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SLEEP AND BIOLOGICAL RHYTHMS

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Worldsleep2011

NEW HORIZONS OF SLEEP RESEARCH FOR OUR PLANET

Kyoto International Conference Centre (ICC Kyoto)

16–20 October 2011

Kyoto, Japan

ABSTRACTS

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PREFACE

Welcome to Kyoto, Worldsleep2011/JSSR

Masako OKAWA[1] and Tetsuo SHIMIZU[2]

[1]Vice President of World Sleep Federation (WSF), President of Asian Sleep Research Society (ASRS) and Chair of Local Organizing Committee, Worldsleep2011, and [2]President of Japanese Society of Sleep Research (JSSR), President of 36th Annual Meeting of Japanese Society of Sleep Research and Vice Chair of Local Organizing Committee, Worldsleep2011

Welcome to Kyoto, a city full of World Heritage Sites in the heart of Japan, and to Worldsleep2011. This congress aims to explore new horizons of sleep research for our planet, by building bridges between Asia and the world in the field of somnology. Kyoto was selected as the venue for Worldsleep2011 at Worldsleep07 in Cairns, Australia. Ever since, we have devoted ourselves to preparation for this meeting.

As you may know, an unimaginable disaster hit eastern Japan on 11 March and Fukushima is still struggling with the accident response. We would like to express our deepest condolences to those who have lost their lives and those who are still suffering from the Great East Japan Earthquake.

While affected areas are recovering, we believe that science should continue to advance. The Local Organizing Committee, the Executive Council of the World Sleep Federation (WSF) and the Japanese Society of Sleep Research (JSSR) jointly decided that Worldsleep2011 should be held as planned in October of this year.

In response to the current situation in Japan, a number of special programs focusing on "disaster and sleep" and "problems related to daylight savings/energy consumption" have been added to the original program. A wide variety of joint symposia are scheduled with the relevant societies. We also have opportunities to hear from senior researchers who have contributed to the advancement of somnology in Japan and overseas. They are expected to provide valuable developmental insights to the young scientists attending.

Furthermore, we are pleased to offer an exciting plenary symposium, entitled "The Future Direction of Global Sleep Medicine," in collaboration with WSF, JSSR and the World Health Organization (WHO). The symposium will provide participants with up-to-date talks on sleep and health, public health policy, and a global picture of policy development and resources for mental health. The impact of sleep health will be revisited from the viewpoint of WHO, which we expect will open up new horizons for our sleep research.

Sleep researchers must keep moving forward and working at any time and any place, even in the face of disaster. We look forward to welcoming our colleagues from around the globe.

Plenary Sessions

Presidential lectures

Pr-1-1

SLEEP, HEALTH AND SOCIETY

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More than 20% of the population in developed nations suffer the consequences of inadequate sleep or a sleep disorder (sleep loss). These sleep health problems are much more common in those at social and economic disadvantage. In Australia, over 30% of truck crashes involve falling asleep often at night and we know that 45% of Australian truck drivers have sleep apnea, one of the most common sleep disorders. Although catastrophic events due to sleep loss such as marine oil spills or nuclear meltdown have obvious public impact, it is the pervasive loss of alertness and widespread occurrence of human error that severely compromises productivity and public safety. The effects of sleep loss are compounded when there is disruption to our internal biological clock (circadian system), which regulates when we sleep and wake and is exquisitely sensitive to light. Biological clock disorders affect 16% of Australians who work shifts, 30% who travel (jet lag) and 10% of patients with chronic insomnia. Sleep loss and biological clock disruption also have clear effects on general health – weight gain, diabetes, hypertension, depression, accelerated dementia, resulting in major health costs and reduced survival. Indeed the WHO has classified shiftwork as a probable carcinogen. The effects of sleep loss vary widely from individual to individual. Failure to recognise may limit efforts to minimise the consequences of sleep loss for our workers, our industries and our community. As the global impact of chronic disease is being increasingly recognised, there are challenges in emphasising the importance of sleep health. Firstly, there is a poor understanding of sleep health issues amongst national and international policymakers. Secondly, there is little international co-ordination for the promotion of healthy sleep. Finally, we need better scientific evidence to support our arguments. As a field we need to overcome "silos" in our thinking and approach. There are opportunities for better international efforts to address challenges in evidence and translation to policy for healthier sleep.

Pr-2-1

NEW HORIZONS OF SLEEP RESEARCH FOR OUR PLANET-SLEEP AND CHRONOBIOLOGY

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The study of sleep and circadian rhythms in humans has provided us with an extensive base of knowledge as to normal behaviour and pathophysiology. In particular, looking at biological rhythms in children with brain damage has provided useful information on development of the circadian system. These children manifest various types of circadian sleep-wake disorders, and blind children tend to show a higher rate of rhythm disorders than sighted children. On the other hand, sleep in old age can best be characterized by a reduced tendency to sleep at night and difficulty in remaining awake during the daytime. Especially elderly patients with dementia are likely to show reversed or irregular day-night sleep-wake rhythms. Several factors have been implicated: 1) sensory deprivation during the day (particularly low light levels); 2) absence of social stimulation; 3) lack of daytime physical and mental exercise; and 4) organic factors such as the degeneration of the suprachiasmatic nuclei (biological clock) in the brain of dementia.

The prevalence of circadian rhythm sleep disorders are increasing in our 24-hour-7 day society. Delayed sleep phase syndrome and even non-24-h sleep-wake syndrome seem to be common and underrecognized in society, typically emerging during adolescence. Psychiatric problems are also common in both syndromes. DSPS and non-24-h sleep-wake syndrome may share common circadian rhythm pathology in terms of clinical progression and biological underpinnings (dysfunctions at the behavioral, physiological and genetic levels). Given the increasing number of patients in modern society suffering from these disorders, treatment and prevention procedures require further attention using behavioral, environmental, and psychiatric approaches.

In our society, where at least a third of the work force must be available for shifts across the 24-h day and 7 days a week, maintaining health and quality of life has become more difficult. Society's sleep problems need to be addressed from 3 perspectives of "somnology" – sleep science, medicine and sleep sociology.

Opening lecture

OL-1-1

EVOLUTION OF LIFE HISTORY STRATEGY IN HUMAN AND NON-HUMAN PRIMATES

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[2]*President, International Primatological Society*

Primates show slow life history traits, such as small litter size, long gestation, long lactation, and long life span. The low growth rate of primates may be caused by a negative association between mortality rates and growth rates, and the juveniles' vulnerability to food shortage and predation may shape their life history traits. Primates may be adapted to the low mortality rates prevalent in their ancestral habitat (tropical forests), since other arboreal mammals such as bats also have low mortality rates. Primates living in the more unpredictable habitats have higher birth rates and earlier age at first reproduction. The great apes (Hominidae: orangutans, gorillas and chimpanzees) that are strictly distributed in and around the tropical forests have the slowest life history traits among mammals. Modern humans also exhibit slow life history traits, while having high birth rate and short inter-birth interval. The presence of childhood, adolescent sterile, and menopause are unique to human life history. High predation pressure, bipedal walk, and encephalization may have promoted such human specific traits outside the tropical forests. Not hunting abilities, but hunted situations (increased mortality), increased human fecundity by reducing the

period of lactation. Establishment of bipedalism prior to encephalization shaped the patterns of somatic and brain development. Brain uses a lot of energy for maintenance and development. Human children attain a large brain by decreasing body growth rate until puberty. High expenditure of brain development may cause the adolescent spurt in body growth. Such situations may have increased dependency of human children on their parents and led the human ancestors to communal breeding. Social adaptations to open lands may have resulted in the creation of human family and the unique patterns of human sleep. From the common feature of sleeping in individual beds among the great apes, human ancestors established communal sleeping without individual beds, which guarantees cooperation and security.

Plenary lectures

PL-1-1

NEUROIMAGING STUDY ON BRAIN PATHOPHYSIOLOGY OF SLEEP DISORDERS

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Sleep is not a simple rest. Active processes occur in brain during sleep. Brain acts differently in different sleep stages. Normal physiologic brain conditions are affected by many sleep disorders. There are many imaging techniques for the evaluation of brain state. Brain MRI shows anatomical structures whereas brain SPECT and FDG-PET reflect the patterns of cerebral blood flow and cerebral glucose metabolism at the time of radiotracer injection. Insomnia patients showed increased global cerebral glucose metabolic rate during the transition from waking to sleep onset, suggesting that there is an overall hyperarousal in insomnia. The CBF patterns were improved after cognitive behavioral therapy in other study. Brain MRI studies in narcolepsy did not show consistent findings. But two studies similarly reported significant decrease of gray matter concentration in bilateral hypothalamus and nucleus accumbens in narcolepsy patients. FDG-PET study showed reduced glucose metabolism in hypothalamus and thalamus in narcoleptics compared to normal controls. A subsequent brain SPECT study revealed hypoperfusion in bilateral anterior hypothalami. These two studies indicate lower waking baseline brain activity in narcolepsy. In a brain SPECT study, cerebral perfusion increased in limbic areas and basal ganglia, thalami, premotor cortex, sensorimotor cortex and brainstem during cataplectic attacks. Obstructive sleep apnea syndrome (OSAS) are usually associated with a reduction in blood oxygen saturation, blood pressure/heart rate changes, decreased of cerebral blood flow, increased intracranial pressure and increased sympathetic tone. We found significant gray matter reduction in bilateral temporal lobe and anterior cingulated gyri, caudate nuclei, thalamus and other brain structures which suggest brain damage induced by chronic sleep apneas. Neuroimaging studies may be useful to elucidate the etiology and consequences in brain of sleep disorders and contribute to the better understanding of cerebral pathophysiology of sleep disorders.

PL-2-1

SLEEP DISTURBANCES, OBESITY AND DIABETES: INTERACTING EPIDEMICS

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During the past few decades, sleep curtailment and sleep disorders have become increasingly prevalent. The epidemic of obesity has been associated with an epidemic of obstructive sleep apnea (OSA). Insomnia is also on the rise. These trends for shorter sleep duration and poorer sleep quality have developed over the same time period as the epidemics of obesity and diabetes. There is good evidence that chronic partial sleep loss and decreased sleep quality may increase the risk of obesity and diabetes. Laboratory studies in healthy volunteers have shown that sleep restriction is associated with an adverse impact on glucose homeostasis. Insulin sensitivity decreases markedly without adequate compensation in beta cell function, resulting in an elevated risk of diabetes. Reduced sleep quality, without change in sleep duration, is also associated with an increased risk of diabetes. Prospective epidemiologic studies are consistent with a causative role of sleep disturbances in the increased risk of insulin resistance and diabetes. Sleep curtailment is also associated with a dysregulation of the neuroendocrine control of appetite. Several studies have observed a decrease in leptin levels and/or an increase in ghrelin levels following sleep restriction. Thus, sleep loss may alter the ability of leptin and ghrelin to accurately signal caloric need. Consistent with the laboratory evidence, more than 60 epidemiologic studies in both children and adults have shown an association between short sleep and higher BMI after controlling for a variety of possible confounders. Multiple studies have shown that OSA is a risk factor for insulin resistance and diabetes, independently of BMI and other confounders. The prevalence of OSA in type 2 diabetes is exceptionally high, averaging 68% across five independent studies. The severity of OSA is an independent predictor of glycemic control. Taken together, the current evidence suggest that chronic partial sleep curtailment and reduced sleep quality may be involved in the current epidemics of obesity, insulin resistance and type 2 diabetes.

PL-3-1

PHENOTYPING IN THE PATHOGENESIS OF OBSTRUCTIVE SLEEP APNEA: IMPLICATIONS FOR FUTURE THERAPIES

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Obstructive sleep apnea is a common disorder with important adverse consequences for afflicted individuals. A better understanding of apnea pathophysiology could lead to improved therapies with the potential to individualize treatment. Deficient pharyngeal anatomy is a common characteristic in patients with obstructive sleep apnea. However, measures of anatomy, generally Pcrt, predict little of the variability in apnea presence and severity. Thus other traits are important as well and likely include: 1. Upper airway muscle responsiveness and effectiveness during sleep: the upper airway response. 2. Arousal threshold to a respiratory stimulus. 3. Loop Gain, a measure of ventilator control stability or instability. We have developed a graphical, mathematical model that incorporates these four traits which can predict who does and does not have obstructive sleep apnea based on these physiologic characteristics. Manipulation of individual traits can affect apnea severity

based on predictions from the model. Examples include decreasing loop gain with oxygen or acetazolamide, increasing arousal threshold with a hypnotic or changes in upper airway anatomy i.e. surgery or mandibular advancement. Although not fully tested, several other observations have resulted from the model: 1. REM predominant apnea occurs in individuals with reasonably poor anatomy, but a substantial upper airway response during NREM sleep. Loss or reduction in the upper airway response during REM sleep likely leads to airway collapse. 2. Some patients have a negative upper airway response i.e. increasing respiratory drives leads to decreased airway patency. Unless this trait can be altered, such patients will likely be difficult to treat with approaches other than CPAP or major manipulation of anatomy. By measuring these traits and utilizing the graphical model, apnea pathophysiology can be better understood and new therapeutic strategies designed.

PL-4-1

THE ADAPTIVE FUNCTION OF SLEEP

J SIEGEL[1]
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Sleep is not a maladaptive state that needs to be explained by undiscovered functions (which nevertheless undoubtedly exist). Rather, the major function of sleep is to increase behavioral efficiency. Greater waking activity does not necessarily lead to increased numbers of viable offspring and, hence, genetic success. Rather, genetic success is closely linked to the efficient use of resources and to the avoidance of risk. Thus, inactivity can reduce predation and injury. It also reduces brain and body energy consumption. Evidence bearing on this hypothesis will be presented.

PL-5-1

UNANSWERED QUESTIONS ABOUT ADOLESCENT SLEEP

MA CARSKADON[1]
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Several decades of research with teenagers in the developed world show a convergence of findings about trends in the developmental pattern of adolescent sleep: the timing of sleep delays and becomes variable and the duration of sleep declines. Several maturational features of the CNS and sleep regulatory processes underlying these changes will be described. In addition, the talk reviews studies indicating that certain sleep teen patterns are associated with negative outcomes for academic achievement, mood and behavior disorders, substance use and abuse, and health. Unanswered questions remain. Progress on these issues may be enhanced if reframe our aproach in a way that better examines individual differences, sleep over extended time frames, and variation in outcomes. Experimental studies are needed as well as studies that may require global cooperation to examine these processes not only in developed countries, but also in developing, undeveloped, and deprived regions. Examining sleep exposures in broader contexts can extend our understanding of adolescent sleep and the roles it plays in brain development, behavior, and health.

PL-6-1

RBD RESEARCH IN JAPAN: PAST, PRESENT AND FUTURE

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In 1986, Schenck et al proposed a new category of parasomnia which is now called as REM sleep behavior disorder (RBD). Since then, nearly a thousand papers have been published on RBD. However, its animal model, cats with bilateral lesions in their pontine tegmentum showing oneiric behaviors during REM sleep, was reported in 1960th by Jouvet et al. Also before 1986, Japanese researchers had reported similar phenomena in patients with diverse etiologies such as delirium tremens (DT) and other withdrawal delirium, experimental delirium by anticholinergic agents, nocturnal delirium in patients with chronic brain damage, neurodegenerative diseases involving the brain stem, brain tumor, and an elderly without obvious etiology which would be the first report of idiopathic RBD. Hishikawa et al (1975) coined the term stage 1-REM without muscle atonia (1-REM) to describe polygraphic pattern seen in patients with DT. The possible mechanism underlying 1-REM would be not only REM sleep without muscle atonia but also stage 1 with REMs by intrusion of REMs and dream content to stage 1 of NREM sleep or by disinhibition of REMs during NREM sleep. After 1986, Uchiyama (1995) reported an incidental Lewy body disease confirmed by autopsy in a patient with idiopathic RBD. Miyamoto (2006) et al reported markedly reduced cardiac 123I-MBIG uptake, consistent with the loss of sympathetic terminals, in idiopathic RBD. These reports indicate that idiopathic RBD would be the latent Lewy body disease. Further study is needed to elucidate this possibility. Japanese researchers are willing to participate in the international study on that topic.

PL-7-1

SLEEP, FATIGUE AND CIRCADIAN RHYTHMS IN CANCER

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Women with breast cancer report poor sleep and fatigue, occasionally before, and frequently during chemotherapy. These symptoms often last for months and even years after the end of primary cancer treatment, significantly burdening quality of life, decreasing their overall functional level, lowering adherence to adjuvant cancer treatment, and potentially affecting survival. Sleep complaints in cancer patients consist of difficulty falling asleep, difficulty staying asleep and frequent and prolonged night time awakenings. Risk factors for insomnia in cancer patients include the cancer itself, treatment, medications, environment, psychosocial disturbances and physical disorders. Women with breast cancer with a symptom cluster of poor sleep, fatigue and depressive symptoms before chemotherapy are more likely to manifest an increase in severity of these symptoms during chemotherapy. In addition, circadian activity rhythms and cognitive function deteriorate during chemotherapy. Objective measures of sleep in cancer confirm fragmented sleep and low sleep efficiency, more restlessness at night during treatment, longer sleep latency, increased wake time during the night, and more prevalent sleep disorders such as sleep apnea and periodic limb movements. Because insomnia in this patient population may be due to a variety of

causes and comorbidities, treatment must be multimodal and may include both pharmacologic, such as hypnotics and behavioral therapies.

PL-8-1

OBSTRUCTIVE SLEEP APNEA AND ATHEROSCLEROSIS – EXPLORING THE LINKS

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Growing evidence support that obstructive sleep apnea (OSA) may exert a causal role in its strong association with cardiovascular disease (CVD). OSA is postulated to initiate or promote atherosclerosis, the vascular pathology underlying majority of CVD. Atherosclerosis is a process of chronic low grade vascular inflammation, involving interplay of endothelial cells and various circulating cells, and an array of vasoactive mediators. Clinical studies have shown that OSA is independently associated with endothelial dysfunction, arterial stiffness, and early imaging features of carotid atherosclerosis. Mechanistically, neutrophils, monocytes and lymphocytes from OSA subjects, compared to that from non-OSA, were found to be more activated and produced more reactive oxygen species, proinflammatory cytokines, leukotrienes, cell adhesion molecules and other pro-atherogenic factors. Systemic increase in oxidative stress and inflammation have been reported in OSA, although results were conflicting. The role of adipocytokines and biomolecules which regulate vascular inflammation have been studied. There are conflicting results of enhanced or impaired repair capacity in OSA as reflected by circulating endothelial progenitor cells. Intermittent hypoxia (IH) exposure is a commonly employed experimental model of sleep apnea. In rodents exposed to IH, development of atherosclerotic plagues appeared to be more definitive in the presence of concomitant high-cholesterol diet or other predisposing factors. IH may exert pro-atherogenic effects via increasing blood pressure, insulin resistance or dyslipidemia. Many in-vitro or in-vivo studies have reported that IH may produce pro-atherogenic effects at cellular level. A lot remains to be learnt regarding end organ/tissue specificity and the change with duration or intensity of IH. Other biologic effects in sleep apnea, notably sleep fragmentation and shear stress to vessel wall, are relatively unexplored. Tissue vibrations from snoring is recently suggested to contribute to carotid artery endothelial dysfunction.

PL-9-1

CIRCADIAN CLOCK AND SLEEP-WAKE CYCLE

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The circadian system in mammals including humans is consisted of the central pacemaker located in the suprachiasmatic nucleus (SCN) and the peripheral clocks in a variety of organs. The SCN circadian pacemaker entrains to the day-night alternation and conveys the information of local time to the peripheral clocks which express overt circadian rhythms. A unique feature of the human circadian system is internal desynchrony between the circadian rhythms and sleep-wake cycle. The internal desynchrony occurs spontaneously under temporal isolation or is induced by an abrupt shift of time cues. When the routine sleep schedule was shifted by 8 hours, the sleep-wake cycle was entrained by the shifted schedule in 4 days on average, whereas the circadian rhythm in plasma melatonin was not entrained but showed a free-run rhythm under dim light conditions. The circadian system was internally desynchronized. Under following free-run session where there was no time-cue, the sleep-wake cycle either phase-advanced or delayed to reestablish the normal phase-relation with the circadian melatonin rhythm in several days. The direction and the amount of phase-shift of the sleep-wake cycle depended on the phase-relation with the circadian rhythm immediately before the phase-shift. These findings strongly suggest that two independent but mutually coupled pacemakers are involved in the human circadian system.The circadian melatonin rhythm in humans is probably regulated by the SCN, but neither the site nor the nature of the sleep-wake cycle is known. There are two animal models, where the behavior rhythms are desynchronized from the SCN circadian pacemaker; one is food-entrainable oscillation (FEO) and the other methamphetamine-induced oscillation (MAO). Both oscillations are independent of the SCN circadian pacemaker. Taking advantage of internal desynchrony, the site of SCN-independent oscillation was explored in the mouse and rat brains. As a result, the dopaminergic system in the brain stem was found to be the most likely site of oscillation, but other brain areas were not completely excluded.

PL-10-1

SLEEP AND STROKE

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A causal link between sleep and stroke has been postulated since the 19th centuries. Despite the frequency of both, sleep disturbances and stroke, this area of research was generally neglected until very recently. For different reasons this area is, however, of clinical and neurobiological interest. First, sleep disordered breathing (SDB) has been shown to represent an independent risk factor for stroke[1]. Recent data raise the possibility that also other sleep disorders (such as restless legs syndrome, periodic limb disorder in sleep, and insomnia) may increase the cardio- and cerebrovascular risk[1–3]. Second, sleep-wake disorders (SWD) such as hypersomnia, insomnia and parasomnias (e.g. restless legs syndrome, REM sleep behavior disorder) can arise from focal brain damage (stroke)[1]. The analysis of this secondary SWD offer unique insights into the neurobiology of sleep-wake mechanisms[1,4]. Third, clinical data support the hypothesis that SDB, SWD and their treatment may affect the short-term and long-term outcome after stroke[1,2,4–6]. Fourth, experimental and clinical data suggest a fundamental role of sleep in neuroplasticity and learning processes. As a consequence, sleep and its modulation (disturbance or enhancement) are expected to affect the recovery after stroke. Also, recovery after stroke may be accompanied by specific changes of sleep microstructure. Few clinical and experimental observation give support this hypothesis[7–10].

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PL-11-1

ALARM CLOCKS ARE MORE COSTLY THAN WE THINK

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Since the circadian clock controls sleep timing, sleeping at the 'wrong' time has consequences. In a large-scale, on-going epidemiological study on sleep behaviour, we find that the disparity between biological and social timing (social jet-lag) affects health. The higher an individual's social jetlag, the more likely he/she is a smoker and the higher his/her alcohol and caffeine consumption. But social jetlag also affects body mass index (BMI), which has been shown to correlate with sleep duration. Although shift-work elicits the most extreme form of social jetlag, the number of people whose body clocks are not aligned to the life they have to lead for social reasons (e.g., work and school times) has increased over the past years. 85% of the population uses alarm clocks to wake up in time on workdays. To quantify social jetlag in real life and to develop counter measures against social jetlag, we have developed algorithms that predict the progression of internal time based on light exposure. These algorithms do not only promote an understanding of the daily relationship between internal and external time in everyday life but also allows us to simulate the effects of alternative social schedules and life-styles based on daily light profiles. Modelling circadian time in real life is of key importance in pending discussions on artificial manipulations of clock time, such as Daylight Saving Time, over-proportioned time zones, or inappropriately early work and school times. Improving the correspondence between biological and social clocks will lead to improved health on a population-wide level.

PL-12-1

FROM THE CLINIC TO THE LABORATORY AND BACK AGAIN: NEW INSIGHTS ON INSOMNIA

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Chronic insomnia is the most prevalent sleep disorder, and accumulating evidence demonstrates the morbidity and functional impairment associated with this condition. Insomnia research has made rapid progress in some areas, such as epidemiology and behavioral treatment, but slower progress in other areas, such as genetics and pathophysiology. A translational approach to insomnia research–moving from the clinic to the laboratory and back again–may help to accelerate progress. This talk with provide examples of how listening to insomnia patients' symptoms can lead to improved assessment methods, and how basic and clinical neuroscience findings can be understood in the context of patient symptoms. The talk will also illustrate how the effects of insomnia treatments can be understood from the perspective of patient symptoms and sleep regulatory mechanisms. Specific data will be presented from studies at the University of Pittsburgh that deal with qualitative research in insomnia, epidemiological and clinical studies, the development of sleep-focused patient-related outcomes (PROs), treatment studies, and functional imaging studies.

PL-13-1

BRAIN CIRCUITRY FOR CIRCADIAN REGULATION OF SLEEP

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The basic outline of the circadian timing system in the mammalian brain has been known for decades, but the specific circuitry, including cell types and neurotransmitters involved in timing wake-sleep and activity cycles, has only recently emerged. In this lecture, we will review recent advances in understanding the pathways that link the external light-dark cycle, through the suprachiasmatic nucleus (SCN) to the circadian control of wake-sleep, with particular emphasis on recent studies using manipulation of gene expression to dissect this system. First, we will examine the retinal input to the SCN from a specific class of melanopsin-containing retinal ganglion cells, and the neurotransmitters those cells may use in resetting circadian phase. We will then review the pathways from the SCN, via a series of relays in the subparaventricular zone and the dorsomedial nucleus of the hypothalamus (DMH), that allow it to influence the wake-sleep circuitry, and the neurotransmitters used in those pathways. Finally, we will discuss the ways in which such signals as food availability and drug delivery can converge on the DMH, and how the DMH can override the SCN, and reshape circadian rhythms. These studies not only help us to understand the circadian basis of normal wake-sleep states, but give us insight into possible approaches to therapies for sleep and circadian disorders.

Plenary symposia

PS-1-1

SLEEP, HEALTH, AND SOCIETY: AN OVERVIEW

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More than 20% of the population in developed nations suffer the consequences of inadequate sleep or a sleep disorder (sleep loss). These sleep health problems are much more common in those at social and economic disadvantage. In Australia, over 30% of truck crashes involve falling asleep often at night and we know that 45% of Australian truck drivers have sleep apnea, one of the most common sleep disorders. Although catastrophic events due to sleep loss such as marine oil spills or nuclear meltdown have obvious public impact, it is the pervasive loss of alertness and widespread occurrence of human error that severely compromises productivity and public safety. The effects of sleep loss are compounded when there is disruption to our internal biological clock (circadian system), which regulates when we sleep and wake and is exquisitely sensitive to light. Biological clock disorders affect 16% of Australians who work shifts, 30% of Australians who travel internationally each year (jet lag) and 10% of patients with chronic insomnia.

Sleep loss and biological clock disruption also have clear effects on general health – weight gain, diabetes, hypertension, depression, accelerated dementia, resulting in major health costs and reduced survival. Indeed the World Health Organisation has classified shiftwork as a probable carcinogen. The effects of sleep loss vary widely from individual to individual. Failure to recognise may limit efforts to minimise

the consequences of sleep loss for our workers, our industries and our community.
As the global impact of chronic disease is being increasingly recognised, there are challenges in emphasising the importance of sleep health. Firstly, there is a poor understanding of sleep health issues amongst national and international policymakers. Secondly, there is little international co-ordination for the promotion of healthy sleep. Finally, we need better scientific evidence to support our arguments.
As a field we need to overcome "silos" in our thinking and approach. There are opportunities for better international efforts to address challenges in evidence and translation to policy for healthier sleep in society.

PS-1-2

SLEEP AND MENTAL HEALTH: WHAT WE KNOW AND STILL NEED TO KNOW

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Sleep problems share complex bidirectional relationships with mental health disorders. These relationships have been most carefully explored for insomnia and depression. Cross-sectionally, depression is the strongest risk factor for insomnia, and insomnia is a nearly universal symptom in patients with depression. Increasing evidence has also demonstrated that insomnia is a risk factor for incident depression, for poor treatment outcome in comorbid depression, and for recurrence of depression following treatment. More recent studies have shown that pharmacologic or behavioral treatment of comorbid insomnia improves outcomes in depressed patients. However, a number of important questions remain. Most important is the mechanism by which insomnia increases depression risk. Future studies should examine the neural circuitry of affect regulation in patients with chronic insomnia to determine similarities and differences compared to patients with depression. Treatment of insomnia could potentially reduce the risk of subsequent depression. However, before widely advocating such treatment, it is important to determine whether insomnia treatment significantly alters affective neural circuits. The relationship between bipolar disorder and sleep also warrants further investigation. Patients with bipolar disorder have significantly disturbed sleep, even between episodes. Developing sleep and circadian interventions to address these sleep disturbances could potentially improve outcomes. Finally, patients with mental health disorders have increased risk for cardiovascular and metabolic disorders. It is important to examine whether sleep disturbances and sleep disorders (such as obstructive sleep apnea) contribute to this risk, and whether appropriate treatment can mitigate the risk.

PS-1-3

PUBLIC HEALTH POLICY AND SERVICES FOR SLEEP AND HEALTH

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In the past half-century, the Ministry of Health, Labour and Welfare, Japan, has focused on improving the health of our citizens. Over the last three decades, the ministry has taken specific actions aimed at reducing premature deaths and enhancing quality of life by implementing a series of measures termed the Nation's Health Promotions: the first period was 1978–1987, the second period 1988–1999 and the third period 2000–2012. Life expectancy and healthy life expectancy at birth for Japan in 2001 were estimated to be 77.9 years and 71.4 years for men and 84.7 years and 75.8 years for women, respectively. With the goal of helping people to live longer lives in better health, the third Nation's Health Promotion, referred to as Healthy Japan 21, is being carried out to achieve 70 goals in the nine fields of non-communicable diseases (e.g., cardiovascular disease, cancer, diabetes mellitus, mental health and oral health), lifestyles (e.g., diet, physical activity and sleep) and behaviors (e.g. tobacco and alcohol use). The accumulated knowledge of sleep in biology, medicine and sociology shows that sleep deprivation or disorders increase the risks for hypertension, diabetes mellitus and depression. It is noteworthy that sleep is included in Healthy Japan 21 as one of the important factors contributing to non-communicable diseases. Good sleep ensured by appropriate interventions might contribute to reducing national afflictions and prolonging healthy life expectancy in the future. My presentation will focus on the following topics: 1) the history of the nation's health promotion in Japan, 2) Healthy Japan 21, and 3) the coming 10 years for our nation's health.

PS-2-1

SLEEP IN YOUNG CHILDREN IN OCEANIA AND ASIA

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Sleep is a vital part of every growing child and significantly impacts the health of the child and the family. Variability in sleep practices occur around the world. Understanding the sleep patterns and problems in different populations would aid in appreciating the impact of these differences. This paper describes the first large scale study on sleep in Asian and Oceania infants less than 36 months old.
Methods: Parents of 23,479 infants and toddlers in Australia, New Zealand, China, Hong Kong, India, Indonesia, Korea, Japan, Malaysia, Philippines, Singapore, Taiwan, Thailand and Vietnam completed an expanded version of the Brief Infant Sleep Questionnaire. Sleep in Chinese infants (n = 10,856, from countries with substantial ethnic Chinese – China, Hong Kong, Indonesia, Malaysia, Singapore and Taiwan) in the region was also compared.
Results: Significant variability in bedtime was seen across the region, ranging from 19:27 (New Zealand) to 22:17 (Hong Kong), $p < .0001$. Total sleep time ranged from 11.6 (Japan) to 13.3 hrs (New Zealand), $p < .0001$. Daytime sleep was less variable. Co-sleeping, room-sharing and bed-sharing varied from 5.8% in New Zealand to 83.2% in Vietnam. Sleep was perceived to be a problem in wide ranging levels across the region (11% in Thailand to 76% in China). Australia and New Zealand infants generally slept earlier, had longer night time sleep, was less likely to co-sleep, more likely to have bedtime routines and had less bedtime difficulties compared to Asian infants. Ethnic Chinese infants from different countries in the region also show variability in sleep. North Asia compared to South-east Asia had little difference in infant sleep but reported more sleep problems.
Conclusions: This study describes the substantial differences in sleep practices and problems across the Oceania and Asian region and also amongst chinese infants across the region. This information will enhance our understanding of sleep practices and problems as well as serve as a baseline for future comparative studies over time, across age groups and between different regions.

PS-2-2

SLEEP IN YOUNG CHILDREN IN THE USA AND AROUND THE WORLD

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Few broad scale studies have been conducted on sleep in young children. Results will be presented from two large scale global studies, which focused on sleep patterns and sleep problems in children ages 0 to 3 years from the United States, as well as from predominantly Caucasian and predominantly Asian countries. Results from the United States reflected clear sleep related developmental changes, including a decrease in daytime sleep and total sleep time, as well as consolidation of sleep during the night, which was manifested in a decrease in frequency and duration of night wakings. Sleep ecology and parental behaviors significantly explained a portion of the variance in the sleep patterns of young children. Parental interventions that encourage independence and self soothing were associated with extended and more consolidated sleep, especially in comparison to more active interactions that were associated with shorter and more fragmented sleep. Furthermore, findings indicated that children from predominantly Asian countries have significantly later bedtimes, shorter total sleep times, increased parental perception of sleep problems, and are more likely to room share than children from predominantly Caucasian countries. These results indicate substantial differences in sleep patterns in young children across culturally diverse countries. In addition, across all countries, three primary factors, that is an early bedtime, a consistent bedtime routine, and falling asleep without parental presence, were most predictive of sleep consolidation and sleep problems. Implications of these results will be discussed.

PS-2-3

CROSS-CULTURAL DIFFERENCES IN SLEEP AND SLEEP DISTURBANCES IN YOUNG CHILDREN. SLEEP IN YOUNG CHILDREN IN SOUTH AMERICA

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Sleep in Young Children in South America.The way children sleep critically affects their ability to think and behave during daytime hours. Most of important studies concerning prevalence of sleep disturbances are based on self-administered sleep habit questionnaires which parents take home or answer by internet. Unfortunately there are few comprehensive studies of sleep patterns and sleep problems among children in South America. There are few studies about the prevalence of bed sharing and factors associated with this sleeping environment. One study from Brazil showed that at 3 and 6 months about 30% of infants slept with their mothers at night. Prevalence of bed-sharing at 3 months was high and associated with single mothers and sharing the home with the infant's maternal grandmother. Another study from Brazil showed a prevalence of co-sleeping at 12 months of 45% and co-sleeping was more common among mothers with low socioeconomic status, less education, younger mothers, mothers with previous births and among children who used to wake at night. In another study the prevalence of breastfeeding at age 12 months was about 60% in the children who bed shared at 3 months and 44% in those who did not; bed sharing at 3 months protected against weaning up to age 12 months. Sleep disorders were highly prevailing in some studies, similar to other studies: bruxism: 12 to 35%, sleep enuresis: 5%, habitual snoring: 15 to 27% and arousal disorders: 10%. A recent study shows that both short sleep duration and increased television viewing were associated with greater body fatness, obesity and higher blood pressure, independently of physical activity level.

PS-2-4

SLEEP IN YOUNG CHILDREN IN EUROPE

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Infant sleep problems are among the most prevalent problems presented to pediatricians and other child-care professionals. The consolidation of sleep during the night, which is referred to as sleeping through the night, is a rapid maturational process during the first year of life. However, surveys show that as many as 20% to 30% of all infants and toddlers do not succeed in achieving this goal and their sleep continues to be fragmented, as manifested by multiple and/or prolonged night wakings, which are considered to be the most prevalent sleep problems during early childhood. If not treated, these night-waking problems are persistent and can last well into adulthood. Other studies indicate that childhood sleep disturbance may have effects that linger into adulthood, such as increased risk for depression. This last decade, numerous studies have been done in Europe to gather normative data on parent-reported child sleep and investigate what factors could influences it, such as, foreign origin, family situation, parents age and education, prenatal and perinatal factors, night feedings, child temperament and psychological trauma. These studies have been done with structured interviews, questionnaires, sleep diary logs, internet surveys but also with objective actigraphy sleep measures. Longitudinal studies have given normative data for sleep characteristics in children in Western societies. Cross-sectional survey have pointed the disparities between the different countries in Europe due to sociocultural and climate differences. The sleep disturbances induce repercussions on children behavioral symptoms but also on physical growth already in infants less than 6 months. Maternal sleep-related cognitions during pregnancy have also a great influence on the infant sleep. During this presentation, we will also report our experience on 500 newborns followed from birth to 2 years of life with questionnaires and polysomnographic recordings every 6 months. Their sleep was evaluated according to the infants characteristics but also to maternal sleep during pregnancy.

PS-3-1

MECHANISMS UNDERLYING OVARIAN HORMONE MODULATION OF SLEEP: WHAT RODENT STUDIES TELL US ABOUT THE IMPLICATIONS ON WOMEN'S HEALTH

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Sleep complaints like insufficient sleep and insomnia are twice as prevalent in women. As quality sleep is imperative for the maintenance of good health, women suffering from sleep disturbances are at risk for affective mood disorders, impaired cognitive function, and increased stress and anxiety. Data from a number of different species, including

humans, strongly implicate a role for gonadal hormones (estrogens, progestins and androgens) in the modulation of sleep. Symptoms of sleep disruption are often coincident with marked changes in the gonadal hormone profile across the female lifespan. What is less clear are the mechanisms underlying such effects. Using the laboratory rat, our group has made inroads into where and how gonadal hormones influence sleep. We have found that (1) estradiol (E2; endogenous or exogenous) attenuates rapid eye movement (REM) sleep with no significant effect on non-REM sleep in the quiescent phase, (2) the E2-induced suppression of REM sleep is NOT followed by a homeostatic rebound and under conditions of induced sleep loss (i.e., sleep deprivation) E2 significantly attenuates the REM sleep rebound, and (3) the suppression of REM sleep correlates with attenuation of neuronal activity (measured via fos expression) in the ventrolateral preoptic area (VLPO) and median preoptic nucleus (MnPN). More recent results demonstrate that both estrogen receptor alpha and beta isoforms are necessary for the attenuation of REM sleep by E2. However, an estrogen receptor antagonist infused directly into the VLPO does not return REM sleep to the non-hormonal baseline suggesting that E2 is not acting directly in the VLPO to suppress REM sleep. Currently, we are investigating E2 actions in other brain regions involved in the modulation REM sleep. The significance of advancing our understanding of the mechanisms underlying ovarian hormone modulation of sleep is the potential to uncover new perspectives on the origins of sleep disturbance in the female brain, which may uncover novel drug targets for the treatment of sleep disorders in women.

PS-3-2

MODULATION OF SLEEP AND RESPONSE TO SLEEP LOSS BY OVARIAN HORMONES IN RATS

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Hormonal changes that occur naturally in women or as a result of medical treatments are associated with changes in sleep patterns. To understand these phenomena and their underlying mechanisms, we used ovariectomized rats with subcutaneous steroid implants. We found that physiological levels of ovarian hormones modulate sleep architecture differently at baseline (24 h) and during recovery (18 or 24 h) after sleep loss. Specifically, estradiol (E), either alone or combined with progesterone (P), promoted arousal in the animal's active (dark) phase by consolidating wake and fragmenting sleep, resulting in an increased light : dark ratio of NREM and REM sleep. A different picture emerged after acute sleep deprivation by gentle handing for 6 h during the second half of the light phase. As expected, all animals showed rebound sleep. However, hormonally treated rats showed greater consolidation of sleep; nevertheless, the total time spent in rebound NREM sleep did not change and sleep intensity, as assessed by NREM EEG delta power, increased for a shorter period of time than in vehicle-treated rats. Possibly as a result of NREM sleep consolidation, individual REM sleep episodes lasted longer in hormonally treated rats, leading to greater REM sleep rebound.

We repeated the same experiments using middle-aged (10–12 months) female rats, and found that sleep-modulatory effects of E and P in these rats are largely similar to those observed in young females, although there are several minor differences that may be attributable to age differences. We also asked whether the modulation of sleep regulation by E is dependent on the female sex of the animal. The results with young castrated male rats indicated that E's effects on baseline and recovery sleep are similar between males and females, but that E's effects on EEG measures associated with sleep and wake states are sex-dependent.

In conclusion, ovarian hormones modulate baseline sleep and recovery sleep differently in both young and middle-aged female rats as well as in male rats.

PS-3-3

SEX DIFFERENCES AND MENSTRUAL-RELATED EFFECTS ON SLEEP

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There are sex differences in sleep behavior with women reporting more sleep problems and a poorer sleep quality than men across a wide age range. Women are at 40% greater risk than men for developing insomnia. The poorer self-reported sleep quality in women appears to relate in part to psychosocial factors, such as depression and anxiety, which are more common in women. In contrast to subjective reports, polysomnographic recordings show that women have better sleep efficiency, with less Stage 1 sleep and fewer awakenings than men across a wide age range, suggesting that objective and subjective assessments are tapping into different constructs of sleep. Women also have more slow wave sleep (SWS) and slow wave activity (SWA, delta, 0.5-4Hz) within the sleep electroencephalograph (EEG) as well as larger amplitude evoked K-complexes than men. This sex difference in slow waves seems to be driven by more than just anatomical differences affecting signal conduction, since women have thicker skulls, smaller intracranial volumes, and smaller absolute volume of cortical gray matter than men. Within women, fluctuating sex steroids during the menstrual cycle, pregnancy, and menopause transition, impact sleep architecture. The most dramatic change in sleep across the menstrual cycle is increased spindle frequency EEG activity in the luteal phase, when progesterone is high, compared with the follicular phase. SWS and SWA, however, do not change across the menstrual cycle. The menstrual cycle influences REM sleep, which is marginally reduced in the luteal phase. Higher progesterone and estrogen levels correlate with a longer latency to REM sleep and less REM sleep, implying a role of these hormones in the REM sleep changes. Women with premenstrual syndrome report a poorer subjective sleep quality in the symptomatic luteal phase yet show similar menstrual-related changes in sleep architecture as controls suggesting that sleep-independent factors such as mood impact their perception of sleep quality. Sleep in women, therefore, is impacted by both biological and psychosocial factors.

PS-3-4

AGE- AND SEX-RELATED DIFFERENCES IN SLOW-WAVE ACTIVITY IN HEALTHY AND DEPRESSED CHILDREN AND ADOLESCENTS

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Major depressive disorders (MDD) are associated with a number of subjective and objective sleep disturbances both in adults and in childhood and adolescence. Prolonged latency to sleep onset and alterations in the timing of the REM and NREM sleep cycles are among the most robust findings. Few studies focus on the sleep regulatory differences

between depressed patients and healthy controls and the moderating influence of age and sex are rarely explored. This presentation will focus on sleep homeostasis and slow-wave EEG activity (SWA) regulation in MDD and discuss how age and sex moderate response to a sleep regulatory challenge, including several large scale studies from the UM sleep research group. The clinical significance and treatment relevance of these findings will also be addressed. Finally, we will also discuss the role of homeostatic impairment as a risk factor for onset of the first episode of depression, presenting recent data on SWA regulation and response to homeostatic challenge in adolescents who are at high-risk for MDD, based on parental history, but who are not yet depressed.

PS-3-5

GENDER DIFFERENCES IN HUMAN PEPTIDERGIC SLEEP REGULATION

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It is well established that certain peptides play a key role in sleep regulation. This knowledge derived from studies which were performed in male animals and humans only. We performed a series of studies to clarify whether gender differences exist peptidergic effects on sleep EEG and nocturnal hormone secretion.
Sleep EEG (23:00 to 07:00) and the nocturnal secretion of growth hormone (GH), cortisol and in some studies of ACTH (22:00 to 07:00) were investigated simultaneously after one night of adaptation after pulstile intravenous injections of peptides or placebo. In detail we examined vs placebo the effects of four bolus injections of 50 ug GH-releasing hormone in 7 young healthy men, and in healthy volunteers (20 m, 20 f) and in drug-free patients with depression (18 m, 16 f, age range 19–76 years), of 25 ug and 50 ug GHRH in 11 young male female volunteers, of 50 ug corticotropin-releasing hormone (CRH) in 7 young male and in 10 young female volunteers, and of 50 ug ghrelin in 10 young and 10 elder healthy male and 10 young and 10 elder healthy female volunteers and in drug-free patients with depression (7 m, 7 f, mean age 41 ± 7 and 37 ± 5 respectively.
Major findings were opposite effects of GHRH between gender as NonREM sleep was promoted and ACTH and cortisol were blunted in male patients and healthy subjects, whereas NonREM sleep was impaired and ACTH and cortisol increased in women regardless whether they were healthy or depressed. Also in the young women sleep was impaired after GHRH, but cortisol remained unchanged. After CRH slow-wave sleep and GH decreased in men. In women the sleep-EEG changes ware more distinct as the time spent in REM sleep increased during the first third of the night, wakefulness increased and stage 3 sleep decreased. Ghrelin promoted NonREM sleep in young and elder healthy men, but not in women. In both sexes GH and cortisol increased after ghrelin. In female, but not in male depressed patients REM sleep was suppressed after this peptide.
Our data show distinct differences in the effects of GHRH, CRH and ghrelin on human sleep and sleep related hormone secretion.

PS-4-1

THE SLEEP HEART HEALTH STUDY: A LOOK BACK AT LESSONS LEARNED

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Sleep-disordered breathing (SDB) or obstructive sleep apnea is a chronic condition that is characterized by partial or complete collapse of the upper airway during sleep. The resulting apneas and hypopneas often lead to reduction in oxyhemoglobin saturation and recurrent arousals from sleep. Although the clinical syndrome of SDB has been known for decades, it was not until 1988 that the National Commission of Sleep Disorders Research (NCSDR) was established by Congress to address the public health importance of SDB and other sleep-related disorders. In 1993, the NCSDR issued a comprehensive report which set forth key research priorities for the field of sleep medicine with the specific acknowledgment that coordinated efforts were needed to define the health-related effects of SDB. At about the same time, the potential morbidity and mortality associated with even moderate degrees of SDB was being increasingly recognized, and the means to efficiently diagnose the condition were becoming readily available. Shortly thereafter, newly available data on the population prevalence of SDB revealed that millions of Americans were affected with this condition with a majority of them being undiagnosed. Given the rising epidemic of obesity and its strong association with SDB, a major initiative was set forth by the National Institutes of Health to define the public health impact of SDB. The Sleep Heart Health Study (SHHS), a product of that initiative, was established to answer many of the pressing questions regarding the clinical consequences of SDB, particularly its effects on hypertension and cardiovascular disease. The primary objective of this presentation is to review the scientific progress made by the SHHS over the last 20 years. Within the context of this presentation, some of the most pivotal findings available to date will be highlighted including the associations between SDB and incident hypertension, cardiovascular disease, stroke, and all-cause mortality.

PS-4-2

PUBLIC HEALTH IMPLICATIONS OF THE BUSSELTON HEALTH STUDY

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There are very few community-based cohorts anywhere in the world with objective quantification of sleep apnea and snoring and sufficient follow-up time to determine whether sleep disordered breathing is a risk factor for cardiovascular disease and premature mortality. Four hundred residents (n = 102 women) of the Western Australian town of Busselton underwent investigation with a home sleep apnea monitoring device in 1990 (MESAM IV). Sleep apnea and snoring were quantified via the respiratory disturbance index (RDI) and percentage of the night spent snoring quantified via a microphone and spectral analyses. All-cause mortality and cardiovascular and stroke hospitalisation status was determined in 397/400 participants (99.3%) after up to 17 years (mean follow-up 16.2 years) by data matching. Diabetic status was also ascertained at baseline and 4 years follow-up. People with a respiratory disturbance index >15/hr in 1990 (n = 18) had a marked independent increased risk of all-cause mortality after 17 years after control for all leading risk factors and snoring (Hazard Ratio 6.0; 2.0–17.6) and may

in time prove to be at increased risk for cardiovascular events (univariate $p = 0.055$) and stroke events (univariate $p < 0.01$) compared to people without sleep apnea (RDI < 5/hr). People with moderate-severe OSA at baseline were also at increased risk for developing diabetes inside 4 years after controlling for both BMI and waist circumference (Multivariate Odds Ratio 13.5; 1.6–114.1). In no analyses was any definition of snoring in either univariate or multivariate models associated with mortality, cardiovascular events or stroke events after 17 years. Snoring may however act as an amplifier of for the effect of sleep apnea on mortality as there was a significant effect modification. We are awaiting ethical approval to match and analyse 20 year outcome data. The Busselton Health Study is one of the small number of community-based cohorts in the world helping to define the public health implications of sleep apnea, who it affects and at what severity should we be worried about it.

PS-4-3

HYPERTENSION AND ATHEROSCLEROSIS IN SLEEP APNEA

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Obstructive sleep apnea (OSA) is independently associated with death from cardiovascular diseases, including myocardial infarction and stroke. Myocardial infarction and stroke are complications of atherosclerosis; therefore, over the last decade investigators have tried to unravel relationships between OSA and atherosclerosis. OSA may accelerate atherosclerosis by exacerbating key atherogenic risk factors. For instance, OSA is a recognized secondary cause of hypertension and may contribute to insulin resistance, diabetes, and dyslipidemia. In addition, clinical data and experimental evidence in animal models suggest that OSA can have direct proatherogenic effects inducing systemic inflammation, oxidative stress, vascular smooth cell activation, increased adhesion molecule expression, monocyte/lymphocyte activation, increased lipid loading in macrophages, lipid peroxidation, and endothelial dysfunction. Several cross-sectional studies have shown consistently that OSA is independently associated with surrogate markers of premature atherosclerosis, most of them in the carotid bed. Moreover, OSA treatment with continuous positive airway pressure (CPAP) may attenuate carotid atherosclerosis, as has been shown in a randomized clinical trial.

PS-4-4

METABOLIC SYNDROME, HYPERTENSION, DIABETES MELLITUS AND SLEEP APNEA IN JAPAN

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Obstructive sleep apnea (OSA), metabolic syndrome (Mets) and short sleep duration are all risk factors for cardiovascular events. There has been no report which has investigated this relationship in an age- and BMI-matched population-based study. An individual who has 3 of 5 risk factors for cardiovascular disease is diagnosed as Mets. Five risk factors usually contain increased waist circumference, high blood pressure, increased fasting glucose, increased triglycerides, and decreased HDL cholesterol. This home cardiorespiratory (type 3) sleep study, using an actigraph, was conducted in 275 males working for an urban company. Retrospective measurements of fasting blood parameters were obtained from the company's periodical inspection data. Average sleep duration was 6.0 h/day. Severe OSA was 7.8 times as likely to be present in subjects with Mets (16.2% of all 68 Mets subjects) as those without (2.4% of 207 non-Mets) ($p < 0.001$). Subject with severe OSA had significantly short sleep duration ($p < 0.05$). Sleep duration in Mets subjects was also significantly shorter than in those without ($p < 0.05$). Respiratory disturbance index (RDI) was related negatively significantly to sleep duration in hypertensive subjects. Multiple regression analyses showed that only in the diabetic subjects, the RDI was independently related to fasting plasma glucose even after adjustment for the confounders. The total cholesterol level was correlated negatively with sleep duration and positively with age and the waist/hip ratio, and that the triglyceride level correlated positively with the RDI, body mass index and alcohol consumption. Sleep duration should be taken into consideration as an important factor in studies investigating the prevalence of OSA and several risk factors for cardiovascular diseases including Mets.

PS-5-1

CORTICAL ACTIVATION CHANGES DURING SLEEP FOR VISUAL PERCEPTUAL LEARNING

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While a growing body of evidence suggests that sleep is beneficial for visual learning, the underlying neural mechanisms are not clear. Here, we investigated consolidation-related brain activation during sleep subsequent to training of a visual task using fMRI concurrently with measurements of EEG, EOG and EMG to obtain polysomnogram.
We employed a texture discrimination task (Karni & Sagi, 1992, Nature). Perceptual learning of this task activates only the region in the primary cortex (V1) corresponding to the trained location (Yotsumoto, Watanabe & Sasaki, 2008, Neuron). The experiment consisted of 2 sleep adaptation sessions, the pre-training sleep session for 90 min on the 3rd night, intensive training of the texture discrimination task 6 hours prior to the post-training sleep session for 90 min, followed by the re-test session of the task. To estimate brain activation in the pre- and post-training sleep, we contrasted BOLD signals during NREM sleep before and after training to during wakefulness before each sleep. NREM sleep periods were identified by the standard sleep scoring criteria on the obtained polysomnogram.
The results indicate that brain activation in the trained region of V1 was significantly higher than in the untrained region of V1 in the post-training sleep, but not in the pre-training sleep. Significant performance improvement was obtained in the re-test session after the post-training sleep and was highly correlated with the brain activation in the trained region of V1 in the post-training sleep. Furthermore, the left dorsolateral prefrontal cortex (DLPFC) was significantly more highly activated than the right DLPFC in the post-training sleep and was correlated with activation of the trained region in V1.
These results suggest that during early NREM sleep after training, consolidation of learning occurs in the trained region of V1 under a control by the prefrontal cortex.

PS-5-2

MEMORY PROCESSING DURING SLEEP: IMPLICATIONS FOR HEALTHY AND DYSFUNCTIONAL MEMORY

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Two approaches will be used to show that sleep is important for memory. First, sleep can enhance memory accuracy, and second, memory difficulties can be exacerbated by poor sleep. In keeping with correlative evidence linking sleep and memory, we used novel auditory stimulation methods to demonstrate selective memory reactivation during slow-wave sleep. Sounds were uniquely associated with specific information learned prior to sleep. Presenting these sounds at a low intensity during sleep led to selective memory improvement for the corresponding information. By extension, memory fidelity in general may depend on the same sorts of memory processing during sleep, particularly during slow-wave sleep. In other experiments, we explored deficits in declarative memory (recall and recognition of facts and events); memory abilities commonly decline in older adults and can be especially problematic in patients with amnestic mild cognitive impairment (aMCI) or Alzheimer's disease. These difficulties are usually ascribed to deficient memory acquisition, but they may also reflect memory stability. That is, if memory processing during sleep is normally operative in the service of stabilizing memory storage and creating new connections among memories (i.e., memory consolidation), then deficient memory access during sleep may contribute to poor memory function during the day. Polysomnographic findings in patients diagnosed with aMCI were consistent with this suggestion. Patients spent less time in slow-wave sleep and showed lower delta and theta power compared to age-matched healthy adults. These sleep disruptions were also implicated in memory consolidation, as evening-to-morning change in memory correlated with delta and theta power during intervening sleep in both groups. In a subsequent study, electrical stimulation delivered during sleep at a frequency in the delta range resulted in larger pre- to post-sleep memory improvements compared to sham stimulation. These results suggest that deficiencies in sleep-dependent memory consolidation can contribute to memory impairment.

PS-5-3

SHIFT IN THE NEURAL NETWORK ASSOCIATED WITH DECLARATIVE MEMORY CONSOLIDATION

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We learn through experiences that we encounter during the wakeful period. Not all information, however, is successfully stored for later retrieval. Memory consolidation pertains to stabilization of the memory trace such that it becomes resistant to forgetting. One theory of memory consolidation posits that initial episodic memory trace is captured in the medial temporal lobe structures including the hippocampus. Over time, the memory trace transforms itself to a more neocortical network based trace. The hippocampus is an ideal brain structure that can encode ongoing episodes very rapidly, but at the same time, is vulnerable to interference and erasure. On the other hand, neocortical memory network is slow in binding distributed elements that comprise a memory, but is more resistant from decay. How this transformation occurs over time is yet unclear, however, evidence for the role of sleep in the consolidation of memories is steadily increasing. If sleep is deprived, we tend to remember less, or the performance improvement is not observed. With sleep, there is a better chance that memory is stabilized and even more, if the brain is stimulated during sleep, memory retention seems to be enhanced. In this talk, I would like to present some data showing the changes in the retrieval network before and after sleep and how functional connectivity during sleep might have an influence on the consolidation process. Furthermore, I would like to show brain responses to the stimulation during sleep which could result in strengthening of the memory.

PS-6-1

SLEEP IN CHILDREN WITH AUTISM SPECTRUM DISORDERS

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Sleep disturbances in children with autism spectrum disorders such as pervasive developmental disorder and Asperger syndrome are extremely common. The etiology of sleep problems in these children is varied and may be linked to homeostatic and circadian dysregulation as well as to features associated with the underlying neurodevelopmental disorder (ie, anxiety, self-injurious behavior, sensory integration deficits). This presentation will focus on the etiology, clinical presentation, differential diagnosis and intervention strategies for children with ASD and sleep problems, using a case-based approach.

PS-6-2

SLEEP IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER

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Sleep disturbances are a significant clinical problem in children with attention deficit hyperactivity disorder (ADHD) and may impact on daytime functioning. There are many potential causes of sleep problems in these children and these range from psychostimulant-related sleep onset delay to bedtime resistance related to comorbid oppositionality to circadian-mediated sleep phase delays. This presentation will outline a comprehensive clinical approach to the diagnosis and management of sleep problems in children with ADHD.

PS-6-3

BEHAVIORAL INTERVENTIONS IN CHILDREN WITH NEURODEVELOPMENTAL DISABILITIES

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Sleep disturbances are highly prevalent in children with neurodevelopmental disabilities. For example, studies have indicated that between 50 to 80% of parents of children with ADHD report sleep problems, with similar percentages reported by parents of children with Autism Spectrum Disorders. The most common sleep disturbance reported is

pediatric insomnia, including bedtime problems and night wakings. Studies have found that behavioral interventions can be highly effective in treating behaviorally based sleep disturbances in these populations. Interventions include implementing positive sleep hygiene practices, developing consistent bedtime routines and reward systems for appropriate sleep related behaviors, and encouraging the ability to fall asleep independently. Behavioral interventions are found to not only improve sleep in children and their parents, but can also reduce parental stress and improve a sense of control and ability to cope in parents. Behavioral interventions are also preferred by parents to pharmacological management, however these interventions can be more difficult to implement than in typically developing children.

PS-6-4

POLYSOMNOGRAPHY IN CHILDREN WITH NEURODEVELOPMENTAL DISORDERS

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Children with neurodevelopmental disabilities have significant sleep disturbances. The use of polysomnography in these children can be challenging given the complexity of their disorders, the medication, regimen, and their ability to tolerate the sleep laboratory. This symposium will summarize the findings on polysomnography that are associated with various disorders such as autism spectrum disorders, Tourette's syndrome and Attention deficit hyperactivity disorders. The challenges and methodological issues related to these disorders will be discussed. Future directions with respect to clinical and research involving these children with neurodevelopmental disabilities will also be discussed.

PS-7-1

RBD: UPDATE ON RECENT STUDIES AND NEW DEVELOPMENTS

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Recent studies and the cumulative clinical & basic science literature on RBD indicate that RBD is situated at a strategic crossroads of the neurosciences and sleep medicine. The formation of the International RBD Study Group in 2009 in Marburg, Germany underscores this assertion. The IRBDSG has sponsored 4 RBD symposia, with the 5th symposium to be held in Japan after the Worldsleep2011 congress. Topics being addressed at these RBD symposia consist of devising research protocols i) for studying primary & secondary endpoints in double-blind, placebo-controlled prospective therapeutic trials utilizing clonazepam and melatonin; ii) for studying the efficacy of putative neuroprotective agents in prolonging the latency period (or preventing the progression) from idiopathic RBD to the emergence of parkinsonism (PD, MSA, DLB). Of relevance to the latter study design are 2 studies that identified risk factors for predicting imminent parkinsonism in iRBD: decreased striatal dopamine transporters uptake together with substantia nigra hyperechogenicity (Iranzo A, et al. Lancet Neurol 2010;11:1070–7); olfaction/color vision abnormalities (Postuma RB, et al. Ann Neurol 2011;69:811–8). The PSG diagnosis of RBD has been clarified, with cut-off scores for tonic & phasic EMG activity identified with high specificity & sensitivity that can be used clinically and for research. (Montplaisir J, et al. Mov Disord 2010;25:2044–51). Automated scoring of the submental EMG in REM sleep is being investigated (Ferri R, et al.), with the development of a REM-atonia-index that can be used clinically & for research. RBD screening and severity questionnaires have been developed. New brain imaging techniques are being used in RBD studies. Research into the strong link between RBD-parkinsonism, RBD-narcolepsy, RBD-PLMs continues on multiple fronts. RBD linked with NREM parasomnias (Parasomnia Overlap Disorder) now also includes sexsomnia and sleep related eating disorder. The brain mechanisms subserving REM atonia, and its loss in RBD, and phasic motor overactivity in RBD are being further elucidated.

PS-7-2

COMBINATION NEUROIMAGING MARKERS PROVIDE CLUES TO THE UNDERLYING NEURODEGENERATIVE DISORDER IN IDIOPATHIC REM SLEEP BEHAVIOR DISORDER

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Idiopathic REM sleep behavior disorder (iRBD) is a parasomnia related to REM sleep that is characterized by nocturnal behaviors in which patients appear to act out their dreams. RBD in PD occurs in 46–50% of PD patients. In about 20% of cases it occurs before the onset of classic walking motor symptoms. Several longitudinal studies have reported the natural course of iRBD. Several procedures such as positron emission tomography (PET), SPECT studies, transcranial ultrasound imaging of the substantia nigra, and cardiac MIBG scintigraphy have been proposed to identify subjects in early stage of Parkinson disease (PD) or dementia with Lewy bodies (DLB). In our study, 6-[18F]-fluoro-meta-tyrosine PET (FMT/PET) template superimposed onto the each individual brain MRI in PD, iRBD, and controls. Regions of interests (ROIs) for striatum and cerebellum were placed over each individual brain template. ROIs were manually drawn on the FMT/PET after overlapping with each individual brain MRI, and striatal ROI was divided into the putamen and caudate. We performed FMT-PET imaging can assess the level of presynaptic dopaminergic nerve for iRBD, PD, and controls. IRBD patients have no signs of parkinsonism and have neuroimaging evidence of almost intact striatal dopaminergic innervations such as controls. Whereas PD patients have parkinsonism by definition and have loss of striatal dopaminergic innervation, as evidenced by decreased striatal uptake. Reduced 123I-MIBG uptake by postganglionic cardiac sympathetic neurons in patients with early stage PD has made this technique a useful early marker of this disease. We determined that these same 123I-MIBG findings were present in patients with iRBD. H/M ratio was significantly lower in RBD, PD and DLB subjects compared to essential tremor and multiple system atrophy (MSA) and PSP. It has been speculated that iRBD might represent a prodromal form of neurodegenerative diseases referred to as synucleinopathies such as PD, MSA, and DLB.

PS-7-3

SIGNIFICANCE OF REM SLEEP BEHAVIOR DISORDERS IN SYNUCLEINOPATHIES SUCH AS PARKINSON DISEASE

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REM sleep behavior disorder (RBD) has been reported to occur in synucleinopathies, such as Parkinson disease (PD) and multiple system atrophy (MSA). We conducted clinical interviews examining RBD symptoms in 49 patients with PD and 16 patients with MSA, and performed polysomnography (PSG) on all the subject patients. Twenty-seven patients with PD (55.1%) and 11 patients with MSA (68.8%) had REM sleep without atonia (RWA) on PSG, a essential physiological marker for RBD. The life time prevalence of RBD symptoms in PD was 38.8% (19/49) and that in MSA was 50.0% (8/16). These findings supported that RBD is frequently co-morbid with synucleinopathies. Uptake of 123I-labeled meta-iodobenzylguanidine (MIBG) in myocardial scintigrams has been shown to be as low in patients with idiopathic RBD as in PD patients. We performed MIBG scintigrams on the above indicated 49 PD patients. The patients were divided into three groups (PD with clinical RBD, PD with subclinical RBD, and PD with normal REM sleep). PD patients with clinical RBD had reduced MIBG uptake compared to those with subclinical RBD and those with normal REM sleep. Multiple linear regression analysis revealed that only the existence of RBD symptoms was significantly associated with reduced MIBG uptake among PD patients. This result suggests that PD patients with clinical RBD have a wider synuclein pathology. Convenient screening tool for RBD in PD patients has been desirable. We evaluated the usefulness of the RBD screening questionnaire (RBDSQ) among 45 patients with PD. We compared RBDSQ scores among the following groups: PD with RBD, PD without RBD, and idiopathic RBD, and estimated the cut-off score for an RBD diagnosis. RBDSQ scores in PD with RBD and idiopathic RBD groups were similar, and the scores were higher than those in the PD without RBD group. A receiver-operator characteristics curve revealed that a total score of 6 points (1 point higher than idiopathic RBD) on the RBDSQ represented the best cut-off value for detecting RBD. RBDSQ could be a useful tool for the screening of RBD in PD patients.

PS-7-4

RBD – PRECLINICAL PD, LBD, OR BOTH?

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Idiopathic RBD is an important risk factor for neurodegenerative disease, in particular, those diseases characterized by deposition of alpha synuclein; Parkinson disease (PD), Lewy body dementia (LBD), and multiple system atrophy. Prospective cohort studies have estimated that between 40 to 65 percent of patients with idiopathic RBD will develop a defined synucleinopathy over 10 years. Systematic follow-up of patients with idiopathic RBD provides an unprecedented opportunity to directly observe the development of a neurodegenerative disease. With observation of early disease, it has become increasingly clear that these conditions overlap. Patients with PD who also have RBD are at higher risk of mild cognitive impairment, develop dementia faster, and have more autonomic dysfunction than those without. Patients with idiopathic RBD who go on to develop Lewy body dementia usually have prominent parkinsonism at onset, and are equivalent to PD patients on quantitative motor testing, autonomic dysfunction, and olfactory dysfunction (hallucinations and cognitive fluctuations appear to develop later). Although there are exceptions (in particular patients with tremor-predominant PD) for most patients with idiopathic RBD and newly defined neurodegenerative disease there is considerable difficulty in deciding which is the appropriate diagnosis. The clinical impression is that of a generally advancing global synucleinopathy, the diagnosis of which depends on whether it is first parkinsonism or cognitive impairment that crosses diagnostic threshold. The implications of these findings for understanding development of neurodegenerative disease in prediagnostic stages and classification of synucleinopathies will be discussed.

PS-8-1

CIRCADIAN RHYTHM DISRUPTION IN PATIENTS WITH SCHIZOPHRENIA AND SNAP-25 MUTANT MICE

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Sleep disturbances comparable to insomnia occur in up to 80% of schizophrenia patients, but very little is known about the contribution of the circadian system to these prevalent disruptions. We have undertaken a systematic exploration of circadian time patterns in 20 schizophrenia patients and 21 healthy control individuals matched for age, sex and being unemployed. Significant sleep/circadian disruption occurred in all patients. Half the patients showed severe circadian misalignment ranging from phase-advance/delay to non-24-hour periods in sleep-wake and melatonin cycles, and the other half showed patterns from excessive sleep to highly irregular and fragmented sleep epochs but normally timed melatonin production. We show that severe circadian sleep/wake disruptions exist irrespective of mood, mental state and antipsychotic treatment regimes. In parallel with our work on human subjects, we have examined both rest/activity behaviour and the expression of molecular elements of the circadian system in Snap-25 mutant mice, blind-drunk (Bdr). Bdr mice are known to display endophenotypes associated with schizophrenia. Our studies show that these mice also show abnormal sleep/wake behaviours that mirror those found in patients with schizophrenia. Further, critical outputs of the molecular clock shows disrupted expression in the suprachiasmatic nuclei (SCN) of mutant mice. These data suggest that the Bdr sleep/wake phenotype arises from a disruption of synaptic connectivity within the SCN that alters the neuropeptide output of the master circadian pacemaker. Collectively these data provide the first direct evidence for overlapping mechanistic pathways between circadian timing and schizophrenia.

PS-8-2

LIGHT-INDUCED IMPAIRMENT OF MOOD AND LEARNING REQUIRES MELANOPSIN-EXPRESSING GANGLION CELLS

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Aberrant light conditions experienced in shift-work and transmeridian travel, as well asseasonal changes in day length, cause mood and cognitive deficits. These are thought toarise from disruptions in sleep and circadian rhythms. However, using an aberrant lightcycle that neither changes the amount of sleep nor abolishes circadian rhythmicity, weshow that light directly regulates mood-related behaviors and cognitive functions in mice.In these animals, depression-like behavior and serum corticosterone levels are increased,while hippocampal long-term potentiation and learning are impaired. Administration oftwo differentially acting antidepressant drugs, fluoxetine and desipramine, restoreslearning in mice exposed to the aberrant light cycle. Furthermore, melanopsin-expressingintrinsically photosensitive retinal ganglion cells are necessary for this disruptive lightenvironment to directly influence mood and learning.

PS-8-3

RHYTHM AND THE BLUES

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Our biological clock counts daily rhythms with approximately 24 hours called circadian rhythm in our body. The mammalian circadian system consists of three components: input, pacemaker, and output. Almost all physiological phenomena including mental states, in addition to sleep-wake cycles, can be considered as circadian outputs. The recent molecular advances revealed that molecular clocks were located not only in the central oscillator, suprachiasmatic nuclei (SCN), but also in peripheral tissues, even in cultured cells. We established both in vivo and in vitro rhythm monitoring system. To understand molecular interaction between circadian rhythm and depression or mood disorders, we investigated circadian rhythm of the learned helplessness (LH) rat, an animal model of depression, at the behavioral and cellular level. The locomotor activity rhythm in vivo and circadian transcriptional rhythm in vitro seemed to be correlated with each other. The phosphorylated glycogen synthase kinase 3beta (pGSK3beta) was likely to be the key molecule that connects behavioral rhythm with cellular ones. Clock genes were included in the downstream targets of GSK3beta. The phenotypes including circadian rhythm in fibroblasts correlate to those in vivo, suggesting that the fibroblasts from the patients can be used as a diagnostic material and a therapeutic tool.

PS-8-4

DEUBIQUITINATION AND BEHAVIOR

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We found that CS mice exhibit an extremely low immobility time (almost no immobility) in both the tail suspension test (TST) and forced swimming test (FST). In these tests, animals are subjected to the short-term, inescapable stress of being suspended by their tail or being forced to swim in a water-filled cylinder. In such situations, the animals rapidly adopt a characteristic immobile posture that has been named "behavioral despair" on the assumption that the animals have given up hope of escaping. These tests have been widely used for assessing antidepressant activity and depression-like behavior. Quantitative trait locus (QTL) mapping using CS and C57BL/6J mice revealed significant QTLs on chromosomes (Chrs) 4 (FST) and 5 (TST and FST). To identify the quantitative trait gene on Chr 5, we narrowed the QTL interval to 0.5 Mb using several congenic and subcongenic strains. Ubiquitin-specific peptidase 46 (*Usp46*) with a lysine codon deletion was located in this region. This deletion affected nest-building, nursing behavior, alcohol preference, muscimol-induced righting reflex etc. The muscimol-induced current in the hippocampal CA1 pyramidal neurons and hippocampal expression of the 67-kDa isoform of glutamic acid decarboxylase significantly decreased in the *Usp46* mutant mice compared to control mice. All these phenotypes were rescued in transgenic mice with bacterial artificial chromosomes containing wild-type *Usp46*. In addition, *Usp46* KO mice exhibited low immobility time in TST. Thus, *Usp46* affects "behavioral despair" and it is implicated in the regulation of GABA action.

PS-9-1

MORPHOLOGICAL AND FUNCTIONAL NEUROIMAGING OF HUMAN NARCOLEPSY

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Human narcolepsy is due to a deficiency of the hypothalamic hypocretin system and presents with a pleomorphic clinical phenotype including sleep-wake, motor, vegetative, psychiatric and cognitive disturbances. Neuroimaging studies have expanded our knowledge of narcolepsy as a complex brain disorder arising from the dysfunction of multiple brain areas in addition to the hypothalamus.
1) Conventional brain MR studies have shown that the brain is grossly intact in primary (idiopathic) narcolepsy[1], whereas in secondary narcolepsy, hypothalamic and brainstem lesions were mostly found[2]. 2) Voxel-based brain MR studies provided inconsistent results[3]. 3) Proton brain MR spectroscopic studies have also been contradictory. Some authors reported alterations in hypothalamus and brainstem[4–5]. 4) Functional brain MR studies documented abnormalities in hypothalamo-amygdala-brainstem-limbic interactions in both aversive and appetitive (reward) experiments, suggesting a dysfunction of the emotional processing in narcolepsy[6–9]. 5) Brain PET studies found both a hypo- and hyper-metametabolism of cortico-subcortical areas during the awake state, and an hypothalamic hypometabolism during cataplexy[10–11]. 6) Brain SPECT studies have shown the activation of an amygdalo-cortico-basal ganglia-brainstem circuit during cataplexy[12]. 7) Brain neurotransmission (ligand) studies suggested changes in serotoninergic and dopaminergic transmission, the nature of which remains unclear[3].

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PS-9-2

DECIPHERING THE GENETIC PREDISPOSITION TO HUMAN NARCOLEPSY

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Human narcolepsy is affected by multiple genetic and environmental factors. In 1984, two independent groups reported the very strong association of HLA-DR2 with narcolepsy (Juji, Honda et al. Tissue Antigens; Langdon et al. Lancet), and the high-risk type is now defined to be HLA DRB1*1501-DQB1*0602 haplotype. Since then, a number of candidate genes have been studied for possible associations, but few common susceptibility polymorphisms have been confirmed. Recent technological development in large-scale SNP (single nucleotide polymorphism) typing has enabled genome-wide association studies (GWAS), and provided opportunities to identify novel susceptibility loci without any prior knowledge of position or function. Our first SNP-based GWAS confirmed the strong association with HLA-DQ region and identified a new susceptibility locus, CPT1B/CHKB (Miyagawa et al. Nat Genet 2008). GWAS by Mignot and international collaborators have identified new susceptibility genes, T cell receptor alpha (TCRA) (Hallmayer et al. Nat Genet 2009) and P2RY11 (Kornum et al. Nat Genet 2011). Another GWAS by Tafti and collaborators reported a new protective HLA haplotypes (Hor et al. Nat Genet 2010). Associations with HLA, TCRA, and P2RY11, as well as elevated autoantibodies against TRIB2 in narcoleptic patients (Cvetkovic-Lopes et al. J Clin Invest 2010) strongly suggest the involvement of autoimmunity in the disease pathogenesis. In addition, association with CPT1B/CHKB and some other genes as well as abnormal serum acylcarnitine levels (Miyagawa et al. Sleep 2011) suggest alteration of fatty acid beta-oxidation in the disease. New technological developments including massive parallel sequencing will contribute to our understanding of the genetic basis of human narcolepsy.

PS-9-3

MOVEMENT DISORDERS IN NARCOLEPSY

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Narcolepsy with cataplexy (NC) is a chronic disease characterized by excessive daytime sleepiness, striking transitions from wakefulness into rapid eye movement (REM) sleep, typically associated with cataplexy and other phenomena due to the abnormal occurrence of REM sleep elements during wakefulness (sleep paralysis and hallucinations) and frequent sleep/wake transitions. Nocturnal sleep in NC is usually disturbed by a large cohort of phenomena: vivid frightening dreams, several nocturnal awakenings, REM sleep behavior disorder (RBD), periodic leg movement (PLM), obstructive sleep apnea (OSA), sleep-related eating disorders and other parasomnias. Frequent abnormalities in both NREM and REM sleep motor regulation result in dissociated sleep/wake states. Higher abnormalities in REM sleep motor regulation were reported with an increased frequency of REM sleep without atonia, phasic EMG events and PLMS in narcoleptic patients when compared to controls. A higher prevalence of RLS was found in NC but with a moderate severity, together with a higher frequency of PLMS and PLMW with an association between the presence of PLMS and measures of REM sleep and daytime functioning disruption. PLMS displayed specific features in idiopathic restless legs syndrome and narcolepsy-cataplexy respectively, with narcolepsy-cataplexy with restless legs showing an intermediate pattern. Motor dyscontrol in narcolepsy is not restricted to sleep, involving also wakefulness with the presence of cataplexy and the increase in periodic leg movements index. Moreover, recently pediatric cases of NC have been reported with a co-occurence with a complex movement disorder at disease onset, a phenomenon that may vanish later in the course of the disease. The coexistence of NC and several motor dysfunctions suggest a common neurobiological defect of motor inhibition. Further studies are warranted to assess clinical course and whether the associated movement disorder is also caused by hypocretin deficiency or by additional neurochemical abnormalities.

PS-9-4

SPECTRUM CONCEPT OF NARCOLEPSY AND ITS CLINICAL SIGNIFICANCE

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In the 2nd edition of International Classification of Sleep Disorders (ICSD 2nd), narcolepsy was separated into the cases with and without cataplexy, and idiopathic hypersomnia into the cases with and without long sleep time. Among these, idiopathic hypersomnia with long sleep time is clearly different in symptomatology with more than 10 h of nocturnal sleep time and a major difficulty to wake up in the morning. However, the other three categories are common in that they have frequent short naps in daytime and show almost normal length of nocturnal sleep time. Based on this, narcolepsy spectrum encompasses idiopathic hypersomnia without long sleep time. Although all the disorders in this spectrum show marked daytime sleepiness, score of Epworth sleepiness scale (ESS) is highest and sleep latency on multiple sleep latency test (MSLT) is lowest in narcolepsy with cataplexy among the disorders. Of note, when dividing the cases with narcolepsy without cataplexy into the group with HLA-DRB1*1501/DQB1*0602 positivity and that without, the latter group shows a lower frequency of sleep onset REM period and longer sleep latency on MSLT compared with the former group, and the sleep latency in this group is quite similar with that in idiopathic hypersomnia without long sleep time. The fragmentation of nocturnal sleep is observed in narcolepsy with cataplexy, but this phenomenon is not observed in HLA negative narcolepsy without cataplexy as well as in idiopathic hypersomnia without long sleep time. In addition, the deficiency of orexin secretion does not exist in HLA negative narcolepsy without cataplexy. These findings suggest that HLA negative narcolepsy without cataplexy is a milder variant of narcolepsy and symptomatic characteristics is not so different from idiopathic hypersomnia except for the increased REM propensity.

PS-9-5

WORK OF DR. YUTAKA HONDA ON NARCOLEPSY AND ITS SUBSEQUENT DEVELOPMENT

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Dr. Yutaka Honda started his passionate interest in narcolepsy while he engaged in the study of his doctoral thesis entitled Clinical studies on the Diencephalon-related Psychic Symptoms published in 1959. He reported 24 patients with psychiatric symptoms associated with vegetative dysfunction and found that somatic/autonomic symptoms and psychic symptoms progress simultaneously and closely connected. Among 24 patients, 16 were narcolepsy and he evaluated their psychic symptoms such as changes in activity, mood and character as well as autonomic functions.

He extended his interests in narcolepsy to various directions, including neuroendocrinological abnormality (disappearance of GH surge), tendency towards obesity and diabetes mellitus, and the HLA association in narcolepsy. The discovery of genetic contribution to narcolepsy triggered subsequent studies, resulting in the identification of novel narcolepsy-related genes. IGFBP3 and CPT1B are among those, identified by expressional gene profiling and genome wide association study, which could be associated with endocrine and metabolic abnormalities found in narcolepsy patients.

He noticed the serious QOL impairment of narcolepsy patients and founded the Japan Narcolepsy Association (JNA) in order to cultivate mutual friendship and facilitate self-help activities among the members. Now JNA developed into an authorized NPO with more than 200 members, fulfilling his one more aim to enhance a better public understanding of narcolepsy. JNA activity was also effective to form a good therapeutic relationship and provided the opportunity for long-term prognosis study of narcolepsy, elucidating the existence of spontaneous remission in narcolepsy.

We are still on the way to understand narcolepsy as a whole from the viewpoint of current knowledge about hypothalamic sleep wake regulation. His observations remain to be addressed how psychic and somatic symptoms are interacted and what neural system contribute psychic to form narcoleptoid personality and occasional psychotic symptoms observed in narcolepsy patients.

PS-10-1

COMBINED CHRONOTHERAPY IN DRUG-RESISTANT DEPRESSION

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There are several advantages to using sleep deprivation for treatment of depression, including early response, a high efficacy rate (approximately 60%), few side effects, and efficacy for drug-resistant depression. On the other hand, its clinical efficacy seems to be hampered by high relapse rates after recovery sleep. Therefore, it has not been widely used to date in many countries. However, methods for increasing and sustaining the efficacy of sleep deprivation have been reported. It is possible to increase and sustain the efficacy of sleep deprivation in combination with medication (antidepressant drug, lithium, etc.), repeated sleep deprivation, bright light therapy, and/or sleep phase advance. In Akita University Hospital, we tried combined chronotherapy, which is total sleep deprivation followed by sleep phase advance (3 days) and bright light therapy (5 days), in drug-resistant depression patients (N = 13, male/female = 8/5, unipolar/bipolar = 10/3). They took ongoing medication without change before and after the chronotherapy. Changes in the depressive state over time were rated using the Hamilton Rating Scale for Depression (HAM-D), the Visual Analogue Scale (VAS), and the Zung Self-Rating Depression Scale (SDS) for 3 weeks. Significant improvements were observed with the chronotherapy in HAM-D, VAS, and SDS. Finally, 8 patients of 13 kept treatment response (50% or more changes in HAM-D). Because we sometimes encounter patients who are resistant to general drug treatment, adding sleep deprivation to the treatment choices may overcome drug-resistant depression and shorten treatment duration.

PS-10-2

RAPID AND SUSTAINED ANTIDEPRESSANT RESPONSE WITH SLEEP DEPRIVATION AND CHRONOTHERAPY IN BIPOLAR DISORDER

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Objectives: The development of a rapid-acting and sustainable treatment for bipolar disorder (BPD) has been a goal for decades. The most widely-documented rapid-onset antidepressant therapy is sleep deprivation (SD) which acts within 24–48 hours in 40–60% of depressed patients. Conventional antidepressants usually require 2–8 weeks to meet response criteria. The delay prolongs suffering, may increase suicidal risk and underlines the urgency of alternative treatment strategies. This the first study to evaluate the combined efficacy of three established circadian-related treatments (SD, bright light, sleep phase advance) as adjunctive treatment to lithium and antidepressants.
Methods: Forty-nine BPD patients were randomly assigned to a chronotherapeutic augmentation (CAT) (SD+BL+SPA) or to a medication-only (MED) group. Clinical outcome was assessed using the Hamilton Rating Scale for Depression (HRSD).
Results: Significant decreases in depression in the CAT versus MED patients were seen within 48 hours of SD.
Conclusions: This is the first study to demonstrate the benefit of adding three non-invasive circadian-related interventions to SD in medicated patients to accelerate and sustain antidepressant responses and provides a strategy for the safe, fast-acting and sustainable treatment of BPD.
Keywords: Sleep deprivation, depression, light therapy

PS-10-3

NEUROIMAGING AND GENETICS OF SLEEP DEPRIVATION IN DEPRESSION: FROM MONOAMINES AND GLUTAMATE TO NEUROPLASTICITY

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Accumulating evidence suggests that plastic processes occurring during wakefulness result in a net increase in synaptic strength in many brain circuits, and that synaptic strength is downscaled to baseline levels

during sleep, when effective cortico-cortical connectivity is broken down. According to this synaptic homeostasis hypothesis of sleep, SD should cause marked changes in neuronal connectivity resulting in major changes of brain metabolism and function which could be related to its antidepressant action.The mechanisms by which prolonged wake increases synaptic strength involve glutamatergic neurotransmission. Glutamate agonists, such as ketamine, cause rapid antidepressant effects similar to SD, and increase mTOR dependent synaptic formation. Some authors speculated that increased AMPA-to-NMDA glutamate receptor throughput in critical neuronal circuits would be a key component of antidepressant mechanisms, indirectly and gradually obtained by monoaminergic compunds and directly caused by drugs influencing Glu neurotransmission.We showed that Glu metabolism is altered by SD, the changes being proportional to both perceived and observed mood amelioration. The effects are well evident in dorsal ACC cortex, where changes in 5-HT function as a function of 5-HTTLPR polymorphism influence neural responses after successful SD. The finding suggests then a role for Glu neurotransmission, and its interaction with monoamines, in the rapid antidepressant effects of SD.

PS-11-1

BRAINSTEM AND SPINAL CORD NEURAL CIRCUITRY OF REM SLEEP AND ATONIA

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REM sleep (or paradoxical sleep) is characterized by cortical and hippocampal activation and muscle atonia. Atonia can be better understood by dividing it into tonic and phasic component, which displays differently in cranial muscles with prominent phasic actvitiy (such as rapid eye movements) and postural muscles with almost no phasic activity. In this talk, I will review the lesion, behavioral and genetic works leading to identify the brainstem and spinal neural circuitry regulating phasic activity atonia, cortical activation and REM sleep timing. I will also review our recent work of the neural circuitry of phasic events of trigeminal motor nucleus (Mo5). Finally, I will discuss how the animal model can help us to understand human REM sleep behavior disorder (RBD).

PS-11-2

COMMON GROUNDS AND DIFFICULT TO RECONCILE DIFFERENCES BETWEEN THE DISFACILITATION AND ACTIVE INHIBITION CONCEPTS OF THE ATONIA OF REM SLEEP

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When rapid eye movement (REM) sleep was discovered, a combination of characteristic motor events was noted: REMs, phasic twitches of facial and distal muscles, irregular breathing, and a flaccid paralysis of axial/postural muscles (atonia). Subsequent observations revealed that, when the atonia occurs, motoneurons are hyperpolarized and receive postsynaptic, glycinergic inhibitiory potentials. Additional experiments led to the concept of a REM sleep-specific descending inhibitory pathway that: (1) originates in the dorsomedial pons; (2) has a synaptic relay in the medial medulla; and (3) includes glycinergic inhibitory premotor neurons that cause the atonia. Evidence supports parts of this concept, some parts still need critical examination, and some have been disproved. Specifically, REM sleep-related depression of activity in hypoglossal (XII) and trigeminal (V) motoneurons is not diminished by antagonism of glycine receptors in the corresponding motor nuclei. This does not disprove the presence of active inhibition but indicates that it is not the main cause of depression of XII or V motoneuronal activity during REM sleep. Similar studies need to be conducted with spinal motoneurons. Forthermore, some orofacial motoneurons become silent during non-REM sleep (atonia). Any additional depression of their activity during REM sleep is not strong enough to suppress the phasic excitations that elicit the frequent and large phasic twitches in orofacial muscles. In the carbachol model of the atonia of REM sleep in which phasic twitches do not occur, the REM sleep-like depression of XII motoneuronal activity can be sufficiently explained as resulting from a combined withdrawal of serotonin- and norepinephrine-mediated, endogenous excitation (disfacilitation). Thus, a one-size-fits-all concept cannot explain the atonia of REM sleep in all muscles. Rather, the atonia is caused by a combination of disfacilitation and active inhibition, with the two mechanisms having different magnitudes in motoneurons innervating axial, distal limb, orofacial and other muscle groups.

PS-11-3

PONTOMEDULLARY REGULATION OF REM SLEEP ATONIA

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The medial pontomedullary reticular formation has been implicated in the control of motor activity. Electrical activation of the medial pons and medulla suppresses motor activity in the decerebrate animal. In the behaving animal, the magnitude of the medial medulla stimulation induced motor suppression has been shown to be state-dependent, with larger suppression of muscle tone in SWS than waking. Pharmacological studies showed that the medial pons, the pontine inhibitory area (PIA), responded to glutamate and acetylcholine, with suppression of muscle tone being induced by these chemicals. On the other hand, injection of glutamate but not acetylcholine into the nucleus magnocellularis (NMC) of the rostroventral medulla induced muscle atonia. The PIA stimulation induced suppression of muscle tone has been suggested to be mediated through the NMC. Anatomical and physiological studies demonstrated that the PIA contains glutamatergic neurons, which project to the NMC and elicit muscle atonia. In vivo microdialysis and HPLC analysis studies revealed that activation of both the PIA and NMC increases glycine and GABA release and decreases norepinephrine and serotonin release into the spinal ventral horn. Our recent study found that an area rostral to the PIA, located at the ventral portion of the junction of the pons and midbrain including the caudal substantia nigra, the ventral mesopontine junction (VMPJ), is also involved in the control of muscle activity in sleep. Sleep pattern was not changed by neurotoxic lesion of the VMPJ. However, this lesion produced periodic leg movements in SWS and increased phasic and tonic muscle activity in REM sleep in the cat, symptoms resembling human REM sleep behavior disorder (RBD). Clinical evidences have shown that RBD and Parkinson's disease are highly correlated. Patients may be diagnosed simultaneously with Parkinson's disease and RBD, or diagnosed with Parkinson's disease and then develop RBD, or vice versa. The anatomical proximity of the VMPJ to the substantia nigra may provide a link between RBD and Parkinson's disease.

PS-11-4

ATONIA MEDIATING MECHANISMS FROM THE FOREBRAIN STRUCTURES TO SPINAL CORD

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Postural muscle tone is defined as tonic muscular tension that permits standing. Although appropriate level of postural muscle tone is regulated in conjunction with any types of movements during wakefulness, it is completely abolished during rapid eye movement (REM) sleep. Abnormality in postural muscle tone may exist behind a variety of movement disorders and sleep-relating disorders. We have identified muscle tone inhibitory system in the cat. This inhibitory system arises from the midbrain cholinergic neurons in located the pedunculopontine tegmental nucleus (PPN). The PPN cholinergic neurons activate cholinoceptive neurons in the medial pontine reticular formation (PRF), which consecutively excite medullary reticulospinal neurons and spinal inhibitory interneurons. At the level of lumbosacral spinal segments, an activation of the inhibitory system exerted postsynaptic inhibition in alpha- and gamma-motoneurons and interneurons mediating reflex pathways, and presynaptic inhibition in primary afferents. These inhibitory effects are possibly mediated by a group of lamina VII interneurons. Microinjections of carbachol (a long-acting cholinergic agonist) and serotonin into the medial PRF altered the level of muscle tone of the decerebrate cats by increasing and decreasing the excitability of the inhibitory system, respectively. The PPN receives efferents from the forebrain structures such as the basal ganglia and the hypothalamus. GABAergic efferents from the substantia nigra pars reticulata (SNr), an output nucleus of the basal ganglia, to the PPN reduced the activity of the inhibitory system. In addition, orexinergic efferents from the prefornical lateral hypothalamus to the SNr and the PPN also reduced the activity of this system via GABAergic neurons. Based on these findings, it is possible that the inhibitory system contributes to muscular atonia during REM sleep. We propose that the dysfunction of this inhibitory system may underlie pathophysiological mechanisms of neurological disorders such as Parkinson disease and narcolepsy.

PS-12-1

HOW INDIVIDUAL GENETIC DIFFERENCES AFFECT DAILY BEHAVIOR

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All facets of human behavior display wide inter-individual variations. In every aspect studied so far, a portion of this difference has been genetically determined, and a portion by environment. Twin studies have shown that interindividual differences in both the circadian clock determining diurnal behavior and the homeostatic one regulating sleep need are likely about 50% heritable – i.e. half is controlled genetically, and half by environmental factors. Using human primary fibroblasts as a model, our laboratory has studied the origins of these differences at a molecular level. Even if the intercellular interactions that determine diurnal behavior are neuronal, the intracellular pathways that control a cell's response to external signals are conserved in most cell types. For example, there exist slave circadian oscillators in most cells of the body that are similar or identical in mechanism to those in the suprachiasmatic nuclei (SCN) of the hypothalamus that regulate circadian behavior. Thus, the molecular period length of human fibroblasts in culture is proportional to the behavioral period of the subjects from whom they were taken.Thus, we can conclude that some circadian variation can be ascribed to direct genetic changes in the circadian clockwork that are visible in peripheral cells: changes in period and amplitude of the circadian clock, for example. Other changes, however, can be ascribed to epigenetic mechanisms. In particular, we show that early in life, circadian properties are plastic, and can be stably modified by environmental light patterns that modify genome-wide methylation patterns. Together, these genetic and epigenetic mechanisms probably account for the wide diversity of human daily behavior.

PS-12-2

POTENTIAL THERAPEUTIC AND DIAGNOSTIC TARGETS FOR CIRCADIAN RHYTHM SLEEP DISORDERS

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We prepared two different topics for this symposium. When clock mutant mice were reared under constant lighting conditions in their early stage, they showed the delay of onset of locomotor activity rhythm under light-dark conditions, similar to delayed sleep-phase syndrome (DSPS) in humans. This result suggests that environmental lighting condition in early life stage may be an important factor for normal circadian rhythm in adults. Administration of melatonin at light-off time could attenuate the DSPS, and mouse activity onset was advanced during administration period. In addition, opioid receptor-like 1 (ORL1) receptor agonist, W-212393 could also rescue the DSPS of clock mutant mice. Thus, this model mouse is helpful to understand the DSPS and also develop potential therapeutic drugs for DSPS. For the purpose of sleep and wakefulness, benzodiazepines and caffeine is used for humans, respectively. Brotizolam administration during late afternoon caused a phase-advance of hamster circadian rhythm with reduction of expression of Per1 and Per2 genes, suggesting that brotizolam may affect circadian rhythm system. Caffeine lengthens the locomotor activity rhythm and bioluminescence rhythm of suprachiasmatic nucleus in Per2-luc KI mouse. Caffeine also lengthens the bioluminescence rhythm of MEF from Per2-luc KI mouse, and decreased the phosphorylation of GSK and increased the phosphorylation of AMPK. Thus, caffeine-induced lengthen of circadian rhythm may be involved in the activation and /or inactivation of various protein kinases. Taken together it is suggested that chemicals induce sleep or wakefulness may have a potential activity to affect the circadian rhythms.

PS-12-3

CIRCADIAN AND HOMEOSTATIC EVALUATION OF SLEEP-WAKE DISTURBANCES INHUMANS

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Circadian and homeostatic processes are key regulatory components of sleep-wake regulation. Quantification of these processes in humans can be accomplished by a variety of protocols, including total sleep-deprivation, partial sleep deprivation and circadian displacement. Relevant outcome variables are numerous and range from waking performance, waking and sleep EEG measures to analyses of the transcriptome in peripheral tissues. Individual differences in these processes are prominent and may be informative of the mechanisms underlying commonly

observed sleep-wake disturbances. Recent data related to the circadian and homeostatic evaluation of sleep-wake disturbances will be presented.

PS-12-4

GENETIC AND PHYSIOLOGIC PHENOTYPING OF CIRCADIAN RHYTHM SLEEP DISORDERS

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Metabolic, physiological, and behavioral processes exhibit 24-hour (h) rhythms in most organisms including humans. These rhythms are driven by a system of self-sustained clocks and are entrained by environmental cues such as cycles of light and dark and food intake. In mammals, the circadian clock system is hierarchically organized such that the master clock in the suprachiasmatic nuclei of the hypothalamus integrates environmental information and synchronizes the phase of oscillators in peripheral tissues. The transcription and translation feedback loops of multiple clock genes are involved in the molecular mechanism of the circadian system. Disorganization of the circadian system is known to be closely related to many diseases including sleep, mood and metabolic disorders. Advanced sleep phase type, delayed sleep phase type and non-entrained type of circadian rhythm sleep disorders (CRSD) are thought to result from malfunction/maladaptation of the circadian system. Dissection of human circadian clock system is indispensable to understand the pathophysiology of CRSD. In this study, we evaluated rhythmic characteristics of physiological functions (core body temperature, plasma melatonin and plasma cortisol levels) from healthy subjects and CRSD patients under a 28-h forced desynchrony protocol in a laboratory environment free from external cues and masking effects for several weeks. Furthermore, we measured clock gene expression in primary fibroblast cells established from individual skin biopsies using a luminescence reporter assay system. Our results demonstrate that there was a significant correlation between the period length of physiological and fibroblast rhythms in the same subjects and suggest that surrogate measurements using fibroblast cells derived from individual biopsies would be a useful tool for assessing individual circadian properties. Here, we have examined and will discuss the phenotypes of CRSD at both the physiologic and molecular levels.

PS-12-5

SOCIAL APPLICATION OF HUMAN SLEEP AND CIRCADIAN PHENOTYPING FOR SHIFT WORKERS

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Introduction: Individuals vary greatly in their tolerance to circadian disruption. The results of two field studies are presented to illustrate the impact of circadian rhythms and sleep-wake disturbances for the shift worker population.
Methods: Experiment 1: 15 shift nurses (mean (S.D.): 41.8(7.9) years; 9 controls and 10 intervention) worked about 12 non-consecutive 8 h nights. The intervention consisted of bright white light exposure and morning neutral grey density goggles. Diurnal sleep was measured at home by Nightcap or PSG. Circadian rhythm of salivary melatonin was assessed before and after night shifts by 36-h constant routines. Experiment 2: 15 police officers (30.1 (5.2) years; 9 controls and 8 interventions) worked 7 consecutive 8-h nights. The intervention consisted of bright white light and orange-tinted goggles at sunrise. Diurnal sleep was measured at home by wrist actigraphy. The amount of UaMT6s excreted during diurnal sleep was assessed at home after night shifts. Circadian rhythm of salivary melatonin and UaMT6s was assessed before and after night shifts during 48-h laboratory visits.
Results: Experiment 1: Intervention group nurses had longer mean (SEM) diurnal TST of 7h20 (0h10) compared to 6h35 (0h08) in controls (Mann-Whitney, $p = 0.05$). The 11.31 (1.13h) phase delay of melatonin was greater in intervention group nurses than the 5.08 (2.32) h delay in controls (ANOVA: $p = 0.03$). Experiment 2: The rate of UaMT6s excreted during diurnal sleep increased faster over the week in intervention versus control group officers (mixed linear model: $p = .0323$), although circadian phase delay was not significantly different. Following night shifts, treatment group officers had greater mean diurnal TST of 6h31 (0h15) compared to the 6h21 (0h28) of control group officers (mixed linear model: $p = 0.0238$).
Discussion: Parameters such as circadian phase and the phase angle of entrainment are useful indexes of sleep-wake disturbances in shift workers. The degree of exposure to light and darkness contribute to the level of circadian adjustment in both studies.

PS-13-1

TURNING AROUND DAYTIME IMPACT OF INSOMNIA IN THE DAILY LIFE OF PATIENTS

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Insomnia is not only defined by a non satisfiyng sleep, but also by daytime consequences of poor sleep on the daily life of patients. However this daytime impact is poorly understood.
Based on two recent studies made in national and international samples, we try to better understand determinants of deleterious daytime life in chronic insomniacs.

- In a Cross-sectional telephone survey in a representative sample of 1004 French young adults (25–45 years old), we assess insomnia, short sleep (total sleep time < 5 hours) and sleep debt. We found significantly more short sleepers in the group of insomniacs than in the non-insomniac group (24.6% vs 17.2%; $p < 0.0001$). Insomniacs with short sleep have significantly more complaints on daytime functionning that those who are non short sleepers (1).
- In an international cross-sectional survey was conducted in 5293 outpatients complaining of sleep disturbances in primary care practice. A sleep questionnaire addressing daytime consequences, insomnia symptoms, socio-demographic characteristics, and daytime impairment was administered by 647 physicians in 10 countries. Overall, 20% to 33% of subjects reported a "severe" daytime impairment associated with sleep disturbances. Patients with several and combined complaints of insomnia showed a higher percentage of severe daytime consequences compared with those suffering from single type of insomnia (initiation or maintenance). Non-restorative sleep insomniacs had less severe daytime impact compared to the other subgroups (2).

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PS-13-2

LONGITUDINAL OUTCOME OF INSOMNIA – PSYCHIATRIC & MEDICAL CONSEQUENCES

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Insomnia is defined as a complaint about sleep continuity and quality that has daytime repercussions. It is a common sleep disorder affecting all age groups across the globe, and carries significant health care burden and morbidities including reduced daytime alertness, fatigue, increased health care utilization, accident risk, reduced productivity and subjective quality of life.

Insomnia is much more common among patients of psychiatric disorders. Over past decade, there is a paradigm shift to conceptualize insomnia as a co-morbidity disorder rather than merely as a symptom of the mental disorders. Prospective studies found that insomnia predisposed to future development of depression, anxiety disorders, and alcoholism abuse. Persistent insomniac symptom was associated with future risk of relapse of depression. Apart from mental adversity, increasing attention has been recently focused on the medical consequences of insomnia. Medical illnesses, such as chronic pain, hypertension, impaired glucose tolerance and diabetes mellitus, and upper respiratory tract infections, were found to be associated with insomnia in both cross sectional surveys and longitudinal studies.

In this lecture, the current literature on the longitudinal psychiatric and medical outcome of insomnia will be discussed especially with reference to the adult and children insomnia longitudinal data from our Hong Kong studies.

PS-13-3

SLEEP AND SUICIDAL BEHAVIORS AMONG YOUTHS

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Suicide risk begins to increase during adolescence. Sleep in adolescence is characterized by delay in the sleep/wake schedule, sleep insufficiency, daytime sleepiness and fatigue, and increased risk for sleep disturbances. Sleep disturbances are likely to lead to suicidal behaviors, since mental disorders are a strong risk factor for suicidal behaviors, and sleep disturbances are, in turn, linked to mental disorders. This presentation will review recent clinical, epidemiological, and biological studies on the relationship between sleep and suicidal behavior and propose potential psychological and biological pathways and future research directions. Clinical studies have shown that suicidal psychiatric patients have more sleep disturbances including insomnia, hypersomnia, or nightmares than nonsuicidal patients. Shorter rapid eye movement latency and increased rapid eye movement activity have been noted to be a marker of suicidality in psychiatric patients. A number of cross-sectional and several longitudinal epidemiological studies have demonstrated that insomnia, nightmares, and sleep insufficiency are associated with elevated risk for suicide. Inadequate sleep increases suicide risk possibly by 1) impairing cognitive judgment or impulse control; 2) increasing irritability, lowering threshold for negative emotional responses; 3) increasing the individual's susceptibility to psychopathology or exacerbating preexisting psychopathology; or 4) by interacting with a number of underlying vulnerable moderators (such as hopelessness, impulsivity). Inadequate sleep or sleep disturbances and suicidal behavior may share neurobiological mechanism, particularly in regard to decreased serotonin functioning. Future studies need to examine the causal relationship neurobiological mechanisms between sleep, psychopathology, and youth suicidal behavior.

PS-13-4

NATURAL HISTORY OF INSOMNIA: FACTORS MODERATING THE COURSE OF INSOMNIA OVER TIME

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Despite the high prevalence and significant burden of insomnia, there is little information about its natural history, risk factors, course, and factors moderating its trajectory over time. This presentation will outline preliminary findings of an ongoing longitudinal study of insomnia in a population-based sample in Canada. A sample of 3464 adults (62% women, mean age of 48 years old) with and without insomnia complaints completed several questionnaires about their sleep, physical and mental health, and several psychological and behavioral characteristics hypothesized to be related to the onset and course of insomnia. These evaluations were completed at baseline, 6 months, and at yearly follow ups for five consecutive years. Data from the first three evaluations (baseline, 6 and 12 months) will be used for this presentation. Among good sleepers, 20.3% developed either insomnia symptoms (17.3%) or an insomnia disorder (3%) during the 1-year follow-up period. Conversely, of those with insomnia symptoms or an insomnia syndrome, the majority reported persistent insomnia (63.5 for symptoms and 90.1% for syndrome) over the course of the one year follow up, whereas 36.8% and 9.9% remitted during the same period. Of all psychological variables examined, depression, anxiety, arousability, emotion-oriented coping style, and stress-related vulnerability to insomnia were associated with (predisposed to) new onset insomnia; conversely, improvements on these variables between any two assessment periods were also associated with remission of insomnia. Of the health-related variables, only general health and pain were associated with new onset insomnia. These findings suggest that several psychological and health-related variables can moderate the course of insomnia over time.

PS-13-5

LIFE STYLE AND GENESIS OF INSOMNIA

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Insomnia is defined as a sleep difficulty that occurs despite adequate opportunity and circumstances for sleep and is associated with various daytime impairments related to the difficulty. Prior studies have indicated that factors having an influence on its genesis are multiple, including gender, age, physical and psychological conditions, life style, etc.

Among these variables, life style or sleep habits has been a target of non-pharmacological therapeutic interventions. Bed time restriction, a cognitive behavior therapy, in which time spent in bed (TIB) is properly shortened has a favorable therapeutic effect on insomnia, suggesting that the length of TIB may have a robust pathogenetic influence on the development of insomnia. However, none of the studies have examined the pathogenetic importance of long TIB in a large sample from the general population. Therefore we conducted an epidemiological survey on sleep problems and habits among the general adult population of Japan and examined the relation between insomnia and sleep habits. Describing prevalence for insomnia subtypes as a function of TIB was of our particular interest. The Nihon University Sleep and Mind Epidemiology Project (NUSMEP) was conducted in 2009, using face-to-face interviews. People aged 20 years or older were selected randomly from all areas of Japan, by using a three-stage-stratified sampling method. Finally 2,559 people (response rate 54.0%) indicated the presence of difficulty initiating sleep (DIS), difficulty maintaining sleep (DMS), early morning awakenings (EMA) and habitual TIB. Multiple logistic regression analyses after adjusting possible confounding effects of age and gender revealed that long TIB (9 hours or longer) was associated with a higher prevalence of all the subtypes of insomnia and that a short TIB (shorter than 6 hours) was associated with a higher prevalence of DIS and EMA. These results suggest that one's setting of TIB may have played a pathogenetic role in the natural history of insomnia and that its detailed mechanism may be different among the subtypes of insomnia.

PS-14-1

HOW ANIMAL KNOWS THE DAYLENGTH

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Animals living outside the tropics use changes in daylength to adapt to seasonal changes in environment, but the molecular and endocrine mechanisms underlying photoperiodic time measurement are not fully understood. The Japanese quail is a robust model for the study of these mechanisms because of its rapid and dramatic response to changes in photoperiod. In the previous study, we have demonstrated that local thyroid hormone catabolism within the mediobasal hypothalamus (MBH) by thyroid hormone-activating enzyme (type 2 deiodinase: DIO2) regulates photoperiodism. Recent functional genomics analysis in quail demonstrated that long days induce thyrotropin (TSH) production in the pars tuberalis (PT) of the pituitary gland, which triggers *DIO2* expression in the ependymal cells (EC) of the MBH. In mammals, nocturnal melatonin secretion provides an endocrine signal of the photoperiod to the PT that contains melatonin receptors in high density. We have also demonstrated the involvement of TSH signalling pathway in mammals by using the TSH receptor null mice. It has been know for many decades that non-mammalian vertebrates detect light by deep brain photoreceptors that lie outside the retina and pineal gland to regulate photoperiodism. We identified expression of a novel opsin (Opsin 5) in the paraventricular organ (PVO), an area long believed to be capable of phototransduction in quail. Functional analysis revealed that Opsin 5 detects short-wavelength light to regulate photoperiodism. I would like to review the current understanding of the mechanism underlying photoperiodism in vertebrates.

PS-14-2

MAMMALIAN CIRCADIAN CLOCKS DETECTING MORNING LIGHT AND EVENING LIGHTS

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Seasonal changes in day-length (photoperiod) and climates affect human circadian rhythms including sleep length and quality. The mechanisms how mammals, especially non-seasonal breeders, know the seasonal changes to alter their physiology and behavior are still poorly understood. Long-lasting hypothesis for measuring day length in nocturnal rodents is the two independent but mutually coupled oscillators, Morning (M) and Evening (E) oscillators, which track dawn and dusk separately and regulate behavioral offset and onset, respectively. By using transgenic mice carrying a firefly luciferase reporter gene for clock genes *Per1* expression and PER2, we explored the mechanisms and site of the photoperiodic clock.

Per1-luc or PER2:LUC knock-in mice which were kept in LD12:12 were exposed to either LD6:18 or 18:6 for 3 weeks. After measuring behavioral rhythms, they were decapitated and serial coronal SCN slices were cultured for recording bioluminescence with a photomultiplier (PMT). In addition, horizontal as well as serial coronal slices were cultured for bioluminescent imaging with a CCD camera, and circadian rhythms in single SCN cells were analyzed.

Irrespective of photoperiods, *Per1* expression rhythms in the anterior and posterior SCN were phase-locked to the onset and offset of behavioral rhythms, respectively, suggesting the localization of E and M oscillators. In addition, the third oscillatory cell group with an early morning peak was detected in the anterior SCN of mice that were exposed LD18:6. No laterality was detected in the cells with early morning or late evening peaks, suggesting that an oscillatory mechanism for photoperiodic regulation of behavioral rhythms may be different from that for behavioral splitting of hamsters in constant light. PER2::LUC rhythms in single SCN cells did not show large phase differences even in LD18:6. Different roles are suggested between *Per1* and *Per2* especially in photoperiodic responses of behavioral rhythms.

PS-14-3

NATURE AND NURTURE IN THE SEASONALITY OF CIRCADIAN RHYTHMS

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The mammalian central biological clock, that times sleep/wake cycles and mediates seasonal responses to light, is composed of ca. 20,000 neurons that express a network of clock genes which generate 24 hour rhythms. Much is known about how clock genes and their variants determine the characteristics of the circadian timing system, but less is known about how environmental influences on the clock during development may affect the clock through epigenetic means. Recently, our laboratory has examined whether exposure to seasonal light cycles during perinatal development can have lasting influence on the characteristics of the brain's biological clock. During the perinatal period mice were exposed to either a short-day winter-like LD 8:16 light cycle,

an equinox LD 12:12 cycle, or a long-day summer-like LD 16:8 light cycle. At weaning, mice were placed into individual cages with running wheels and either continued on the same seasonal light cycle, or switched to the opposing cycle (long to short; short to long) for 4 additional weeks of maturation. At 7 weeks of age either the molecular rhythms of the suprachismatic nucleus (SCN) biological clock, or running wheel behavior in constant darkness was assayed. We tested for i) persistent effects of perinatal photoperiod by testing for main effects of developmental photoperiod across both the maintained and reversed continuation groups, and for ii) interactions of perinatal photoperiod with subsequent changes in seasonal photoperiod by comparing across all groups. We found that i) there are persistent changes in the waveform and period of individual clock neurons induced by perinatal seasonal light cycles that are also evident as altered circadian behaviors, and ii) that changes in clock neurons induced by perinatal exposure to seasonal light resulted in altered circadian responses to subsequent seasonal change. These results show that in addition to the genetic determination of clock properties by clock genes that can be lasting epigenetic influence of environmental signals to the clock during development.

PS-14-4

SEASONALITY IN HUMAN SLEEP AND MOOD IN HEALTH AND DISEASE

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Seasonality used once to pervade our lives. The change in daylength throughout the seasons was as important for human physiology as for other organisms that needed to adapt to survive and reproduce. Until the widespread use of electric light (and indoor work) and heating/air conditioning, there is evidence for a spring peak in conception rates. Epidemiological studies indicate some remnant of seasonality in sleep under daily entrained conditions – longer in autumn/winter than in spring/summer (by ca. 15 mins), whereas the changes in sleep under freerun during temporal isolation are much greater (by ca. 1 h). Women sleep longer than men at all times of year. A wide range of behaviours and illnesses still show seasonal variations – from physical activity to metabolic syndrome, from sympathetic outflow to schizophrenia birth rate to suicide. At the neurotransmitter level, serotonin function changes with season. Seasonal affective disorder is one example of a mood disorder related to shifts in the circadian system (lower amplitude, phase delay). More generally a winter lowering of mood is associated with a shift towards eveningness, and evening chronotypes have a higher prevalence of depressive disorders.

PS-15-1

DISCOVERY AND HISTORY OF OREXIN

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Orexin A and orexin B (also known as hypocretin 1 and hypocretin 2) are hypothalamic neuropeptides that were discovered thirteen years ago. Orexin producing neurons are localized exclusively in the lateral hypothalamus, the classical feeding center. Subsequently, several studies suggested that orexin deficiency causes narcolepsy in humans and other mammalian species, highlighting roles of this hypothalamic neuropeptide in the regulation of sleep and wakefulness. Studies of efferent and afferent systems of orexin-producing neurons have shown that the orexin neuronal system has close interactions with systems that the regulate emotion, energy homeostasis, reward, and arousal. Orexin neurons receive abundant input from the limbic system, which might be important for increasing arousal during emotional stimuli. We found that orexin neurons are also regulated by sleep active neurons in the ventrolateral preoptic area. These cells also have been also thought to be regulated by peripheral metabolic cues, including ghrelin, leptin and glucose, suggesting that orexin neurons might provide a link between energy homeostasis and vigilance states. Orexin neurons project to numerous brain regions, with especially strong inennevation to the monoaminergic/cholinergic nuclei, suggesting that orexin neurons affect the activity of these nuclei to regulate sleep/wakefulness states. These observations suggest that orexin neurons are involved in sensing the body's external and internal environments, and regulate vigilance states accordingly. In this symposium, we will discuss the input and output systems of orexin neurons and their roles in sleep/wake regulation.

PS-15-2

AFFERENT AND EFFERENT CONTROL OF THE OREXIN SYSTEM

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The orexin/hypocretin neurons play key roles in the maintenance of wakefulness and the regulation of REM sleep. The importance of these cells is clear in mice lacking the orexin neurons that have narcolepsy and fail to rouse in response to hunger. Over the last few years, much has been learned about the factors that drive activity in the orexin neurons and the key projections of the orexin neurons that ultimately affect wakefulness and sleep.

As expected, inputs to the orexin neurons arise from brain regions implicated in the control of sleep/wake behavior, but they also originate from areas that govern emotions, stress, hunger, and circadian rhythms. The orexin neurons receive inputs from state-regulating regions such as the preoptic area, basal forebrain, lateral and posterior hypothalamus, periaqueductal gray matter, raphe nuclei, and lateral parabrachial nucleus. Inputs also arise from limbic regions including the allocortex, lateral septum, bed nucleus, amygdala and CRF neurons. Signals related to circadian rhythms are relayed via the subparaventricular zone and dorsomedial nucleus.

The orexin neurons innervate a wide variety of brain regions from the cortex to the spinal cord, and some of these projections are especially important for normal state control. We produced mice in which a loxP-flanked gene cassette disrupts production of the OX1 and OX2 orexin receptors, but Cre recombinase can globally or focally restore normal orexin receptor signaling. At baseline, mice lacking OX2R show signs of moderate sleepiness, and expression of OX2R only in the tuberomammillary region completely rescues their ability to produce long wake bouts. Restoration of OX1R and OX2R signaling in the basal forebrain also improves the maintenance of wakefulness, demonstrating that signaling through these regions is sufficient to improve sleep/wake behavior.

These anatomic connections show that the orexin neurons are uniquely positioned to integrate a variety of interoceptive and homeostatic signals to increase behavioral arousal under basal condition and in response to a variety of challenges.

PS-15-3

OREXIN NEURONS AS SENSORS OF EXTRACELLULAR NUTRIENTS

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In order to maintain body energy balance through regulation of food intake and energy expenditure, the brain has to measure body energy levels. A key direct strategy for doing this was discovered by Yutaka Oomura and co-workers in the 1970s, who found that there are specialized glucose-sensing neurons in the lateral hypothalamus (LH). Their identity remained unclear until 2003, when Takeshi Sakurai and co-workers showed that glucose-inhibited neurons in the LH contain orexin. Our recent work indicates that inhibition of orexin cells by glucose is mechanistically unusual in that it may not require conventional glucose metabolism. Moreover, our data suggest that glucose inhibition of orexin cells is subject to paradoxical negative modulation by increased background energy levels. We also investigated the effects of other macronutrients on orexin cells, and show that nutritionally-relevant mixtures of dietary amino acids alter the orexin cell activity in the opposite direction to glucose. This suggests that orexin neurons are not simple energy sensors, but may detect the balance between different macronutrient in the diet. We propose a hypothesis for how nutrient-specific modulation of orexin cells may promote consumption of a balanced diet.

PS-15-4

NEUROCHEMISTRY OF HYPERSOMNIA

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Our recent progress in understanding the pathophysiology of hypersomnia is particularly indebted to the 1999 discovery of narcolepsy genes (i.e., hypocretin receptor and peptide genes) in animals and the subsequent discovery (in 2000) of hypocretin ligand deficiency in idiopathic cases of human narcolepsy-cataplexy. This discovery in human narcolepsy lead to (A) the establishment of a new diagnostic test (i.e., low CSF hypocretin levels) and (B) development of hypocretin replacements to be used in the treatment of hypocretin deficient narcolepsy. In contrast, the pathophysiology of hypocretin non-deficient narcolepsy is still debated. Similarly, the pathophysiology of idiopathic hypersomnia, another defined primary hypersomnia, is largely unknown.Anatomical and functional studies demonstrate that the hypocretin systems integrate and coordinate multiple wake-promoting systems (such as monoamine and acetylcholine systems) to keep subjects fully alert. Among theses wake-promoting systems, we are particularly interested in the hypocretin-histamine interactions since hypocretins excite histaminergic neurons in the posterior hypothalamus through hypocretin receptor-2, one of two hypocretin receptors that play critical roles in creating the narcolepsy phenotype.In this talk, the roles of hypocretin-hitsmaine interaction in primary hypersomnia will be discussed. Further knowledge of the neurochemistry of hypersomnia will most likely lead to the development of new treatments and management strategies for patients with hypersomnia of various etiologies.

Educational lectures

EL-1-1

NEUROBEHAVIORAL DYNAMICS OF SLEEP RESTRICTION AND RECOVERY

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This talk will review the effects of sleep loss on human neurobehavioral functions over periods longer than the typical acute sleep deprivation study. Although acute total sleep loss experiments suggest the effects are quickly recovered by intensification of sleep as manifest in EEG slow wave energy, more chronic experiments reveal longer time constants in degradation and recovery of neurobehavioral functions. Studies have found that chronic reduction of sleep can result in waking neurobehavioral deficits that become progressively worse over days, and that the rate of accumulation of waking deficits is a function of the magnitude of the sleep restriction. Thus, chronic sleep restriction induces slow changes (days to weeks) in neural processes mediating alertness, attention and aspects of cognitive functioning. A recent experiment suggests extended recovery sleep duration is critical to liquidation of these slow (cumulative) changes. If this is the case, time off work during and following consecutive days of chronic sleep restriction must receive more scrutiny for the extent to which it provides adequate recovery sleep duration and thereby reverses the (slow) cumulative neurobehavioral effects of sleep restriction. A related issue is the length of the recovery period required between multi-day work periods. Although recovery time is often allowed to be minimized in duration in work regulations, based on the assumption that people will utilize the majority of the off-work time for sleep, it appears this may not be the case. A failure to understand the criticality of chronic sleep restriction and recovery sleep duration in the health and safety of people appears to be the greatest challenge to preventing fatigue-related accidents and adverse outcomes.

EL-2-1

GENETICS OF SLEEP DISORDERS

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Enormous efforts have been undertaken in the last decade to identify genes for complex diseases and traits. Sleep, as a behavior, is from the genetic point of view a highly complex trait and sleep disorders in general are complex diseases. Narcolepsy and Restless Legs Syndrome (RLS) are two emblematic disorders of sleep and recent advances in their molecular genetics opened new avenues. RLS is a common disorder affecting up 10% while narcolepsy is rare and affects less than 0.05% of the general population. RLS is familial in up to 60% and narcolepsy in less than 10% of cases. Although single genes with autosomal dominant inheritance are evidenced by linkage studies in both conditions, no causative gene has yet been identified. The extraordinary success of genome-wide association studies (GWAS) led to recent such attempts in RLS and narcolepsy. Identified variants (except one) revealed small effect sizes and even when several such variants were identified in RLS, the added effect size remains negligible in regards to the overall heritability. Obviously, as in many other complex disorders, GWAS are of limited help in discovering a substantial genetic contribution to complex traits such as sleep disorders. Other strategies such as

large-scale, high-resolution comparative genomic hybridization and next generation sequencing technologies combined with linkage analysis in families might help identifying causative genes.

EL-3-1

THE NEURONAL NETWORK RESPONSIBLE FOR PARADOXICAL (REM) SLEEP AND ITS DYSFUNCTIONS CAUSING NARCOLEPSY AND REM BEHAVIOR DISORDER

P-H LUPPI[1]
[1]*team "Physiopathology of the neuronal network of the sleep-waking cycle" of the CRNL, UMR 5292 CNRS/U1028 INSERM, Lyon, France*

Since the discovery of rapid eye movement (REM) sleep (also known as paradoxical sleep; PS), it is accepted that sleep is an active process. PS is characterized by EEG rhythmic activity resembling that of waking with a disappearance of muscle tone and the occurrence of REMs, in contrast to slow-wave sleep (SWS, also known as non-REM sleep) identified by the presence of delta waves. I will describe an updated integrated model of the mechanisms responsible for the sleepwake cycle. This model introduces the notion that the entrance and exit of PS are induced by different mechanisms. I will hypothesize that the entrance from SWS to PS is due to the intrinsic activation of PS-on GABAergic neurons. These populations of neurons would inhibit during PS all waking systems and a population of PS-off GABAergic neurons. This population of PS-off GABAergic neurons tonically inhibits during waking and SWS the glutamatergic neurons triggering the state of PS localized in the pontine sublaterodorsal tegmental nucleus (SLD). The exit from PS would be induced by the inhibition of the PS-on GABAergic neurons by waking systems such as the pontine and medullary noradrenergic neurons and the hypothalamic hypocretin. Finally, I will propose hypotheses on the mechanisms responsible for two main sleep pathologies, REM sleep behavior disorder and narcolepsy.

EL-4-1

EPIDEMIOLOGY, INSOMNIA, MENTAL DISORDERS

MM OHAYON
Stanford Sleep Epidemiology Research Center, School of Medicine, Stanford University, USA

Abstract not arrived.

EL-5-1

VIOLENT PARASOMNIAS- FORENSIC IMPLICATIONS

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All brain states are now recognized as permeable, dynamic, and interactive. Additionally, the various components of sleep may dissociate or oscillate rapidly which may result in State Dissociation. In such situations transitions from wake to sleep or from NREM to REM may proceed until switching errors arise resulting in states that are not stable and not yet fully declared. As each state is an entity which is physiologically and experientially distinct, an overlapping of states transpire whereby the physiologic and experiential remnant of each state can be dissected, studied, and understood. A salient example of State Dissociation would be the Parasomnias, specifically REM Behavior Disorder whose condition can be understood as an overlap between wake and REM sleep. SLEEP FORENSICS was first formally defined at the 5th Congress of the WFSRSMS (WorldSleep07) in Cairns, Australia. SLEEP FORENSICS is defined as the application of the principles and tools of neuroscience as applied to Somnology and Sleep Medicine that have been widely accepted under international peer-review to the investigation in understanding unusual, irrational, and/or bizarre human behaviors associated with alleged criminal behavior which is to undergo further examination in a conflict resolution legal atmosphere and/or courtroom. This lecture will develop a current and up-to-date neuroscientific approach to understanding violent behaviors arising from sleep while contrasting the often conflicting paradigms of LAW vs. SCIENCE. Upon defining the new and developing field of SLEEP FORENSICS the speakers will proceed to review the broad spectrum of criminal and civil allegations associated with SLEEP FORENSICS based upon their extensive medico-legal experience from their formal international forensics program with both the law enforcement and legal communities involving over 230 case referrals from 2006–2011.

EL-6-1

CIRCADIAN RHYTHM, HUMAN, SLEEP-WAKE

CA CZEISLER
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Abstract not arrived.

EL-7-1

SLEEP APNEA SYNDROMES

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Sleep Apnea is a complex disease, its pathogenesis and management derived from genetic and environmental factors. An apnea occurs through a reduction in ventilatory drive, and recurrent apnea results from longer-term influences such as loop gain. Patients could have a pre-determined susceptibility for breathing instability and the appearance of recurrent apneas. Mathematical models predict an association between recurrent apneas and chemosensitivity, and a post-hypoxic response could promote ventilatory stability or recurrent apnea. The trait of post-hypoxic frequency decline (Han, Subramanian et al. 2001) as well as periodic and unstable breathing is present in the C57BL/6J (B6) mouse during wakefulness (Han, Subramanian et al. 2002) and under anesthesia (Gonsenhauser, Wilson et al. 2004). The finding of periodic breathing in B6xA/J recombinant inbred mice (Han, Subramanian et al. 2002) and chromosomal substitution strains confirm an inherited basis, but also indicate that the expression of post-hypoxic ventilatory decline is not necessary for its expression. To date, we know that that buspirone (Yamauchi et al, 2008), acetazolamide (Yamauchi et al 2007), and inhibition of hydrogen sulfite production (Donovan et al, in press) will reduce or eliminate post-hypoxic apnea, and pharmacologic inhibition of neural nitric oxide synthase will lengthen events (Price, Han et al. 2003). Chromosome 1 from the A/J strain protects the B6 from the expression of recurrent apneas, not only in the setting of reoxygenation but also spontaneous sighs during resting breathing (Yamauchi et al 2008). Such a pre-clinical model is a starting point for understanding mechanisms and treatments that sensitize (or desensitize) the control system in regard to ventilatory stability, and is broadly applicable to breathing instability in several medical and neurological conditions.

EL-8-1

MOLECULAR CHARACTERIZATION OF HUMAN SLEEP VARIANTS

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Sleep disruption and duration has been shown to have significant impact on human health, quality of life, and life expectancy. Among humans, it is clear that the biological need for sleep varies dramatically. Natural short sleepers have a lifelong tendency to sleep only 4–5 hours per night and to awaken refreshed and energetic. Natural long sleepers biologically require 9–10 hours/night to feel well rested. The reason for these differences is not known and no genetic forms of either phenotype have been described. In contrast to sleep (where almost nothing is known), there is a wealth of information on the genetics of clock function across species. Sleep and circadian function are distinct processes that interact in living organisms. Although these two systems can operate independently, recent studies indicate a more intimate relationship. Despite the exciting developments in the last decade on the neuronal pathways involved in wakefulness, sleep induction/maintenance, and molecular characterization of the circadian clock, the mechanism that controls how much sleep we need is entirely unknown. We've undertaken a Human Genetic approach to identify genes/pathways involved in sleep. We've identified families with autosomal dominant transmission of Natural Short Sleep (NSS) and Natural Long Sleep (NLS) phenotypes and identified a mutation causing familial NSS (FNSS). The mutation is in Dec2 a gene encoding a transcription factor. Mice engineered to carry the human FNSS mutation also sleep less. It is interesting that they also have a metabolic syndrome. Identification of mutations that give rise to alterations in sleep requirement represents a unique opportunity for delving into the molecular regulatory mechanisms of sleep homeostasis. Understanding of human sleep homeostasis has the potential to produce an enormous impact on our understanding of many biological pathways including brain functions (vigilance, short-term and long-term memory, executive function, math processing, cognitive speed, and spatial orientation), behavior, health, and longevity.

Educational symposia

ES-1-1

HUMORAL AND NEURAL REGULATION OF SLEEP – LESSON FROM PROSTAGLANDIN D_2-INDUCED SLEEP

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Prostaglandin (PG) D_2 is the most potent endogenous sleep-promoting substance thus far reported. PGD_2 is produced by lipocalin-type PGD synthase localized in the leptomeninges, choroid plexus, and oligodendrocytes in the brain, and is secreted into the cerebrospinal fluid as a sleep hormone. PGD_2- stimulates DP_1 receptors localized in the leptomeninges of the basal forebrain and the hypothalamus, and increases the local concentration of extracellular adenosine. Adenosine acts as a paracrine sleep-promoting molecule to activate adenosine A_{2A} receptor-expressing sleep-promoting neurons in the basal forebrain and/or ventrolateral preoptic area (VLPO) and to inhibit adenosine A_1 receptor-possessing arousal neurons. An intracerebroventricular infusion of PGD_2 or adenosine A_{2A} receptor-agonists induces non-REM sleep and increases the expression of fos protein in VLPO. The activation of VLPO neurons is associated with a decrease in the fos expression in the histaminergic tuberomammillary nucleus (TMN), one of the arousal centers. The neural network between VLPO and TMN is considered to play a key role in the regulation of vigilance states. The i.p. injection of $SeCl_4$, a selective inhibitor of L-PGDS into mice decreased the PGD_2 content in the brain and inhibited sleep in a dose-dependent manner, during the light period when mice normally sleep. The $SeCl_4$-induced insomnia was not observed at all in gene-knockout (KO) mice of L-PGDS or DP_1 receptor. A novel DP_1 antagonist ONO-4127Na reduced sleep of rats by 30% during infusion at 200 pmol/min into the subarachnoid space under the rostral basal forebrain. Caffeine, a non-selective antagonist of adenosine A_1 and A_{2A} receptors, inhibited sleep in wild-type mice in a dose-dependent manner and induced complete insomnia for several hours after an i.p. injection at 15 mg/kg. The caffeine-induced insomnia was also observed in A_1 receptor KO mice but not at all in A_{2A} receptor KO mice. These results indicate that the DP_1 and A_{2A} receptor system is critical for physiological sleep.

ES-1-2

KEY ROLES OF THE HISTAMINERGIC SYSTEM FOR THE SOMNOGENIC EFFECT OF PROSTAGLANDIN D_2 AND ADENOSINE

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This talk presents an overview of the current knowledge about the role of histamine in mediating wakefulness in mammals with a focus on the somnogenic effects of prostaglandin (PG) D_2 and adenosine, and on the arousal effects of PGE_2 and orexin. PGD_2 activates DP_1 receptors (R) to promote sleep by stimulating them to release adenosine. The released adenosine activates adenosine $A_{2A}R$ and subsequently excites the ventrolateral preoptic area (VLPO), one of the sleep centers in the anterior hypothalamus. VLPO neurons then send inhibitory signals to down-regulate the histaminergic tuberomammillary nucleus (TMN), which contributes to arousal. A_1R is expressed in histaminergic neurons of the rat TMN. Adenosine in the TMN inhibits the histaminergic system via A_1R and promotes NREM sleep. Conversely, both endogenous PGE_2 and orexin activate the histaminergic system through EP_4R and OX2R, respectively, to promote wakefulness via histamine H_1R. Furthermore, the arousal effect of ciproxifan, H_3R antagonist, depends on the activation of histaminergic systems. These findings indicate that VLPO and TMN regulate sleep and wakefulness by means of a "flip-flop" mechanism during sleep-wake state transitions.

ES-1-3

DIURNAL VARIATION OF PROSTAGLANDIN METABOITES D AND LIPOCALIN TYPE PROSTAGLANDIN D SYNTHASE IN HEALTHY VOLUNTEERS

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Introduction: There is a bi-directional relationship between sleep and inflammation. Insufficient sleep leads to increased inflammatory mediators, and activation of the host defense system leads to sleepiness and sleep. The prostaglandins (PGs) are mediators of inflammation, and PGD synthase in serum is elevated in association with sleepiness. PGE2 is associated with pain sensitivity and increases with sleep loss. For these reasons, we explored the diurnal and sleep-loss associated changes in the urinary metabolites of PGD, PGE (PGDm and PGEm, respectively) and lipocalin type prostaglandin D synthase (l-PGDs) in healthy volunteers undergoing 63 hrs of sleep deprivation (SD).
Methods: Twenty-three subjects were randomized (1:2) to sleep or SD conditions, respectively. Twenty-three subjects (10f/13m) between 23 and 56 years were included. Following extensive screening (habitual sleep time, healthy profile based on blood chemistry and medical history, ECG, overnight PSG and exercise stress tests), volunteers stayed in the clinical research center for 7 days, and six nights. The first 2 nights were adaptation and baseline (BL), followed by 2 nights of SD or normal control sleep of 9 hrs, followed by recovery sleep of 2 nights. Urinary in- and output was measured for the second BL, last 24 h of SD and the first 24 h recovery. Urine from the 9 h bed period was pooled and analyzed for nighttime samples; urine was pooled for 15 h wake periods and made up the daytime samples. Data were analyzed using SPSS mixed model analysis, with condition (deprivation/control sleep); day of protocol, and diurnal (day/night), as fixed factors (repeated).
Results: PGDm and l-PGDs showed significant diurnal rhythms in the absence of sleep deprivation effects ($p > 0.04$ for the metabolite and $p < 0.001$ for the synthase, respectively). PGEm showed a trend ($p < 0.06$) towards higher levels in the SD condition at night during SD.
Conclusion: The PGD system shows diurnal variation in the absence of SD changes. Daytime levels were higher than nighttime, despite continuous wakefulness.

ES-1-4

HUMORAL REGULATION OF SLEEP: PAST, PRESENT AND FUTURE

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Studies conducted by Ishimori at the beginning of the 20th century demonstrated that factors accumulated in brain during wakefulness that induced subsequent sleep. These initial studies were forgotten as sleep research during the mid-20th century was dominated by neuroanatomists. In the 1960 s, investigations in the laboratories of Kornmuller, Monnier, Pappenheimer and Uchizono focused on humoral sleep regulatory mechanisms. Pappenheimer and Krueger demonstrated that during prolonged wakefulness factor S, subsequently determined to be muramyl peptide, increased in brain and could induce deep sleep. Subsequent studies of sleep factors demonstrated that interleukin-1, tumor necrosis factor, and prostaglandin D2 were immunomodulators that also were powerful inducers sleep. During the period from 1983 to present, much has been learned of mechanisms by which immunomodulators contribute to the regulation / modulation of physiological sleep and in the alterations in sleep during immune challenge. Epidemiological studies demonstrate that chronic insufficient sleep is a risk factor for hypertension, cardiovascular disease, metabolic syndrome, obesity, insulin resistance and diabetes. Each of these pathologies is characterized by inflammation, suggesting that immunomodulators may be a mechanistic link between chronic insufficient sleep and multiple diseases that plague society today.

ES-2-1

OVERVIEW OF STUDIES UTILIZING ANALYSIS OF THE TRANSCRIPTOME

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Analysis of changes in the transcriptome with sleep/wake and sleep deprivation has proven to be a powerful strategy. Knowledge of genes changing expression with behavioral state has led to hypotheses about the functions of sleep-synaptic homeostasis, macromolecular synthesis in brain-as well as identifying that sleep deprivation leads to the unfolded protein response in brain. Recently our group has extended these studies to ask the question whether sleep/wake and sleep deprivation affects gene expression in peripheral organs controlling for diurnal time (heart and lung), i.e., is sleep only for the brain? There were genes that increased expression in specific molecular pathways in both organs

with sleep and different genes in both organs that increased expression with sleep deprivation. Thus, at a molecular level, sleep is not only for the brain. Genes changing expression in brain with behavioral state could do so as a consequence of the state and/or be involved in its control. High throughput video-based phenotyping strategies to assess sleep, combined with new mouse resources, can quickly address this question. Currently transcriptome analysis is moving in two new directions. First, RNA seq is being used to assess changes in all genes in the genome, including small RNAs. About 25% of all genes are not represented in current microarray chips. Second, analysis is moving to study of identified neuronal populations as well as glia based on novel transgenic animals and utilizing techniques such as manual plucking. Application of these new approaches to the study of changes in the transcriptome with sleep/wake and sleep deprivation will be described.

ES-2-2

MOLECULAR AND NEUROANATOMICAL SIGNATURES OF SLEEP DEPRIVATION

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Sleep deprivation (SD) leads to a suite of cognitive and behavioral impairments, although the molecular consequences of SD in the brain are poorly understood. Using systematic immediate-early gene (IEG) mapping to detect neuronal activation, the consequences of SD were mapped in forebrain regions. SD both induced and suppressed IEG expression in subregions of neocortex, striatum, and other brain regions. Laser microdissection and cDNA microarrays were used to identify the molecular consequences of SD in 7 brain regions. In situ hybridization (ISH) for 222 genes selected from the microarray data and other sources confirmed that robust molecular changes were largely restricted to the forebrain. In the neocortex, SD activated gene expression in an areal, layer-, and cell type-specific manner and preferentially activated excitatory neurons. The neocortex and suprachiasmatic nuclei (SCN) exhibited differential regulation of the same genes such that SD and Waking-related effects were evident in the neocortex whereas time-of-day effects were evident only in the SCN. Analysis of the ISH data for 222 genes (publicly accessible at http://sleep.alleninstitute.org) provided a molecular and anatomic signature of the effects of SD. In a separate set of studies, we identified a population of cortical GABAergic neurons that express neuronal nitric oxide synthase (nNOS) and also express FOS specifically during sleep in three different species. FOS expression in cortical nNOS neurons varies across the diurnal cycle in conjunction with the natural occurrence of sleep; SD experiments further demonstrate that the extent of activation of these cells is proportional to homeostatic sleep drive. Cortical nNOS neurons receive subcortical inputs from serotonergic and cholinergic neurons and have intracortical efferent projections. We propose that cortical nNOS neurons are critical integrators that link state-dependent afferent inputs to cortical slow wave activity and the homeostatic response to SD. [Supported by NIH R01 HL059658].

ES-2-3

INTEGRATIVE ANALYSIS OF GENOME WIDE DATA SETS FOR SLEEP AND CIRCADIAN RHYTHMS

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The analysis of high throughput data sets requires analytical techniques that can highlight important results in a specific biological context. Understanding of the relevant physiology, and a proper selection of relevant features and data, can greatly influence the utility of the results. Our recent work on identifying novel core clock genes through the integrative analysis of diverse genome-wide data sets provides an illustrative example of one such computational approach. Using naive Bayesian integration we enumerated key features that characterize core circadian genes. For each feature we then developed a simple, quantifiable metric that encapsulates it. We combined our own data with previously published data sets to determine how those metrics were distributed among known clock genes and within the genome at large. These distributions were used to quantify the total evidentiary support that a given gene was a core clock component. The output of this analysis is a ranking of genes by the probability that they play a role in the clock. This list, was, as expected, greatly enriched for known core clock genes. However several novel candidates were identified. In order to demonstrate the utility of this approach we then experimentally characterized one novel candidate. Gm129, which we have dubbed Chrono, demonstrates many features of a core clock gene. Over-expression studies demonstrate that it functions as a Cry1/Cry2 independent repressor of Clock/Bmal1 mediated transcription. Additional data from a mammalian 2 hybrid screen shows direct physical interactions between Gm129 and the clock genes Bmal1 and Per2. Knockdown experiments in the NIH3T3 cellular model system demonstrate a short period phenotype.
Additional examples from the analysis of microarray results relating to sleep deprivation will be used to illustrate the use of unsupervised machine learning algorithms and, in particular, the value of looking beyond standard metrics of differential gene expression.

ES-2-4

USING MICROARRAYS TO IDENTIFY NOVEL BIOMARKERS

ES ARNARDOTTIR[1], EV NIKONOVA[4], KR SHOCKLEY[5], AA PODTELEZHNIKOV[4], KQ TANIS[4], DJ STONE[4], G MAISLIN[3], T GISLASON[1,2], J RENGER[4], CJ WINROW[4], AI PACK[2,3]
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Introduction: The aim of this study was to find changes in gene expression in human blood in response to sleep deprivation and recovery sleep.
Methods: Fourteen healthy subjects that were relatively resistant to sleep deprivation (low responders) and markedly impaired (high responders), based on performance in a psychomotor vigilance task (PVT), were chosen for the study. Blood mRNA expression was measured using microarrays in a normal sleep-wake cycle, 24 hours of sleep

deprivation and 8 hours of recovery sleep. Significance of differences in gene expression was assessed by multivariate ANOVA model. Selected candidate genes were confirmed by qRT-PCR. Biological pathway enrichment analyses were performed using Target and Gene Identification system (TGI) with correction for multiple comparisons.
Results: 7976 gene transcripts had a circadian rhythm in normal sleep-wake cycle (false discovery rate, FDR < 5%). A much higher number of biological pathways peaked during the day than the night. Only 2 genes changed expression significantly during sleep deprivation (FDR < 5%), both significantly involved in lipid metabolism. 28 known genes were suggestive at a less stringent threshold ($p < 0.001$). Again, these genes were involved significantly in lipid metabolism. 31 known genes could separate high and low responders in sleep deprivation ($p < 0.001$). Further differences were observed in recovery sleep with 131 genes found to differ significantly between normal sleep and recovery sleep in high responders and two genes in low responders.
Discussion: This is the first study to use peripheral tissue to identify different human behavioural states. Despite profound circadian signature observed in normal sleep-wake, a small number of genes change expression in response to sleep deprivation and recovery sleep in blood. Importantly, individuals resistant to sleep deprivation have some differences in molecular signatures compared to those markedly impaired. These findings may help further blood biomarker development to successfully monitor healthy or diseased sleep homeostasis.

ES-3-1

ON THE NEURONAL REGULATION OF SLEEP-WAKEFULNESS-NEUROPHYSIOLOGICAL APPROACHES-

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Sleep and wakefulness are controlled by a sophisticated orchestration of a variety of neural populations. Based upon the clinical studies and classical brain lesion or stimulation studies in animals, the hypothalamus has been considered to contain sleep and waking centers. Slow wave sleep is prompted in the proptic area, especially in the ventrolateral preoptic area (VLPO). Neurons in and around the VLPO become active during slow wave sleep and with an inhibitory neurotransmitter, GABA, affect inhibitory influences on the waking active neurons in the waking centers. For the regulation of wakefulness, the neurons in the hypothalamus and brainstem play a crucial role, including the orexinergic neurons in the perifornical hypothalamus, histaminergic neurons in the posterior hypothalamus (tuberomammilary nucleus), noradrenergic neuron in the locus coeruleus and serotonetgic neurons in the dorsal raphe nucleus. These neurons are most active during waking, decrees firing during slow wave sleep and completely cease from firing during REM sleep. In addition, some of the cholinergic neurons in the laterodorsal tegmental nucleus (LDT) and pedunculopontine tegmental nucleus (PPT) become active during waking as well as during REM sleep. They would also some roles in the regulation of waking. A pile of evidence, showing that the cholinergic agonist (carbachol) injected in the mesopontine tegmental area induces REM sleep, have suggested that the cholinergic neurons in the LDT/PPT have a role in the regulation of REM sleep. Some of the cholinergic neurons in the LDT/PPT are most active during REM sleep, least active or almost silent during waking. In addition to the cholinergic neuron, gulutamatergic neurons ventral to the LDT are also important for REM sleep. They receive cholinergic excitation to keep higher firing during REM sleep. These cholinergic and glutamatergic REM sleep active neurons receive GABAergic inhibition during waking, and release from the inhibition of these GABAergic neurons would be a powerful trigger for initiation of REM sleep.

ES-3-2

PHYSIOLOGICALLY BASED QUANTITATIVE MODELING OF SLEEP DYNAMICS

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Arousal state is largely controlled by the ascending arousal system of the brainstem, which projects to the corticothalamic system that produces the commonly observed EEG signatures of arousal state. Quantitative modeling of sleep-wake dynamics is described, using a physiologically based model of the brainstem and hypothalamus with realistic parameters that describe the properties and couplings of neural populations, accumulation and clearance of homeostatic sleep drive, circadian and pharmacological influences, and stimuli. After calibration against a small set of experiments, predictions and analyses of a much wider variety of phenomena are made. Verifications against numerous experimental data are described, including normal arousal dynamics, sleep deprivation and recovery, shiftwork, pharmacological influences, arousal threshold, sleep latency, and subjective fatigue, some of which enable quantification of what have previously been subjective measures. Links to arousal-related EEG changes are then made by coupling the output of the ascending arousal system to a physiologically based model of the cortex and thalamus. Successful prediction of sleep patterns in a variety of terrestrial and aquatic mammals using the same model is also briefly discussed.

ES-3-3

INSIGHTS FROM MATHEMATICAL MODELING OF SLEEP-WAKE BEHAVIOR

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Mathematical modeling has a rich history of helping to shape the way we think about sleep. In recent years, advances in experimental investigations have enabled mathematical models of sleep-wake behavior to become increasingly grounded in the physiology of the system. This strong physiological basis links models to existing data and has the potential to enhance the impact and utility of these models by allowing them to generate precise, experimentally testable predictions. Furthermore, mathematical models can provide detailed, dynamic descriptions of system physiology over time to complement experimental data in which the spatial and temporal scope is often necessarily limited by experimental methodology. In this talk, I will review some of the modeling approaches we have developed to investigate sleep-wake behavior. Using a modeling formalism based on neurotransmitter-mediated interactions among neuronal populations involved in sleep-wake regulation, we have examined mechanisms of state transitions, simulated the effects of localized microinjection of neurotransmitters on sleep-wake behavior, probed interactions between circadian and sleep-wake regulatory systems, and explored the role of orexin/hypocretin in the production and maintenance of sleep. I will summarize these results while focusing on both the ways in which experimental data has been incorporated into the formulation of these mathematical models and the symbiotic relationship that exists between model predictions and future experiments.

ES-3-4

FROM FLIP-FLOP TO CYCLES: NEURAL REGULATION MECHANISM OF SLEEP-WAKE STATES

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So far, many hypotheses have been proposed on regulatory mechanism of sleep-wake states. They are roughly classified into the following categories, although their objectives are more or less different from each other.

(1) Prey-predator dynamics: The reciprocal interaction between cholinergic and aminergic systems is considered to regulate nonREM-REM cycle (McCarley and Massaquoi, 1986).
(2) Multiple flip-flops: The regulatory mechanism of sleep-wake states is interpreted as a multiple flip-flops involving the nuclei in the preoptic hypothalamic area, the aminergic neurons, and the glutamatergic and GABAergic neurons in the brainstems (Saper et al., 2001).
(3) Neural diagram: The glutamatergic and GABAergic systems in the brainstem interacting with each other or their cascade are considered to regulate REM generation (Sakai et al., 2001; Luppi et al., 2006). Because (2) and (3) are rather conceptual, their realization and resulting dynamics are not given. Actually, there have been many mathematical models produced based on these idea. Mathematical modeling of regulatory mechanism of sleep-wake states tends to be more focused on circuit implementation to reproduce physiological phenomena rather than the time scale of state alternation. However, for biological reality what kind of actual process determines the time scale is essential. A flip-flop or bistable system is realized by self-excited systems mutually coupled by inhibitory connections, where excitation may come from external systems. Formation of flip-flop is not a sufficient condition for alternation of multiple states, but an unstabilizing mechanism of each state is essential to determine the time scale of state alternation, i.e., minutes in rodents and hours in human. Actual determinant factors for such a slow dynamics are not identified, which have not been seriously concerned so far. This situation is the same as in (1) and (3). Such slow dynamics cannot be attributed only to neural synaptic interactions. Possible biological processes are discussed from the modeling viewpoint.

ES-4-1

AROUSAL-RELATED LAPSES OF RESPONSIVENESS: CHARACTERISTICS, DETECTION, AND UNDERLYING MECHANISMS

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Lapses of responsiveness ('lapses') are complete transient disruptions in sensory-motor performance. They are a surprisingly frequent phenomenon in healthy subjects – even when not sleep-deprived – and particularly so when engaged in extended monotonous tasks. They are of particular importance in the transport, military, and medical sectors in which there is a need to maintain sustained attention for extended periods and in which lapses can lead to multiple-fatality accidents.
Lapses can be broadly divided into four main types:

- Sleep events (>15 s) – Extended loss of consciousness.
- Behavioural microsleeps (~0.5–15 s) – Brief loss of consciousness, with clear behavioural indications of drowsiness.
- Lapses of sustained attention – Not directly related to level of arousal and can occur when alert, fatigued, or drowsy.
- Lapses of task-orientated attention – Diverted attention.

Our primary focus is on microsleeps, with contributions covering aspects of behavioural detection and characterization, EEG-based characterization and detection, and determination of the underlying mechanisms in the brain via simultaneous recordings of whole-brain BOLD fMRI, 64-ch. EEG, eye video, and EOG, while performing a continuous 2-D visuomotor tracking task. In addition to improving our understanding of what happens in the brain during microsleeps, it is hoped that improved knowledge of the spatiotemporal dynamics of microsleeps will allow us to substantially improve the early detection, and even prediction, of microsleeps and to use this as the basis for a non-invasive early-warning systems with the potential to save many lives.
My talk will (i) provide an introduction to lapses, (ii) overview their importance in the real world, (iii) overview what several research studies have revealed about microsleeps, and (iv) summarize some of the remaining challenges in this fascinating and important area.

ES-4-2

CAPACITY LIMITS OF INFORMATION PROCESSING WHEN SLEEP DEPRIVED

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Our capacity to process information declines when sleep deprived. Perceptual processing capacity refers to our residual capacity to process peripheral distractors after processing a central task. Visual short term memory capacity refers to the number of visual items we can perceive and remember over a few seconds.
Perceptual processing capacity limitations may not be evident at lower perceptual load but can be uncovered at higher load using functional magnetic resonance adaptation. Indeed our ability to allocate attention to a specific visual category may be compromised during sleep deprivation but the extent to which this occurs relates to the temporal predictability of target appearance. Imaging visual cortex provides a means of uncovering loss of attentional selectivity, which in turn is a contributor to impaired cognition in the setting of sleep deprivation.
Visual short term memory is indeed affected by sleep deprivation but for reasons not obvious from observing behavior. We found deficits in engagement of fronto-parietal activation usually engaged in task performance that suggests a memoranda independent effect on neural activation that can be remedied in vulnerable persons by pharmacologic means.

ES-4-3

A MOBILE EEG DEVICE FOR ON-LINE ASSESSMENT OF SLEEP QUALITY

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The polysomnography (PSG) which senses multiple physiological signals including EEG, ECG, EMG and EOG signals is a traditional and common device used to diagnose the participants sleep problems in clinic. People who have the sleep problem will pre-register to do the

sleep quality experiment in clinical sleep laboratory. However, long waiting process and sleep environment adaption are the major challenges for performing the sleep experiment. Even the participant can proceed the sleep experiment in clinic, he/she should wear the traditional PSG system with many cables of the multiple physiological signals and paste of conductive gels on each sensor. These preparation procedures are quite complicated and time consuming. Also, the participant will feel uncomfortable and not easy to sleep in clinic which will cause low efficiency of data acquisition and low accuracy of sleep stage classification. In this study, a mobile and wireless EEG system which consists of innovative foam-based dry EEG sensors, miniaturized circuits and the novel form factor had been developed for EEG signals acquisition in an arbitrary environment. We further developed an intelligent sleep-stage classification system based on the EEG signals acquired only through a few forehead EEG sensors. Experimental results show that the classification accuracy of the proposed system is close to the performance of the clinical PSG system. The best advantage of the developed sleep-stage classification system using the mobile and wireless EEG is that people can easily don and doff the EEG device with great comfort to do the self-evaluation of sleep quality at home.

ES-5-1

NARCOLEPSY AND IDIOPATHIC HYPERSOMNIA

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Narcolepsy and Idiopathic Hypersomnia are main sleep disorders categorized in Hypersomnia of Central Origin, in which the primary cause of daytime sleepiness is not disturbed nocturnal sleep or misaligned circadian rhythms. The fundamental symptom is excessive daytime sleepiness (EDS) defined as the inability to stay awake and alert during daytime, resulting in unintended drowsiness or lapses into sleep. Typical narcolepsy (with cataplexy) and typical idiopathic hypersomnia (with long sleep time) have their characteristic symptoms not only in EDS (short refreshing naps and long nap with awakening difficulty) but in the other features such as cataplexy in narcolepsy and sleep drunkenness in idiopathic hypersomnia.

The pathologic mechanism underlying peculiar narcolepsy symptoms (summarized as sleep wake phase fragmentations and dissociated REM sleep manifestations) are now explained well as the instability of sleep state switching model based on the hypocretin/orexin deficiency in narcolepsy, which is used as a diagnostic biomarker of narcolepsy with cataplexy. Various clinical characteristics of idiopathic hyperosmnia are described, such as autonomic dysfunction, frequent fatigue and preference of evening chronotype. But none of them are pathognomonic nor explain the disease pathophysiology. Idiopathic hypersomnia remains to be a diagnosis of exclusion.

There exist similar but not typical hypersomnia patients and ICSD2 employ operational diagnostic procedures on these cases, defining narcolepsy without cataplexy and idiopathic hypersomnia without long sleep time according to the number of sleep onset REM periods during MSLT. Whether these criteria form independent clinical entities or not awaits further validation study.

Treatments include pharmacological and non pharmacological intervention, such as an instruction for daily life style. Stimulant is effective in most narcolepsy patients but not predictable in idiopathic hypersomnia patients. Clinical course (onset and prognosis) is studied in narcolepsy but not well known in idiopathic hypersomnia.

ES-5-2

SYMPTOMATIC NARCOLEPSY AND HYPERSOMNIA

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Narcolepsy symptoms can also occur during the course of other neurological conditions (i.e., symptomatic narcolepsy). In our recent meta analysis, 116 symptomatic narcolepsy cases reported were analyzed. As several authors have previously reported, inherited disorders (n = 38), tumors (n = 33), and head trauma (n = 19) are the three most frequent causes of symptomatic narcolepsy. Although it is difficult to rule out the comorbidity of idiopathic narcolepsy in some cases, literature review reveals numerous unquestionable cases of symptomatic narcolepsy. These include cases with HLA negative and/or late onset and cases where the occurrence of narcoleptic symptoms runs parallel with the rise and fall of the causative disease. Notably, the review of these cases (particularly those with brain tumors) clearly illustrates that the hypothalamus is most often involved.The same review also lists about 70 symptomatic excessive daytime sleepiness (EDS) cases associated with these neurological conditions. Prevalence of symptomatic EDS is likely much higher. For example, several million USA subjects suffered chronic brain injury, 75% experienced sleep problems, and about 50% among them reported sleepiness. In the current talk, involvements of the hypocretin system in symptomatic narcolepsy and EDS will be discussed. We will also report unique EDS cases occurring in the course of MS patients with symmetrical hypothalamic inflammatory lesions, which together with hypocretin ligand deficiency, contrasts with the characteristics of classic MS cases, but share the clinical characteristics of neuromyelitis optica.

ES-5-3

KLEINE-LEVIN SYNDROME

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Kleine Levin syndrome (KLS) is a rare encephalitis (1 per million) characterized by relapsing-remitting episodes of hypersomnia plus cognitive and behavioral disturbances. Patients are mostly male (68%) and adolescents (81%), with mean onset at 15 years. The first episode is triggered by an infection in 72% of patients. Patients experience an average of 7 to 19 episodes of 10 to 13 days each, relapsing every 0.5 to 12 months. Episodes recur more quickly in patients with childhood onset. The median disease course is 8–14 years, with longer course in men, in patients with hypersexuality, and when onset is after age 20. During episodes, all patients have hypersomnia and heavy fatigue (with sleep lasting 15 to 21 h per day), cognitive impairment (apathy, confusion, slowness, amnesia) and a specific feeling of derealization (dreamy state, altered perception). Less frequently, they experience megaphagia (66%), hypersexuality (53%), depressed mood (53%), hallucinations and photo/phonophobia. Patients have normal sleep, vigilance, mood, and eating attitude between episodes, but may have increased body mass index and mild attention problems. Structural brain imaging, CSF and serological inflammatory markers are normal. EEG slowing is notable in 70% of cases during episodes. Sleep structure varies from hypersomnia with initial decrease in slow wave sleep then in REM sleep, to hypo-arousal with low sleep efficiency. The brain scintigraphy may show hypoperfusion of the frontal, temporal internal and angular gyrus

areas during and between episodes. Factors of vulnerability include birth and developmental problems, Jewish heritage and genetics (5% multiplex families). The association of KLS with HLA DRB1*201, found in a small series, is not replicated in a larger independent sample. There is no increased family history for neuropsychiatric disorders. Some stimulants (amantadine, but rarely modafinil and amphetamines) and mood stabilizers (lithium, valproate) have a moderate efficacy.

ES-5-4

HYPERSOMNIA ASSOCIATED WITH MOOD DISORDERS

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Insomnia is recognized as an essential aspect of mood disorders. Insomnia is included in diagnostic criteria for major depressive episode in DSM-IV-TR. Many reports have suggested the potential causal role of insomnia in the development of depression in patients who have no previous history of depression and in predicting relapse in patients with depression in remission. Decreased need for sleep (e.g., feels rested after only 3 hours of sleep) is one of the criteria for manic episode in bipolar disorders. On the other hand, epidemiologic data suggest hypersomnia is present in 10–14% of patients with various mood disorders. Some research reported that hypersomnia is more indicative of bipolar than unipolar depression. Particularly, hypersomnia is one of the important criteria for seasonal affective disorder. In this lecture, we focus primary on the observable sleep-wake disturbance in the manic and depressed phases in patients with bipolar disorder and secondary on the fundamental etiological agent in mania. From the observation, total sleep time and early morning awaking are thought to be important predictors of future manic episodes.

Industrial symposia

IS-1-1

INTERACTION OF MELATONIN AND LIGHT ON WAKE & SLEEP EEG AND THERMOREGULATION

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Pineal melatonin is primarily a neuroendocrine transducer of external time (i.e. light dark cycle) promoting an increased propensity for "dark appropriate" behavior. The most unequivocal characteristic of endogenous melatonin is its utility to be used alone or in combination with core body temperature as a phase marker of the endogenous circadian pacemaker located in the suprachiasmatic nuclei. However, there are three major reasons, which imply that melatonin could also play an important role in the regulation human sleep-wake behavior:

1) The endogenous melatonin rhythm exhibits a close temporal association with the endogenous circadian component of the sleep propensity rhythm and thermoregulation.
2) There is evidence that exogenous melatonin is able to induce sleep when the homeostatic drive to sleep is insufficient, to inhibit the drive for wakefulness emanating from the circadian pacemaker and to induce phase shifts in the circadian clock such that the circadian phase of increased sleep propensity occurs at a new desired time.
3) Light's acute alerting response depends on its capacity to suppress endogenous melatonin levels during the biological night.

Thus, melatonin's soporific and chronobiotic properties make it an optimal candidate for treating sleep, in addition to circadian rhythm disorders.

IS-1-2

EFFECTS OF RAMELTEON ON TEMPERATURE AND SLEEP PHYSIOLOGY DURING CIRCADIAN MISALIGNMENT

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Abstract not arrived.

IS-1-3

MELATONIN AND MELATONIN RECEPTOR AGONIST IN THE TREATMENT OF CIRCADIAN RHYTHM SLEEP DISORDERS

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Circadian rhythm sleep disorders (CRSD) are conditions in which sleep timing fails to be synchronized with the internal or external environment. While CRSD associated with shift work or jet lag is a consequence of socially evoked acute sleep misalignment relative to the circadian pacemaker, chronic CRSDs including delayed or advanced sleep phase type (ASPT or DSPT), and non-entrained type (NET) are featured by chronic sleep misalignment caused by an improper entrainment of the circadian pacemaker. In the chronic CRSD, entraining the patient's circadian pacemaker properly relative to the external environment is the goal of the treatment, i.e., a timed bright light exposure, or a timed administration of melatonin or its receptor agonists (MRA). Melatonin's efficacy on CSRD is based on its phase-resetting property as a function of a phase response curve (PRC). In healthy subjects a melatonin administration in the early evening induces a phase advance and that in the early morning produces a phase delay. Since the initial demonstrations that a 5-mg or 10-mg dose of melatonin reset circadian rhythms in patients having DSPT or NET, many case reports as well as a few placebo-controlled trials have confirmed its efficacy administered in the early evening. Recently, lower doses (0.5 mg) of melatonin administered daily in the early evening was reported to be equally or even more effective in entraining the blind patients with NET. After the recent introduction of ramelteon, a MRA, in the medical practice of insomnia, a significant phase-shifting effect in forced bedtime-advance experiments has been reported when a smaller dose (a half or quarter tablet) was administered. The greater efficacy of melatonin and MRA in relatively smaller doses in the treatment of CRSD may be interpreted as providing a more discreet temporal signal to the circadian pacemaker than higher doses. In addition to the systematic review mainly on DSPT and NET, I propose the use of MRA in the treatment of other types of CRSD.

IS-1-4

RAMELTEON'S EFFECTS ON INSOMNIA

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Hypnotic effects of melatonin and melatoninergic drugs are mediated via MT1 and MT2 receptors. They differ fundamentally from GABAergic hypnotics. Melatoninergic agonists enhance sleep initiation and reset the circadian clock to phases allowing persistent sleep. Ramelteon is rapidly taken up, reaching Tmax between 0.75 and 0.94 h. Its half-life in the circulation amounts to about 1 to 2 h which is much longer than that of melatonin (20–30 min). The metabolite M-II has a half-life 2 to 5 h longer can reach concentrations that are 20- to 100-fold higher than ramelteon.

Ramelteons effects on sleep in insomnia patients has been shown in subjective and objective sleep parameters (polysomnography) in short and long term studies. At doses of 4 or 8 mg it reduces sleep onset latency, improves total sleep time and sleep efficiency/sleep quality. This has been demonstrated in several double-blind, placebo controlled studies on a total of more than a thousand adult or elderly subjects with primary chronic insomnia. All the effects were statistically significant, but the improvements of sleep maintenance remained moderate. No further improvements are obtained with 16 and 32 mg. However, due to the high affinity for both receptors, higher long life, and the long term effect of the M-II metabolite, the effect on sleep maintenance is better than that of other melatonergic drugs.

Ramelteon does not cause next-day hangover, sedation, withdrawal effects, insomnia rebound, tolerance or dependence, and cognitive impairment. It does not induce behavioural changes, as sometimes observed with non-benzodiazepine receptor antagonists. Taken during the daytime it causes drowsiness and therefore should be taken at the right circadian time at evening/night. In COPD patients with insomnia it does not affect respiratory parameters and improves sleep efficiency and number of nocturnal awakenings.

Despite otherwise good tolerability, its use in children, adolescents, and during pregnancy has not been studied enough, and should be avoided. It should not be applied in patients with immunological diseases. Inhibitors of CYP1A2 may raise ramelteon levels.

IS-2-1

AN INTERNATIONAL SURVEY ON QUALITY-OF-LIFE AND UTILITY SCORES IN CHRONIC INSOMNIACS COMPARED TO GOOD SLEEPERS OF JAPAN, FRANCE AND UNITED STATES OF AMERICA

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Context: Chronic insomnia has a recognized impact on health-related quality-of-life (HRQoL) but data on utility scores across countries are lacking.

Objective: To assess HRQoL and utility scores in people with chronic insomnia compared to good sleepers in three countries (USA, France, and Japan).

Design: Cross-sectional survey (SLEEPI-i) of 4067 persons in the US (n = 1298; 478 good sleepers and 820 patients with insomnias), France (n = 1858; 998 good sleepers and 860 patients with insomnias) and Japan (n = 911; 506 good sleepers and 405 patients with insomnias). Enrollment and data collection using consumer panels were web-based in the US and France, and via a postal survey in Japan. People with chronic insomnia (>6 months) were selected based on Insomnia Severity Index scores (ISI).

Method: Severity of insomnia was assessed using the ISI score and HRQoL was assessed using the self-administered Short-Form SF-36 Health Survey. Utility scores were derived using the algorithm developed by Brazier et al. Multivariate analyses were used to adjust for potential confounding factors.

Results: In all countries, people with chronic insomnia (40% treated) reported lower SF-36 scores in each of eight domains compared with good sleepers ($P < .0001$). Chronic insomnia was associated with significantly lower utility scores compared with good sleepers (mean scores 0.63 versus 0.72 in the US, 0.57 versus 0.67 in France and 0.67 versus 0.77 in Japan, $P < .0001$).

Conclusion: This survey suggests that chronic insomnia is associated with significant impairment of HRQoL and decreased utilities which were similar across the different geographical regions studied.

IS-2-2

GUIDELINE FOR THE EVALUATION AND MANAGEMENT OF CHRONIC INSOMNIA: USA PERSPECTIVE

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Insomnia is a highly prevalent health problem, with nearly 50% of the US adult population reporting symptoms of insomnia and 10–15% having chronic insomnia. Insomnia is often co-morbid with a myriad of medical and psychiatric disorders. Insomnia is also associated with decreased productivity and increased risk of accidents. A recent study on insomnia and work performance of US workers concluded that insomnia is associated with substantial workplace costs, equivalent to annualized population-level estimates of 252.7 days and $63.2 billion. The personal, clinical and socioeconomic implications of untreated insomnia are substantial.

There is undoubtedly a need for practical clinical guidelines to assist health care professionals, particularly in primary care to diagnose and treat patients with insomnia. In 2008, an evidence and consensus based clinical guideline for the evaluation and management of chronic insomnia in adults was published in the US. An innovative aspect of this guideline is the multiple tiered approach to both the evaluation and management that considers the chronic nature of insomnia, the fact that biological and behavioral/environmental factors are involved, and that patients may have several concurrent insomnia diagnoses.

How these approaches can be tailored for special populations such as the elderly and those with co-morbid disorders is an important area for development. The recent advances in the understanding of the neurobiology and behavioral mechanisms underlying insomnia disorders can identify specific insomnia phenotypes, which in turn will lead to more precise diagnosis and personalized approaches for the management of insomnia to improve global health.

Kessler RC et al. Insomnia and the performance of US workers: results from the America Insomnia Survey. SLEEP 2011;34(9):1161–1171

Schutte-Rodin S et al. Clinical guideline for the evaluation and management of chronic insomnia in adults. J Clin Sleep Med 2008;4(5):487–504

Bloom HG, et al. Evidence based assessment and management of sleep disorders in older persons. JAGS 2009 May;57(5):761–89

IS-2-3

IMPORTANCE OF SLEEP TO SUPPRESS CARDIOVASCULAR EVENTS AFTER THE GREAT EAST JAPAN EARTHQUAKE

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The magnitude 9.0 Great East Japan Earthquake that hit Tohoku in the northeast region of the main island, Honshu, on March 11, 2011, was followed by a devastating tsunami that has taken lives of 20,000 or more people. After the earthquake, cardiovascular diseases (CVD) were observed about twice much, particularly during sleep period. The 2 major mechanisms of the earthquake-induced CVD are hypertension and thrombotic tendency caused by stress, poor sleep quality, and high-salt intake. Poor sleep and disrupted circadian rhythm increase salt sensitivity through sympathetic activation and increased aldosterone synthesis. High salt intake as well as increased salt sensitivity causes new-onset of hypertension after the earthquake.

To better assess and reduce risks for disaster-associated CVD, we developed the web-based Disaster Cardiovascular Prevention (DCAP) network on the basis of previous evidences of The Great Hanshin Awaji Earthquake occurred 16 years ago (Kario, et al. J Am Coll Cardiol 1997;29:926–33. Hypertens Res 2003;26:355–67) and have begun to implement it in the survivors of the Great East Japan Earthquake (Kario, Nishizawa, et al. Lancet 2011, Sept 1). Rapid assessment by the DCAP network demonstrated that insomnia and unrecognized hypertension were the most frequent diseases among the suffered people.

Recent studies demonstrated that insomnia (both reduced sleep duration and poor sleep quality) is a new risk factor of hypertension and CVD. Poor sleep quality is particularly important leading cause of nocturnal hypertension with disrupted circadian rhythm of blood pressure (BP) (non-dipper and riser patterns). Treatment of insomnia reduces high BP and restores disrupted circadian rhythm of BP particularly in patients with uncontrolled morning hypertension.

To control hypertension is essentially important for effective prevention of CVD in forthcoming winter season. The "Good sleep", defined by adequate sleep period and improved sleep quality, and salt restriction are especially important for synergistic protection against CVD in stressful conditions.

IS-2-4

MAKING JAPANESE CONSENSUS REPORT ON THE MANAGEMENT OF INSOMNIA IN GENERAL PRACTICE

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It has been widely documented that most patients with insomnia first consult a general practitioner. Thus, various kinds of hypnotics are prescribed mainly by general practitioners or non-sleep-medicine expert physicians. A study using Japanese insurance data revealed that about 70% of hypnotic prescriptions were made by non-specialists. However, most general physicians seem to be unaware of both the potential morbidity associated with insomnia and the importance of sleep health. In addition, most people having sleep problems do not tell their primary physicians about the problems. Thus, we carried out a project to establish a comprehensive consensus report on the management of insomnia aiming at standardization of optimal treatments in general practice. In 2009, board members (BMs), consisting of 3 sleep medicine experts and 3 other non-sleep medicine expert physicians, conducted a survey to explore the information that clinicians actually need in the clinical practice of insomnia. Based on the survey, the board members selected the 10 most important topics and asked 11 expert clinicians (topic investigators: TIs) with different specialties to review and establish the statement for each topic. In December 2009, the BMs, the TIs and other specialists gathered to discuss and determine the contents of the consensus report. Professor Phyllis C. Zee joined the meeting as an advisor. After a peer review by specialists outside the panel, the consensus report was finally confirmed by the BMs in July 2010 and submitted to a journal. A comprehensive index summary as a synopsis of the final statements is as follows: 1) Significance of insomnia treatment, 2) Insomnia to be treated, 3) Goal of the insomnia treatment, 4) Appropriate sleep hygiene education, 5) Strategy for hypnotics treatment, 6) Drug therapy for insomnia in the elderly, pregnant women and children/adolescents, and 7) Diagnostic and therapeutic strategy of insomnia in general practice. We expect that this review paper will contribute to the advancement of the management of insomnia in general practice.

IS-3-1

SLEEPINESS AND SAFETY: WHERE BIOLOGY NEEDS TECHNOLOGY

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Humans remain the root cause of 50% to 90% of all operational failures and disasters. Sleepiness and the neurobehavioral consequences of inadequate sleep contribute to this human error rate, because modern industrialized economies use time as an expendable commodity, requiring more people to be awake more of the time, and thereby frequently exceeding the biological limits on safe human performance. Time use studies indicate that time for compensated work and travel are two major reasons people sleep less. This trend is likely to continue to increase in modern societies as the global population expands to 7 billion and beyond. Although the biological dynamics of human sleepiness and its effects on performance are increasingly understood, the use of technology to predict, prevent, detect and intervene before human error occurs is a relatively new area, but one of great promise for managing sleep/fatigue-related risk. This talk will review the growth of human activity relative to biological limits on safe human performance; the nature of human performance deficits as sleepiness increases; and recent technology development initiatives from the transportation, security and aerospace domains designed to help humans avoid sleepiness/fatigue-related catastrophic errors. These technologies range from (1) prediction of vulnerability to sleepiness and of the timing of sleepiness; (2) brief objective probed assessments of sleepiness; and (3) online, real time continuous evaluations of sleepiness-alertness. Promising examples of these approaches for rapidly detecting sleepiness in the workplace and will be discussed, along with the challenges to bringing these technologies forward relative to individual behaviors and social policies and attitudes.

IS-3-2

NIGHT WORK SLEEPINESS

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Night work is associated with an increased accident risk often attributed to sleepiness. This attribution is based on inference in the sense that sleepiness normally results from activity at the circadian trough or from reduced sleep or, frequently, from both. Rarely, however, is sleepiness actually measured in relation to accidents, near accidents, or corresponding situations. Here we present data showing physiological indications of physiological sleepiness during night work in, as well as subjective reports of sleepiness. Sleep intrusions is seen during work at night and subjective reports reach very high levels. Sleepiness seems to be the major problem in shift or night work (much more so than sleep problems). Night shift levels at the end of the night shift reach levels like those after one night of total sleep loss. Morning shift levels of sleepiness are similar to those of mid-night shift levels or those after a week of 4 h sleep per day or those seen in burnout patients. In a series of studies of driving on rural roads and motorways we have described the levels of sleepiness reached and related this to measures such as unintentional line crossings and driving interrupted because of dangerous sleepiness. The results indicate that shortly before driving is interrupted reported sleepiness is increased to very high levels (corresponding to those seen just before driving off the road in a simulator) and sleepiness intrusions in the EEG and EOG increase., as well as blink duration. About 40% of normal drivers reach high danger levels. Finally, night or morning work are seen as major overall problems by around 14% of those exposed in a national representative sample (N = 4000), but that is only in the middle of the ranking list of problem prevalence (low influence on work hours, short leadway, short time off between shifts are the worst factors). However, night work is seen as the leading risk in terms of health, sleepiness and impaired risk.

IS-3-3

EPIDEMIOLOGY OF DAYTIME SLEEPINESS

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Excessive daytime sleepiness (EDS) is a frequent complain in modern society. As an average the prevalence is between 5% and 15%. In sleep clinic populations sleep apnea is the most common cause followed by narcolepsy. An increase has been noted recently in some countries. The prevalence of narcolepsy varies between 20 and 50/ 100,000 persons. The highest figures are from Japan (160 to 590/ 100,000) and the lowest from Israel. Using the Ullanlinna Narcolepsy Scale (UNS) the prevalence is between 15 and 34/ 100,000. The incidence of narcolepsy is estimated to be 0.74/ 100,000 person-years for narcolepsy with cataplexy and 1.37/ 100 000 for narcolepsy with or without cataplexy. In Finland, during 2002 to 2009 the annual incidence has been around 0.8/ 100,000 inhabitants (95% confidence interval 0.6–1). The average annual incidence among subjects under 17 years of age has been 0.3/ 100,000. In 2010 in subjects aged 4 to 16 years there was an increase in the incidence to 5/ 100,000. Among adults over 20 years of age the incidence rate in 2010 was 0.9/100,000, which equals the average incidence figure in 2002–2009. The increased risk associated with vaccination amounted to 6/ 100,000 vaccinated persons in the 4 to 19 age group during 8 months after vaccination. The risk of a vaccinated person, aged 4 to 19, was 12.7 times the risk of an unvaccinated person (www.thl.fi). No increased incidence of narcolepsy was observed among children under the age of four or among adults over the age of 19. A somewhat weaker increase has occurred in Sweden. In China an increase of childhood narcolepsy in 2010 has been related to H1N1 infection contrary to Finland where the link seems to be with the adjuvanted vaccine and not with the H1N1 infection. No link has been found with vaccines without adjuvants. Recent findings about the changes in incidence of narcolepsy will be discussed during the congress.

IS-3-4

ACCIDENTS RISK IN SLEEP DISORDERS

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Sleep disorders are not uncommon and have been widely reported throughout the world. They have a profound impact on industrialized 24-h societies. Consequences of sleep problems include impaired social and recreational activities, increased human errors, loss of productivity, and elevated risk of accidents. Conditions such as behaviorally induced insufficient sleep syndrome, CNS hypersomnias, shift-work, jet lag, and sleep apnea warrant public health attention, since daytime sleepiness due to these sleep disorders may affect performance of daily activities such as driving a car. The increased risk seems to relate with the symptom severity of excessive daytime sleepiness, and many studies have shown a clear dose-response relationship with respect to the severity of respiratory disorder indices in OSAS to the driving risk. Treatment of sleep apnea with nasal continuous positive airway pressure appears to reduce the risk of traffic accidents to the one of the general population, but the effects of wakefulness-promoting drugs on driving ability is limited. The countermeasures for excessive daytime sleepiness are effective only in the cases with acute sleep loss. There is a need for a social awareness program to educate the public about the potential consequences of various sleep disorders in order to reduce the number of sleep-related traffic accidents.

IS-3-5

MOVEMENT DISORDERS IN NARCOLEPSY

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Narcolepsy with cataplexy (NC) is a chronic disease characterized by excessive daytime sleepiness, striking transitions from wakefulness into rapid eye movement (REM) sleep, typically associated with cataplexy and other phenomena due to the abnormal occurrence of REM sleep elements during wakefulness (sleep paralysis and hallucinations) and frequent sleep/wake transitions. Nocturnal sleep in NC is usually disturbed by a large cohort of phenomena: vivid frightening dreams, several nocturnal awakenings, REM sleep behavior disorder (RBD), periodic leg movement (PLM), obstructive sleep apnea (OSA), sleep-related eating disorders and other parasomnias. Frequent abnormalities in both NREM and REM sleep motor regulation result in dissociated sleep/wake states. Higher abnormalities in REM sleep motor regulation were reported with an increased frequency of REM sleep without atonia, phasic EMG events and PLMS in narcoleptic patients when compared to controls. A higher prevalence of RLS was found in NC but with a moderate severity, together with a higher frequency of PLMS and PLMW with an association between the presence of PLMS and measures of REM sleep and daytime functioning disruption. PLMS

displayed specific features in idiopathic restless legs syndrome and narcolepsy-cataplexy respectively, with narcolepsy-cataplexy with restless legs showing an intermediate pattern. Motor dyscontrol in narcolepsy is not restricted to sleep, involving also wakefulness with the presence of cataplexy and the increase in periodic leg movements index. Moreover, recently pediatric cases of NC have been reported with a co-occurence with a complex movement disorder at disease onset, a phenomenon that may vanish later in the course of the disease. The coexistence of NC and several motor dysfunctions suggest a common neurobiological defect of motor inhibition. Further studies are warranted to assess clinical course and whether the associated movement disorder is also caused by hypocretin deficiency or by additional neurochemical abnormalities.

IS-4-1

METABOLIC RISK OF SLEEP APNEA

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Abstract not arrived.

IS-4-2

EFFECTS OF INTERMITTENT HYPOXIA ON SEVERAL PARAMETERS FOR CARDIOVASCULAR RISK FACTORS

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Pathophysiology of obstructive sleep apnea (OSA) is characterized by repeated events of intermittent hypoxia (IH), sleep fragmentation and arousals. Chronic IH consists of ischemia and reperfusion periods, and ischemia/reperfusion injury can produce oxidative stress. IH is a pathologic phenomenon that is characteristic of OSA, while sustained hypoxia (SH) is observed in normal physiological processes. In vitro, IH causes different effects on cells, compared to SH. In mice, chronic IH increases atherosclerotic changes in combination with high cholesterol diet, and causes insulin resistance in lean mice, independent from autonomic nervous system. Among clinical parameters of OSA, apnea hypopnea index (AHI) and oxygen desaturation index (ODI) represent IH, while % time of desaturation SH. We have investigated the relationship between these OSA parameters and several cardiovascular and metabolic biomarkers in OSA patients, and compared between the effects of IH and those of SH. We revealed that plasma ghrelin, a biomarker of obesity was associated with AHI or ODI rather than % time of desaturation. Platelet aggregability was also related with IH but not SH. In contrast, the heme oxygenase-1/bilirubin pathway, which can be induced by various stresses including hypoxia was related with % time of desaturation rather than AHI or ODI. Plasma thioredoxin (a biomarker of oxidative stress) and plasma adiponectin (an adipokine) correlated with both IH and SH. These findings suggest that IH and SH can affect different pathways and biomarkers that are related with cardiovascular complications in patients with OSA. We would discuss different aspects of IH and SH in OSA, based on our clinical studies. In addition, we would also show some of our cellular experiments of hypoxia exposure.

IS-4-3

MOLECULAR EFFECTS OF OBSTRUCTIVE SLEEP APNEA: SUMMARY AND PERSPECTIVES

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Obstructive Sleep Apnea (OSA) causes intermittent hypoxia (IH), sleep fragmentation, hypercapnea, and intrathoracic pressure swings. Most of the molecular effects of OSA have been attributed to IH. Molecular effects of IH can be classified as systemic and tissue-specific. Systemic effects to large extent are governed by activation of sympathetic nervous system resulting in hypertension, exuberant hepatic gluconeogenesis and adipose tissue lipolysis with ensuing increases in free fatty acids (FFA). Excess of free fatty acids impairs insulin signaling resulting in insulin resistance and activates NF-kappa B resulting in systemic inflammation. Tissue specific effects of IH have been described in the different areas of the brain, heart, pancreas, liver, arterial wall and adipose tissue and attributable to oxidative stress with activation of NADPH oxidase and hypoxia inducible factor 1 (HIF-1). Of note, HIF-2, which is up-regulated by sustained hypoxia, is inactivated by IH. Oxidative stress in different areas of the brain induces hypersomnolence and memory deficit. Excessive production of reactive oxygen species up-regulates NF-kappa B increasing synthesis of pro-inflammatory cytokines TNF alpha, IL-6, IL-8, adhesion molecules and leukotrienes, and activating renin-angiotensin system and secretion of endotheline. IH up-regulates a transcription factor of liver lipid biosynthesis sterol regulatory element binding protein 1 and a downstream enzyme stearoyl coenzyme A desaturase 1, which causes hepatic steatosis and hyperlipidemia. In adipose tissue, IH increases biosynthesis of leptin and angiopoietin-like protein 4 (Angptl4), while insulin sensitizer adiponectin is decreased. Angptl4 inactivates a key enzyme of lipoprotein clearance, lipoprotein lipase which also leads to dyslipidemia. Finally, up-regulation of HIF-1 in the liver and adipose tissue may lead to tissue fibrosis. Thus, multidimensional effects of IH may cause a cognitive dysfunction, atherosclerosis, non-alcoholic steatohepatitis, insulin resistance and type 2 diabetes.

IS-4-4

CARDIOVASCULAR AND METABOLIC CONSEQUENCES OF OBSTRUCTIVE SLEEP APNEA: MECHANISMS

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In the past two decades, obstructive sleep apnea (OSA) has been identified as a common clinical condition. Epidemiological studies have confirmed a high prevalence of the disease in middle-aged adults.

OSA is associated with marked cardiovascular and metabolic morbidities, leading to a significant increase in mortality. Sympathetic activation, oxidative stress and systemic inflammation have been shown to be the main intermediary mechanisms associated with sleep apnea and intermittent hypoxia. There are now convincing data regarding the association between hypertension, arrhythmias, stroke, coronary heart disease, increased cardiovascular mortality and OSA. Data in OSA models and animal models are now available that support the link between sleep apnea and atherosclerosis and dysmetabolism. The desaturation-reoxygenation sequence is a typical pattern that is coupled with a majority of respiratory events and thought to be responsible for most of the associated cardiovascular morbidity. This sequence leads to oxidative stress and the production of reactive oxygen species (ROS). Numerous studies have reported increased oxidative stress using various biological markers, although comorbidities such as diabetes, hypertension or obesity may account for part of these results. The increased levels of ROS contribute to generation of adhesion molecules, activation of leukocytes and production of vascular and systemic inflammation. All these mechanisms are presumably responsible for vascular endothelium damage. They have been extensively studied in intermittent hypoxia model in rodents and more recently in normal volunteers.

IS-5-1

GENETIC UNDERPINNINGS OF VENTILATORY CONTROL

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Abstract not arrived.

IS-5-2

OSA PHENOTYPE AND BREATHING IRREGULARITY

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In polysomnography, each single apnea is classified into three groups, obstructive apnea, central apnea, and mixed apnea according to the presence of respiratory effort. Sometimes we see these three types of apnea coexisting during a night; however we diagnose by which type of apnea is predominant. Thus, if most of the respiratory events are obstructive apnea and/or mixed apnea, it would be OSAS, and if central apnea can be seen frequently we diagnose it as CSAS. Cherniack has suggested in 1979 that the interaction of respiratory output to the upper airway and diaphragm may determine the expression of apnea types, such as central and obstructive. Thus, individuals may manifest apneas with both obstructive and central components. The relative proportion of these components would depend on individual factors, which may be genetic or secondary to a medical condition. With this concept, we have been focusing on resting breathing pattern variability during wakefulness since we consider resting breathing might be not only a window to explore the central respiratory control system, but also a new tool to distinguish clinically important OSAS phenotypes. In this session, first, we will present that irregular breathing during wakefulness and poor adherence to CPAP were seen in mixed apnea dominant OSAS which is one of the particular phenotypes of OSAS. Second, we will introduce the possibility of breathing irregularity as a marker for CPAP acceptance in patients with obstructive apnea dominant OSAS (pure OSAS).

IS-5-3

MECHANICAL PROPERTIES AND COMPENSATORY NEUROMUSCULAR RESPONSES OF THE UPPER AIRWAY IN OBSTRUCTIVE SLEEP APNEA

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Obstructive sleep apnea (OSA) is characterized by repetitive obstruction of the upper airway that results in recurrent hypoxemia and arousal from sleep and increases in cardiovascular morbidity and mortality. Upper airway obstruction during sleep can result from alterations in either the passive structural pharyngeal properties or from disturbances in neuromuscular control. When the neural mechanisms are depressed under sleep, the sequential interaction between anatomical balance and compensatory neuromuscular response against upper airway obstruction become the key factors controlling upper airway patency during sleep.When the upper airway first obstructs, the upper airway musculature remains in a relatively hypotonic or passive state. Initially, mechanoreceptor activity in airway pressure receptors and pulmonary stretch receptors can produce immediate alterations in respiratory timing in experimental animals and sleeping humans. Recent evidence suggests that a prolongation of the inspiratory duty cycle can help stabilize ventilation during periods of upper airway obstruction. Thereafter, upper airway obstruction can elicit compensatory neuromuscular responses that can mitigate the obstruction during spontaneous breathing in sleeping and anesthetized subjects. As upper airway obstruction persists, disturbances in gas exchange ensue, leading to increases in upper airway neuromuscular activity, improvements in airway patency and greater ventilatory stability (active state). When compensatory mechanisms are inadequate to stabilize ventilation, upper airway obstruction often terminates in an arousal from sleep and the prompt restoration of upper airway patency. The main issue of this presentation is to summarize the current understanding of mechanisms for maintaining upper airway patency during sleep and anesthesia and discusses the developmental aspects of the mechanisms, based on the quantitative analysis of upper airway collapsibility using the concept of inspiratory flow limitation.

IS-5-4

THE NEUROBIOLOGY OF OBSTRUCTIVE SLEEP APNEA

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Structural features of the upper airway are the root cause of the obstructive sleep apnea (OSA) syndrome but the interaction between the neural mechanisms that promote sleep with those that control breathing is ultimately responsible for the perturbed breathing because OSA patients

generate adequate ventilation when awake. During wakefulness, OSA patients have elevated upper airway muscle tone when compared to healthy individuals. This elevation is likely caused by: (1) reflex activation by more negative than in healthy persons inspiratory airway pressure; and (2) enhanced tonic, wake-related drive relayed to upper airway motoneurons from a host of sources that are collectively referred to as the wakefulness stimulus for breathing. To date, excitatory effect mediated by norepinephrine and serotonin have been positively identified in animal studies as major mediators of the wake-related drive to upper airway motoneurons. In animals with fully patent upper airway, these drives decline gradually from a maximal level during active wake to total abolition during rapid eye movement sleep. In cats, endogenous serotonergic drive predominates, whereas in rats, norepinephrine has a stronger endogenous excitatory effect. Other state-dependent neurochemicals that excite upper airway motoneurons include histamine, acetylcholine and orexin, but their endogenous effects remain to be characterized. In rats subjected to moderate chronic-intermittent hypoxia (CIH) for 35 days, sprouting of noradrenergic terminals occurs in the hypoglossal (XII) motor nucleus which innervates the genioglossus muscle, a major upper airway dilator, and XII motoneurons exhibit enhanced immunoreactivity for alpha$_1$-adrenergic receptors. In anesthetized rats pre-treated with CIH, antagonism of these receptors reveals an enhanced endogenous noradrenergic drive to inspiratory-modulated XII motoneurons. Collectively, these findings suggest that CIH contributes to the adaptive increase in wakefulness of upper airway muscle tone in OSA patients. [Support: HL47600, HL-71097.]

IS-6-1

RESTLESS LEGS SYNDROME: CLINICAL ASPECTS, COMORBIDITY AND TREATMENT OPTIONS

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Abstract not arrived.

IS-6-2

CURRENT DIAGNOSTIC AND MANAGEMENT STRATEGIES OF RESTLESS LEGS SYNDROME IN UNITED STATES

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Abstract not arrived.

IS-7-1

AUGMENTATION AND COMPLICATIONS DUE TO DOPAMINE THERAPY

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The most relevant complication of dopamine therapy in RLS is augmentation. It is characterized as an overall worsening of symptoms despite therapy. According to current augmentation criteria, RLS is paradoxically worsened or improved (sometimes) despite increasing or reducing of dopaminergic drug dose respectively. Alternative criteria for augmentation include earlier temporal onset of symptoms by four hours without / or by two hours with additional occurrence of other features. Augmentation has been observed around 15 years ago, but early reports used different definitions, were based on case reports or retrospective case series only. Later, augmentation was described in up to 60% of l-dopa treated patients (Hogl B, 2010), and in up to 30% of dopamine agonist treated patients. Only recently, prospective double-blind trials were performed with appropriate testing for augmentation. Results are difficult to compare because of varying durations of the studies, different methods to assess augmentation, etc. The longest available controlled trial of RLS therapy with (retrospective) assessment of augmentation by experts was performed with rotigotine. It showed a low augmentation rate of 13.2% over 5 years (Oertel W, Lancet Neurol 2011). Reports from clinical populations treated for up to 10 years showed that during ongoing treatment with persistent response, nevertheless in the majority of patients, some more or less subtle signs of evolving augmentation can be present (Allen R, Sleep Med 2011). Clinicians should carefully evaluate dopaminergically treated RLS patients for evolving signs of augmentation, and try to reduce the risk for augmentation by keeping the dose low and iron body stores non-depleted. Other complications of dopaminergic treatment, such as gambling have been observed also in RLS. Patients should be warned and regularly questioned for any symptoms of impulse control disorders. Daytime sleepiness and involuntary sleep onset may occur rarely in RLS, but overall ESS improved with dopaminergic treatment due to the improvement of sleep (Kallweit 2009).

IS-7-2

PATHOPHYSIOLOGY OF RLS FROM GENETIC RESEARCH PERSPECTIVE

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There are major controversies with regard to the localization of the neural structures and the nature of neurotransmitters involved in the physiopathology of RLS. Neuroimaging studies and therapeutic results obtained with opioids and L-dopa and the detrimental effect of antihistamine have led to neuropharmacological hypotheses regarding the physiopathology of RLS PLMS. Studies of brain iron and RLS consistently found significant abnormalities supporting the putative concept that a brain iron deficiency causes RLS in many patients.
On the other hand, there are substantial evidences for a genetic contribution to RLS. Twin studies showing higher concordance rate in monozygotic than dizygotic twins, familial aggregation of RLS with strong percentage of positive family histories, multigenerational pedigrees with multiple affected individuals and increased sibling risk for RLS support genetic contribution. The significant familial aggregation of RLS has

encouraged linkage analyses of large multiplex families. Several loci for RLS have been mapped in RLS families supporting the view that RLS is a genetically heterogenous complex trait, but no causative genes and mutations have been identified in the linked families. Association studies have also looked at candidate genes for RLS. Genes related to dopaminergic transmission (D1 to D5 receptors, tyrosine hydroxylase, dopamine-B-hydroxylase) were first investigated but no association was found. Genome-wide association study of RLS provided robust evidence of the presence of common sequence variants in four candidate loci/genes strongly associated with unrelated RLS cases: MEIS1, BTBD9, MAP2K5 and PTPRD on chromosomes 2p, 6p and 15q, respectively, associated with a more than 50% increase in risk for RLS. The link between these genetic mutations and the physiopathology of RLS is largely unknown but a recent study has shown that RLS-associated MEIS1 risk variant influences iron metabolism.

IS-7-3

OVERVIEW OF CURRENT RLS THERAPY WITH DOPAMINE AGONISTS

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Restless legs syndrome (RLS) is a "sleep-movement-pain"-disorder with a prevalence of 2%–10(caucasian)%. The diagnosis is clinically achieved by asking 4 specific questions. The severity of RLS is assessed by the International RLS Study Group Severity Scale (IRLS). It consists of 10 questions each with a numerical value of 0–4 (4 = worst). For intermediate (IRLS > 15) to severe (IRLS = 20–30) RLS, the internationally recognized first line pharmacotherapy for RLS are dopamine agonists – and according to expert opinion also for mildly affected RLS patients. 3 non-ergot dopamine agonists-pramipexole, ropinirole and rotigotine – are approved in various markets for RLS-based on numerous "Evidence based Medicine class I" trials – with an effect size of at least 6 points in the IRLS. These clinical efficacy data are supported by objective measures (i.e. reduction in PLM – or arousal index) obtained in double blind placebo controlled polysomnographic studies. In comparison to their use in Parkinson's disease, in RLS non-ergot dopamine agonists are employed at a dosage of a factor of 3 to 4 times less. They are well tolerated in RLS. Augmentation, a long term complication in RLS and considered to be occur under short acting dopaminergic therapy such as L-dopa, appears to occur less with long acting dopamine agonists (Trenkwalder et al., 2008). This statement has received support from a recently published study of 295 patients with severe RLS, who received transdermal (24 hour patch delivery) rotigotine over a 5 year open label follow up period. 126 patients completed the trial. 39% of patients who completed the trial were classified as "symptom free (RLS remitter – IRLS = 0)". Clinically significant augmentation under a therapy of 1–3 mg rotigotine/day was reported to be 5.1% during the 5 years (Oertel et al., 2011). In summary, non-ergot dopamine agonists are the pharmacotherapy of choice for RLS. (Trenkwalder et al. Mov. Disord 2008; Oertel et al Lancet Neurol 2011).

IS-7-4

RESTLESS LEGS SYNDROME IN ENDSTAGE RENAL DISEASE

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Undoubtedly, restless legs syndrome (RLS) is one of the common symptoms in patients with endstage renal disease (ERSD), and the prevalence of the disorder has been estimated at 20 to 60% of ESRD population. Of note, although the prevalence of RLS in general population is clearly lower in Asia compared with Western countries, the rate is quite similar between the countries, suggesting that RLS in ESDRD occurs beyond racial difference. When evaluating the prevalence of RLS among each renal dysfunction category, the rate becomes higher among the cases in grade 3 or above, and sharply rises in grade 5 (=ERSD). Moreover, it has been known that RLS symptoms in most of ERSD patients disappear shortly after renal transplantation. Considering these, accumulation of uremic toxin to a certain amount can be hypothesized to be responsible for the occurrence of RLS, but a candidate toxic substance has not been found to date. In clinical settings, severity of RLS symptom and consequent nocturnal insomnia in ERSD patients is likely to be higher than those in patients with idiopathic RLS, and the former group accompanies larger amount of periodic limb movements during sleep compared with the latter group. As for treatment, dopaminergic drugs are thought to be the first line in uremic RLS similar with idiopathic RLS. However, the drugs which are eliminated from kidney should be contraindicated in ESRD patients. In addition, we should consider the drug which can suppress RLS symptom both in nocturnal period and periods while undergoing haemodialysis when the symptom is likely to become worse.

IS-7-5

RLS-RELATED NEUROPATHY

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Restless legs syndrome (RLS) is characterized by a desire to move the extremities, often associated with paresthesias or dysesthesias, motor restlessness, worsening of symptoms with rest with relief by activity, and worsening of symptoms in the evening or night. Numerous forms of neuropathy, including hereditary, diabetic, alcoholic, amyloid, motor neuron disease, poliomyelitis, and radiculopathy, have been associated with RLS.

Investigating the association between RLS and neuropathy, however, the association between RLS and peripheral neuropathy remains controversial.

On the other hand, aging deeply influences several morphologic and functional features of the peripheral nervous system. Morphologic studies have reported a loss of myelinated and unmyelinated nerve fibers in elderly subjects, and several abnormalities involving myelinated fibers.

Polydefkis et al reported that 36% of RLS patients neuropathy was identified. Three patients had pure large-fiber neuropathy (LFN), two had mixed LFN and small sensory fiber loss (SSFL) and three had isolated SSFL. The SSFL group had a later onset of RLS ($p < 0.009$), reported pain in their feet with RLS more frequently ($p < 0.001$), and tended to have no family history of RLS ($p < 0.078$). Patients with LFN did not have similar associations with age at onset, family history status,

or presence of pain. They conclude that the results suggest that two forms of RLS exist. Thus in some case of a later onset or aged RLS may have neuropathy as a co morbidity due to aging. Therefore, for later onset or aged RLS not only dopaminergic drugs but also drugs for neuropathy such as pregabaline should be considered as a therapeutic drug.

Abstract symposia

AS-1-1

COGNITIVE BEHAVIOR THERAPY FOR INSOMNIA IMPROVES SLEEP AND DECREASES PAIN IN OLDER ADULTS WITH CO-MORBID INSOMNIA AND OSTEOARTHRITIS

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Fully a quarter of older adults experience significant and chronic osteoarthritis (OA) pain and co-morbid insomnia. This co-morbid pain and insomnia has significant negative impact on physical function and on quality of life and can result in depression, impaired cognitive function and increased healthcare utilization and related costs. Chronic pain initiates and exacerbates sleep disturbance, and disturbed sleep in turn maintains and exacerbates chronic pain and related dysfunction. Since both OA pain and sleep disturbance are common among older adults, and adversely affect physical function, quality of life, and health care costs, there is a compelling rationale for integrated management of both pain and sleep in OA. The likely reciprocal effects of pain dysfunction and sleep disturbance suggest potential benefits of such an integrated approach. In a secondary analysis of a well conducted CBT for insomnia (CBT-I) trail in older adults with co-morbid OA and insomnia we demonstrated that CBT-I treated OA subjects had both significantly improved sleep and reduced pain both post treatment and at one year follow-up relative to attention control OA subjects; despite neither treatment condition including any pain management information. This preliminary finding as well as our ongoing randomized clinical trial, Cognitive Behavioral Therapy for Arthritis Pain and Insomnia in Older Adults (LIFESTYLES) testing the effectiveness of an integrated cognitive behavioral therapy for pain and insomnia (CBT-PI) intervention versus a cognitive behavioral therapy for pain (CBT-P) intervention and an education only attention control (EOC) in a large sample of older adults with co-morbid OA and insomnia drawn from a primary care population will be discussed.

AS-1-2

THE ROLE OF SELF-HELP CBT-I IN THE MANAGEMENT OF INSOMNIA SYMPTOMS ASSOCIATED WITH CHRONIC DISEASE

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Introduction: Aging-related increases in sleep symptoms are closely associated with chronic diseases which both increase with age and substantially elevate the odds of persistent insomnia symptoms. Self-help approaches, based on the principles of CBT for insomnia (CBT-I), could offer a low-cost, first-line treatment option within a stepped care model. This presentation examines the utility and limitations of self-help approaches to insomnia management among older people with insomnia associated with long-term conditions.
Method: In a single centre, pragmatic, 2-arm randomized controlled trial, 98 participants who received a manualized program of supported self-help cognitive behavioral therapy for insomnia (CBT-I) were compared with 95 participants receiving treatment as usual (TAU). Participants were: aged 55–87; diagnosed with a chronic condition; and reporting insomnia symptoms (as defined by DSM-IV-TR). The primary outcome was sleep quality, measured by the Pittsburgh Sleep Quality Index (PSQI). Secondary outcomes were the Insomnia Severity Index (ISI), the subjective sleep efficiency index, the Fatigue Severity Scale (FSS), and the Brief Pain Inventory.
Results: Self-help CBT-I improved sleep quality and sleep efficiency, and reduced insomnia severity and sleep medication use; it did not, however, impact fatigue or pain severity.
Conclusion: This trial supports the use of simple, manualized self-help in a stepped-care model for patients with comorbid insomnia symptoms.

AS-2-1

SEASONAL CHANGES OF OBSTRUCTIVE SLEEP APNEA SYNDROME (OSAS) IN CHILDREN

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Pediatric obstructive sleep apnea syndrome (OSAS) is a disorder in children characterized by recurring episodes of upper airway complete and/or partial obstruction during sleep, resulting in intermittent hypoxemia and hypercapnia, frequent awaking and sleep pattern breaks. At present, polysomnography provides the gold-standard tool for evaluating the presence and severity of OSAS in children The pathophysiology of pediatric OSAS is multifactorial, with enlargement of the lymphoid tissues of Waldeyer's ring contributing to abnormalities of craniofacial/pharyngeal structure and coordination of upper airway tone. In addition, pediatric OSAS may be implicated pathophysiologically by allergies and respiratory viruses. However, its seasonal distribution has been rarely reported. This study population, 554 cases comprised children from the Good Sleep Center, Nagoya City University Hospital and the Toyohashi Mtes Sleep Disorder Center, during the period January 2003 to June 2011 for an assessment of their need for treatment because of nighttime snoring, apneas, or difficult breathing. Children with known genetic syndromes, craniofacial anomalies, neurologic disease, upper airway anomalies, any underlying disease predisposing to upper airway obstruction, asthma, or perennial allergy were excluded. All cases received polysomnography, and the rusults diveded to the months of the day when they received examination. Significant differences of seasonal changes were found in children under six years old. Since adenotonsillectomy is the most common treatment for the age children, careful diagnosis should be accomplished with consideration of seasonal distribution.

AS-2-2

VASCULAR DYSFUNCTION IN CHILDREN WITH OBSTRUCTIVE SLEEP APNOEA: IS IT ONLY OBESITY?

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Obstructive sleep apnoea (OSA) is a common condition in children, and is characterized by repeated episodes of complete and or partial upper airway obstruction during sleep resulting in gas exchange disturbances, frequent arousals and distortion of sleep architecture. There is robust scientific literature to suggest that if the condition is left untreated, significant complications like neurocognitive dysfunction, insulin resistance and hypertension could result. Of particular interest and clinical importance are the cardiovascular sequelae that may develop in children with OSA. These sequelae not only exert an immediately significant effect on cardiovascular health during childhood, but may also affect cardiovascular outcomes later during adult life. With the recent global epidemic of childhood obesity, the association between obesity, OSA and risk for cardiovascular diseases is even more difficult to ascertain, since subjects with either of these disorders often have common risk factors for cardiovascular complications. In this lecture, the author will share with you research on the association between childhood OSA and cardiovascular complications that have thus far been described with reference to the confounding factor of obesity.

AS-3-1

NON-VISUAL LIGHT RESPONSES IN HUMANS

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Exposure to light at night resets circadian rhythms and inhibits synthesis of the sleep-promoting hormone melatonin. These non-visual light responses are mediated by melanopsin-containing retinal ganglion cells. Melanopsin cells are most sensitive to short-wavelength blue light but also receive input from rod and cone photoreceptors. In the first part of my talk, I will present evidence that visual photoreceptors contribute substantially to non-visual light responses at the beginning of light exposure and at low irradiances, whereas melanopsin is the primary circadian photopigment in response to long-duration light exposure and at high irradiances. In the second part of my talk, I will discuss the impact of exposure to room light at night on melatonin regulation. In a series of laboratory studies, we found that exposure to room light before bedtime suppressed melatonin strongly, resulting in a later melatonin onset in about 99% of individuals. Hence, chronically exposing oneself to electrical lighting in the late evening disrupts melatonin signaling and could therefore potentially impact sleep. Our findings also suggest, however, that appropriately timed exposure to room light, or light therapy that optimizes stimulation of melanopsin and visual photoreceptors, could potentially be used to treat circadian disruption, with effects similar to exposure to bright polychromatic white light.

AS-3-2

NON-VISUAL EFFECT OF LIGHT AND SLEEP: NEW FINDINGS FROM THE STUDIES IN CHILDREN AND MELANOPSIN GENE POLYMORPHISM

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Human in modern society are surrounded by many factors which disturb circadian rhythm and sleep. Light is the most powerful synchronizer of the human circadian clock. Although exposure to morning light reset human circadian rhythm to 24 hours, light at night delays circadian rhythm. Other than the effect on circadian rhythm, light has various effects such as effects on melatonin secretion, alertness, and pupillary light response. These effects are called "non-visual effects" or "non-image forming effects", are induced by light signals projecting to the hypothalamus in the brain. It is known that there are large individual differences in these physiological responses to light. The researchers have shown that the light-induced melatonin suppression might be influenced by many factors such as age, light history, season, and ethnics. In recent our study, we found that children was more sensitive to light-induced melatonin suppression than adults. In modern society, sleep time in children has been decreasing and sleep timing has been also delaying. Although it is unclear that the causal relationship between light at night and delayed bed time in children, we should pay more attention to the lighting environment for children. As another new finding, we found that single nucleotide polymorphism of melanopsin gene (OPN4) was associated with pupillary light response and sleep timing. This finding suggests that individual difference in non-visual response to light affects human circadian rhythm and sleep timing. We might have to consider lighting environments for individuals.

AS-4-1

A CROSS-NATIONAL COMPARISON OF TEEN SLEEP BETWEEN AUSTRALIA AND THE U.S.: THE ROLE OF SCHOOL START TIME, PARENTAL LIMIT-SETTING AND EXTRA-CURRICULAR ACTIVITIES

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Study aims: To test whether cultural differences in school start times, parental involvement in setting bedtimes and extra-curricular commitments explain the difference in total sleep time on school nights between adolescents in Australia and the U.S.
Participants: 385 adolescents aged 13–18 years (X = 15.6, SD = 0.95; 60% male) from Australia and 302 adolescents aged 13–19 years (X = 16.03, SD = 1.19; 35% male) from the United States.
Methods: Adolescents completed the School Sleep Habits Survey during class time, followed by an 8-day Sleep Diary.
Results: After controlling for age and sex, culture explained a significant 12.1% of the variance in sleep duration. Australian adolescents obtained an average of 47 minutes more sleep per school night than those in the U.S. There were significant differences between the two countries on all mediator variables. Australian adolescents were more likely to have a parent-set bedtime (17.5% vs 6.8%), start school later

(8:32am vs 7:45am) and spend less time on extra-curricular activities (1h37m vs 2h41m) than their U.S. peers. These mediators were significantly associated with sleep duration, with parent-set bedtimes, later school start times and less hours spent on extra-curricular activities being associated with more total sleep. After controlling for mediator variables, culture still explained a significant, but smaller 5.5% of the variance in school night sleep duration, consistent with partial mediation.
Conclusions: In addition to biological factors, extrinsic cultural factors significantly impact upon the sleep of adolescents. The present study highlights the importance of considering a comprehensive, ecological approach to adolescent sleep.

AS-4-2

A CROSS-CULTURAL COMPARISON BETWEEN AUSTRALIAN AND DUTCH ADOLESCENTS, THAT RELATES CHRONIC SLEEP REDUCTION TO SLEEP MEASURES AS WELL AS TO SCHOOL PERFORMANCE

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Sleep problems and its severe negative consequences on daytime functioning have worldwide been reported. Still, very little research is done that compares these relationships in cross-cultural studies. Although adolescents often experience insufficient and poor sleep, sleep variables such as total sleep time do not account for individuals sleep need and sleep debt and may be an inadequate representation of adolescents' sleep problems and its daytime consequences. This problem can be overcome by measuring chronic sleep reduction. Besides, by measuring symptoms of chronic sleep reduction, individual sleep need and sleep debt can be taken into consideration. We aim to investigate whether chronic sleep reduction and its relationship to subjective (surveys, sleep diaries) and objective (actigraphy) sleep variables as well as to school performance are comparable in Dutch and Australian adolescents. Subjective sleep variables were measured with surveys and sleep diaries of five school nights. Sleep of the same five nights was monitored with actigraphy. School performance was assessed with self-reports. Similar relationships between chronic sleep reduction, sleep variables and school performance were found in both samples, indicating that these relationships are culturally independent. Chronic sleep reduction was associated with a higher sleep need, less time spent in bed, shorter sleep durations (diary), and longer sleep onset latencies. Interestingly, total sleep time and sleep efficiency (actigraphy) were not related to chronic sleep reduction in both samples. School performance was related to chronic sleep reduction, whereas the relationship between grades and other sleep variables was weak or absent. This cross-cultural comparison shows that sleep problems and their relationship with school performance seem to be culturally independent phenomena. Furthermore, our results highlight the idea that chronic sleep reduction may be a good indicator of adolescents' insufficient and poor sleep than other sleep variables such as total sleep time.

AS-5-1

CLINICAL SIGNIFICANCE OF PHASE DETERMINATION OF MELATONIN RHYTHMS FOR THE TREATMENT OF CIRCADIAN RHYTHM SLEEP DISORDERS

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Both the circadian and homeostatic processes contribute to sleep timing and sleep structure in humans. Circadian rhythm sleep disorders (CRSD) are characterized by misalignment of endogenous circadian rhythms with the desired or required time for sleep. Reliable estimate of circadian rhythm phase is essential for effective diagnosis and treatment of circadian rhythm sleep disorders. The onset of melatonin secretion under dim light conditions (dim light onset melatonin; DLMO) is one of the most reliable and feasible markers for assessing the circadian pacemaker and determination of most favorable timing for exogenous melatonin administration in the treatment of CRSD. According to the phase response curve (PRC) to melatonin, which nearly forms a mirror image of the PRC to light, exogenously administered melatonin in the early evening could induce circadian phase advance and contribute to the treatment of CRSD with delayed sleep phase type or non-entrained type. Sleep phase per se can't be a reliable alternative marker to DLMO due to large inter-individual variation of interval between sleep onset and DLMO as well as presence of internal desynchronization. Using saliva for assessing melatonin levels is relatively non-invasive and acceptable diagnostic method even for child patients. An additional advantage of salivary DLMO determination is that patients can collect saliva samples at home setting by themselves. In this study, we applied salivary DLMO monitoring at home starting at 6 hours before usual sleep onset time for patients with CRSD, and estimated the efficacy of DLMO-based melatonin therapy for them. We discuss the usability of salivary DLMO monitoring in the clinical settings and the favorable timing of exogenous melatonin administration for the treatment of CRSD.

AS-5-2

CLINICAL PRACTICE OF CIRCADIAN RHYTHM SLEEP DISORDERS

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Circadian rhythm sleep disorders (CRSDs) are serious conditions, which are consist of being unable to adapt internal circadian rhythms to socially determined light-dark schedules, and are often linked to physical and psychological disturbances and social maladaptation. Especially, delayed sleep phase disorder (DSPD) brings major clinical problems to many adolescents and young adults. Weitzman and colleagues firstly described this condition in 1981, and so far various clinical methodologies have developed as assessments and treatments for endogenous CRSDs; however, they still have much to be evolved. Firstly, there are some assessment tools such as sleep diary, actigraphy, the Morningness-Eveningness Questionnaire, endogenous melatonin measurement, and core body temperature measurement; however each of them has substantial limitations in the clinical use. Secondly, the treatments such as exogenous melatonin administration, bright light exposure and chronotherapy have been applied for CRSDs, but they

have still insufficient evidences except for melatonin. Additionally, other interventions that strengthen the social cues, such as behavioral therapy or environmental therapy with temporal hospitalization, have scarcely studied. Thirdly, there are some other problems with the comorbid psychiatric disorders. Many psychiatric patients show sleep-wake rhythm disturbance, and it has been considered that the remission of the primary psychiatric condition should also lead to the resolution of the secondary sleep problems. However, residual sleep-wake rhythm disturbance often seems to affect the course of the comorbid psychiatric disorders conversely, and also prevents the patients from returning to social activities; therefore, some chronobiological interventions may also be needed for this condition. In this symposium, I would like to present the overview of these clinical practices of CRSDs, and then discuss their future directions.

AS-6-1

CRANIOFACIAL COMPARISONS BETWEEN ASIAN AND CAUCASIAN PATIENTSWITH OBSTRUCTIVE SLEEP APNEA

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This study was designed to compare two groups of adult men from Asian and Caucasian ethnic backgrounds with obstructive sleep apnea who were selected by matching age, gender, skeletal pattern, body mass index, and respiratory disturbance index. Pretreatment cephalometric radiographs and overnight polysomnograms of 30 Chinese and 43 Caucasian patients with Class II, Division 1 malocclusions were analyzed to investigate if there were craniofacial and upper airway structural differences between the two ethnic groups. The Chinese group, when compared with the group of Caucasian patients, revealed more severe underlying craniofacial skeletal discrepancies with significantly smaller maxilla and mandibles, more severe mandibular retrognathism, proclined lower incisors, increased total and upper facial heights, and steeper and shorter anterior cranial bases. However, no significant differences were found between the two groups in posterior facial height, ratio of upper to lower anterior facial height, and the position of hyoid bone, maxilla, and upper incisors. With regard to soft tissue and upper airway measurements, there were no significant ethnic differences in tongue and soft palate size, vertical length of oropharynx, and anteroposterior dimensions of the upper airway at most of the levels except for a larger super-posterior airway space, a larger nasopharynx and oropharynx cross-sectional area, and a smaller tongue height in the Chinese group. There appear to be a number of craniofacial and upper airway structures that differ between the two groups that may be relevant to the treatment of obstructive sleep apnea in various ethnic populations.

AS-6-2

ANATOMICAL BALANCE OF THE UPPER AIRWAY IN JAPANESE AND CAUCASIAN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Obesity and craniofacial abnormalities are common features of patients with Obstructive Sleep Apnea (OSA). Anatomical balance between the size of the craniofacial rigid enclosure (formed by the dentitions, cervical vertebrae, maxilla, and mandible) and the amount of soft tissue (e.g. tongue) influences the upper airway space and is involved in the pathogenesis of OSA (Tsuiki et al. 2008, Isono 2009). In this study, we investigated whether this anatomical balance was different between races in OSA people. Blind measurements of tongue cross-sectional area and craniofacial dimensions were performed two dimensionally through lateral cephalograms in 78 Japanese patients with OSA and 63 Caucasian OSA subjects after matching gender (male), age, and apnea hypopnea index. Sagittal tongue size, sagittal maxillomandibular dimensions, and body mass index (BMI) were compared between the groups. While BMI was significantly higher in Caucasians than in Japanese patients ($p < 0.001$), tongue size ($p = 0.27$) and maxillomandibular dimensions ($p = 0.46$) were not different between the races. These findings suggest that anatomical balance does not differ between Japanese OSA people and Caucasian OSA persons under the same OSA severity. [Support: JSPS 21406033].

AS-7-1

INTERACTION OF SEXUAL AND SLEEP PROBLEMS RELATED TO EPILEPSY ABSTRACT SYMPOSIA: EPILEPSY RESEARCH: OVERALL OUTCOMES RELATED TO SLEEP

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Epilepsy affects approximately 1–3% of the global population, including men and women of all ages, with different levels of severity. Sexual life is particularly impaired in patients with epilepsy. However, it is difficult to clearly differentiate the specific impacts of the disease from the impact of antiepileptic drugs on sexual function. The aim of this study was to evaluate sexual behavior of adult male rats in an experimental model of epilepsy. Initially, the animals were exposed to nine training sessions to acquire sexual experience. After this training period, the same rats were given pilocarpine to induce seizures (350 mg/kg i.p). Once the animals had a stable seizure frequency, sexual behavior were evaluated during three sessions. The results showed that both sexual motivation and sexual performance were markedly impaired during the sessions compared with the baseline response. These findings will aid in understanding the interaction between sexual behavior and epilepsy as well as translate possible human clinical questions involved in this relationship into experimental contexts.

AS-8-1

POLICY IMPLICATIONS OF SOCIOECONOMIC INEQUALITIES IN SLEEP: RESULTS FROM INTERNATIONAL COMPARATIVE STUDIES ON BRITISH, FINNISH AND JAPANESE CIVIL SERVANTS

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Introduction: In general, the lower the socioeconomic status (SES), the poorer the sleep. In Japanese civil servants, low grade employees had poor sleep, and the sleep inequalities reduced after adjustment for psychosocial stress at work, work hours, and work-family

conflicts. These results suggest that sleep inequalities are generated from socioeconomic inequalities in work and family characteristics. International comparisons may provide further understanding of sleep inequalities and their international variations.
Methods: The participants were 3 civil servants populations from Britain, Finland, and Japan. We evaluated whether the magnitude and patterns of sleep inequalities differed among employees from 3 different countries, and whether sleep inequalities and their international variations were explained by work and family characteristics.
Results: In men, low grade employees had difficulty falling asleep. After adjustment for work characteristics, the sleep inequalities decreased in all populations. After adjustment for family characteristics, while the sleep inequalities further decreased in the Japanese population, the inequalities remained unchanged or rather slightly increased in the British and Finnish populations. In women, while low grade employees had difficulty falling asleep in the British and Finnish populations, the reverse was true for the Japanese population. In the British and Finnish populations, the sleep inequalities slightly decreased when work characteristics were adjusted for, but slightly increased when family characteristics were adjusted for. In the Japanese population, the sleep inequalities remained unchanged after adjustment for work and family characteristics.
Conclusions: Work and family characteristics more or less explained SES inequalities in sleep and their international variations. Understanding SES inequalities in work and family characteristics and their international variations provide more effective and efficient health policies for reducing SES inequalities in sleep.

AS-8-2

EXAMINING A PATHWAY BETWEEN SOCIAL INEQUALITY IN SLEEP AND HEALTH RELATED BEHAVIORS USING THE NATIONAL CHILD DEVELOPMENT STUDY

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Previous studies showed a detrimental effect of adult alcohol misuse on sleep; however, little is known in relation to sleep and with other health related behaviours across lifecourse.
We used the data from the National Childhood Development Study for this study (born in Great Britain, 1958, Men = 5937, Women = 5718) to examine early social determinants for sleep inequalities and the lifecourse pathways of alcohol use and smoking. We also examined the effect of lifecourse alcohol use on sleep quality in middle adulthood. Path analysis was used to identify significant paths between variables. Men and women were analyzed separately.
Findings of path analysis showed gender specific patterns in sleep inequalities. Men with socially disadvantaged background had problems with duration of sleep, while the same background contributed to women's difficulties in falling asleep. Men's smoking status at age 42 directly contributed their difficulties in falling asleep; this was partially due to accumulation of the habit stemming through disadvantaged social upbringing and poor cognition and psychosocial mal-adjustment in childhood. On the other hand, women's alcohol use at age 42 directly contributed to their experiences of waking up during sleep. Their drinking habit accumulated over time stemming through affluent social upbringing. However, smoking at age 16 which endorsed by poor social upbringing, cognition and psychosocial adjustment, contributed to their alcohol use at age 33, which led to their difficulties in staying sleep.
In sum, social inequality in sleep is prevalent in men observed in a direct path from their social background and through the pathway of socially patterned smoking habit.

AS-8-3

ECONOMIC DIFFICULTIES AND POOR SLEEP: LONGITUDINAL ASSOCIATIONS AND INTERNATIONAL COMPARISONS

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Background: Sleep problems tend to be socioeconomically patterned, but contribution of economic difficulties to sleep over and above socioeconomic position, is poorly understood. Childhood and current economic difficulties have been associated with sleep problems in cross-sectional studies. However, impact of changes in economic difficulties on subsequent sleep problems has not been addressed. In this presentation, childhood and current economic difficulties and their associations with adult sleep problems are reviewed. Additionally, novel findings from ongoing international comparative prospective study are presented. Furthermore, in addition to changes in economic difficulties, multiple socioeconomic circumstances are simultaneously taken into account.
Methods: In addition to a literature review, prospective cohort data from Finnish (n = 6328) and British (=5002) public sector employees were analyzed. Childhood and current economic difficulties, and other indicators of socioeconomic position, were assessed at baseline and follow-up. Sleep problems referred to difficulties initiating and maintaining sleep as well as nonrestorative sleep.
Results: Sleep problems were prevalent and increased over time in ageing employees. Persistent and increasing economic difficulties remained associated with subsequent sleep problems after multiple adjustments, although less consistently in the British cohort. Sleep problems were also associated with income and housing. Although findings vary between studies, material situation shows more consistent associations with sleep than other indicators of socioeconomic position.
Conclusion: Supporting people to cope with their economic situation might prevent sleep problems and their adverse health consequences.

AS-9-1

OSA AND INTERMITTENT HYPOXIA: FROM CLINICAL RESEARCH TO HYPOXIC EXPERIMENTS AND VICE-VERSA

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Obstructive Sleep Apnea (OSA) is a disorder combining intermittent hypoxia (IH), sleep fragmentation and respiratory efforts. OSA is frequently associated with Excessive Daytime Sleepiness (EDS) and excess in traffic accidents. It also leads to frequent cardiovascular and metabolic consequences. However, obesity and visceral adiposity represent major confounding factors in OSA. Thus both the complexity of the disease and the limited access to the evaluation of intermittent hypoxia consequences at the tissue level in patients, have limited our under-

standing of sleep apnea pathophysiology and the development of specific treatments. The intermittent hypoxia model was developed both in normal volunteers and in rodents, in order to study the cardiovascular and metabolic consequences of OSA, without the confounding factors met in humans. IH is associated with increased blood pressure, impaired vasoreactivity and structural arterial remodeling leading to atherosclerosis, cardiac remodeling, and myocardial infarction. For instance, there is now substantial evidence that intermittent hypoxia in rodents, as a partial model of sleep apnea, triggers atherogenesis. Blood pressure alterations and hemodynamic strains on the vascular wall, impairment in vascular reactivity, lipid metabolism dysregulation, activation of pro-inflammatory transcription factors at the vascular wall level are among the key-factors promoting vascular remodeling. Also, several biological markers potentially linked with early atherosclerosis development have been evidenced as involved in OSA patients. Further studies are needed to identify at-risk subjects prone to develop vascular changes since OSA treatment may either be initiated earlier or combined with specific drug treatments.

AS-9-2

INTERMITTENT HYPOXIA IN RODENTS: EVIDENCE FOR A ROLE OF HYPOXIA IN METABOLIC CHANGES AND ATHEROSCLEROSIS

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Obstructive sleep apnea (OSA) is characterized by intermittent hypoxia (IH) during sleep. OSA leads to high cardiovascular morbidity and mortality attributable to metabolic abnormalities induced by chronic IH, including dyslipidemia, atherosclerosis, insulin resistance, glucose intolerance and non-alcoholic steatohepatitis (NASH). We have developed a mouse model of IH, which mimics the oxygen profile in patients with OSA, and have shown that chronic IH induces VLDL secretion, dyslipidemia, atherosclerosis, insulin resistance and steatohepatitis in mice. Our findings suggest that chronic IH increases hepatic lipid biosynthesis and VLDL secretion up-regulating a key enzyme of hepatic lipid biosynthesis stearoyl coenzyme A desaturase 1 (SCD-1) via hypoxia inducible factor 1 (HIF-1). Chronic IH also inhibits clearance of chylomicrons (CM) and VLDL contributing to postprandial hyperlipidemia, which may lead to atherosclerosis. IH decreases CM and VLDL clearance by inactivating lipoprotein lipase (LPL) in adipose tissue. In turn, LPL inactivation is likely mediated by HIF-1 induced up-regulation of angiopoietin like protein 4, a powerful LPL inhibitor. Finally, sleep apnea in humans and IH in rodents raise circulating free fatty acid (FFA) levels in proportion to the severity of hypoxia suggesting that IH leads to exuberant lipolysis in adipose tissue. The FFA influx into the liver may accelerate assembly of pro-atherogenic VLDL, induce insulin resistance, hepatic steatosis and inflammation leading to NASH. Sympathetic nervous system (SNS) is a major regulator of lipolysis. We propose that IH of OSA causes metabolic dysfunction by augmenting adipose tissue lipolysis, which is induced by SNS through the carotid bodies. In summary, our data suggest that IH of OSA may induce metabolic dysfunction and atherosclerosis by 3 major mechanisms: 1) up-regulation of hepatic lipid biosynthesis; 2) down-regulation of lipoprotein clearance; 3) exuberant adipose tissue lipolysis.

AS-9-3

CLINICAL TRIALS ADDRESSING OSA ASSOCIATED CARDIOVASCULAR AND METABOLIC OUTCOMES: PAST, PRESENT AND FUTURE

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Intermittent hypoxia (IH) is inducing oxidative stress and consequently promotes inflammation, endothelial dysfunction and cardiovascular morbidity. Effective treatment of OSA may represent an important target for improving cardiovascular risk. Large-scale randomized controlled trials (RCTs) demonstrating the benefits of OSA treatment with respect to hard cardiovascular outcomes (e.g., cardiac events and death) are then necessary. An alternative is to design shorter-term RCTs using surrogate cardiovascular end points such as endothelial function, carotid intima-media thickness or arterial stiffness. Research efforts should also be directed at identifying novel treatment interventions that affect the specific pathophysiology of cardiovascular consequences of OSA. The most effective strategy for reducing OSA-induced hypertension remains to be delineated. In OSA patients, the blockade of angiotensin II receptors reduces blood pressure fourfold more than CPAP. Recent studies suggest that spontaneous overnight fluid shift from the legs to the upper body is associated with obstructive sleep apnea. Spironolactone is potentially interesting for reducing this overnight fluid shift and then improving both blood pressure and the severity of OSA. This hypothesis remains to be validated in RCTs. Our group has demonstrated that the leukotrienes pathway is activated in OSA-induced atherosclerosis. We have also described a specific inflammatory profile in aortic walls of mice exposed to IH with a key role of the chemokine RANTES. A 5-lipoxygenase inhibitor or anti-inflammatory drugs like statins need to be evaluated as able to prevent atherosclerosis progression in OSA. Response to CPAP therapy in terms of cardiovascular and metabolic outcomes differs in non-obese and obese patients. The failure of CPAP to alter metabolic or inflammatory markers in obese OSA emphasizes the need to offer a combination of multiple modalities of treatment including weight loss and physical activity.

AS-10-1

CAN A COMPOSITE ANALYSIS OF AUTONOMIC AND VASCULAR SIGNALS PREDICT CARDIOVASCULAR RISK? THE ASI APPROACH

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Introduction: Analysis of multiple continuous physiological signals obtained during sleep may provide a novel method to assess cardiovascular (CV) risk. The novel autonomic state indicator (ASI) algorithm combines information from arterial oxygen saturation (SpO2) and a photoplethysmographic pulse wave signal and computes a CV risk index.

Methods: Subjects (n = 327, 227 male, age 55.1 ± 13.6 yrs, BMI 30.1 ± 6.4 kg/m2) referred to five sleep centers in Germany and Sweden were studied. The occurrence of CV risk factors was assessed and subjects were classified by four established CV risk matrixes (Framingham, EU-SCORE, PROCAM and ESC/ESH). Peripheral pulse wave was measured by overnight digital photoplethysmography. The ASI algorithm extracted patterns of the peripheral pulse wave and SpO2 signal by amplitude and time/frequency analysis. Five derived parameters (hypoxic variation, vascular augmentation, cardio acceleration, cardio-respiratory coupling and pulse wave amplitude) were used to determine the final ASI score (range 0–1).
Results: The computed ASI CV risk index was significantly associated with the ESH/ESC risk matrix ($r = 0.48$, $p < 0.0001$), the Framingham risk score ($r = 0.42$, $p < 0.001$, the PROCAM score ($r = 0.45$, $p < 0.001$) and the EU-SCORE ($r = 0.36$, $p < 0.001$). Moreover, the ASI CV risk index was elevated in patients with an already established CV endpoint (MI and/or stroke, n = 29) compared with the remaining patients (0.72 ± 0.43 vs. 0.47 ± 0.38, $p = 0.002$).
Conclusions: The ASI technique appears to provide a possibility to recognize subjects with increased CV risk based on recording of physiological signals. Interestingly, the sleep period appears to be a particularly useful window for assessment. This technique, based on a modified pulse oximeter, may be useful in both sleep and cardiovascular medicine. [The study was supported by Weinmann GMBH, the Swedish Heart and Lung Foundation and the University of Gothenburg].

AS-10-2

NOCTURNAL TRANSCUTANEOUS CARBON DIOXIDE MONITORING: A NEW MESSAGE FROM AN OLD TECHNIQUE

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The transcutaneous carbon dioxide measuring technique was developed in the 1970ies. As non-invasive estimate of the arterial pCO2, the method is considered unreliable, since the signal is affected by vasoconstriction and vasodilatation.
Falling asleep is characterized by gradual vasodilatation whereas arousal from sleep is associated with temporary vasoconstriction. We have previously shown that the transcutaneous carbon dioxide signal can be used to monitor these sleep-induced autonomic events in the peripheral vascular bed.
Fully relaxed parasympathetic state during sleep is indicated by levelling-off of the tcCO2 signal at higher level than what occurs during wakefulness. Partial upper airway obstruction with flow limitation is a parasympathetic event, during which the tcCO2 increased further above the plateau level. Repetitive episodes of obstructive sleep apnea result in lowering the tcCO2 below the nocturnal plateau but above the level during wakefulness.
Endothelial dysfunction (failure of vasodilatation during sleep) is detected as difficulties in reaching or maintaining the nocturnal tcCO2 plateau. In 103 women aged 46 the nocturnal transcutaneous CO2 parameters were the best predictors of the endothelial function estimated during wakefulness with ultrasound measurements of the brachial artery (Aittokallio et al. 2009). The nocturnal transcutaneous CO2 signal can also predict metabolic abnormalities including low HDL concentration in the serum (Virkki et al 2008).
The peripheral CO2 is a product of ventilation and perfusion, which is controlled by the autonomic nervous system. The old transcutaneous CO2 measured during sleep is a new tool to study the interactions between sleep, metabolism and endothelial function.

AS-11-1

TO LAPSE OR NOT TO LAPSE: A QUESTION OF PRIOR SLEEP, CIRCADIAN TIMING AND ENVIONMENTAL DISTRACTERS

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Introduction: Well controlled laboratory studies reveal attention lapses increase due to both acute and chronic sleep restriction. Here, we look at the lapse outside the confines of a controlled laboratory setting, and describe the incidence of an attention lapses as a function of prior wake, circadian timing, and environmental distracters.
Methods: Study 1 involved participants completing psychomotor vigilance tests (PVTs), with and without extraneous distractions, at 10pm and 4am. Distraction comprised a TV (with sound) operating in the periphery. Time synchronized video footage was obtained simultaneously. Here, lapses were categorized as occurring with the eyes open (EO), eyes closed (EC) and due to distraction (DIS). For study 2, participants (trainee physicians) completed PVTs while working an extended duration work shift in the hospital (acute sleep loss). This was repeated on six successive occasions (chronic sleep loss).
Results: For study 1, lapses increased significantly due to time awake/time of day. This impairment was further exacerbated by the presence of a distracter. While lapses increased in incidence as a function of time awake/time of day, only lapses due EC increased in duration. Lapses due to DIS increased when the distractor was present ONLY at 4am (time*distraction interaction). For study 2, lapses significantly increased due to acute and chronic sleep loss, with a significant acute*chronic sleep loss interaction.
Conclusions: Field and laboratory data indicate PVT lapses change as a function of prior wake and time of day, with lapses due to an eye closure being the most vulnerable to these factors. When sleepy, an external distractor exacerbates PVT lapses attributed to looking away, ostensibly as the sleep brain seeks stimulation.

AS-11-2

A PARADOXICAL RELATIONSHIP BETWEEN USUAL SLEEP EFFICIENCY AND BEHAVIOURAL MICROSLEEP PROPENSITY FOLLOWING A SINGLE NIGHT OF SLEEP RESTRICTION

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Sleep-deprived people, or those performing extended monotonous tasks, can exhibit brief episodes when performance is suspended and they appear to fall asleep momentarily – behavioural microsleeps (BMs). BM rates have been shown to be highly variable between normally-rested people but relatively stable between sessions. This study aimed to determine whether there is a relationship between BM propensity when normally-rested or after a night of sleep restriction (4 h time-in-bed) and measures of sleep (i.e., wrist actigraphy, Epworth Sleepiness

Scale, Pittsburgh Sleep Quality Index, and Horne-Ostberg Morning-Eveningness Questionnaire). BMs were identified based on eye-video and tracking response characteristics during a continuous 20-min tracking task undertaken during the afternoon (1.30 or 2.30pm). Analysis was completed on data from n = 8 healthy people (age 26.3 ± 5.6 y (mean ± SD) [5 F, 3 M]). Mean actual sleep was 8.1 ± 1.0 h for the night prior to the normally-rested session and 3.5 ± 0.2 h for the night prior to the restricted session. Sessions were 1 week apart and counterbalanced. There was an increase in the number of BMs from the normally-rested to restricted session (mean 2.5 vs 33.0, p = .047, range 0–10 vs 0–100). There was a strong correlation between BM propensity in the restricted session and sleep efficiency during the week prior to the sleep restricted night (r = 0.85, p = .007). There were also trends for correlations between BM propensity in the restricted session and sleep efficiency (r = 0.61, p = .10) and sleep onset latency (r = –0.64, p = .09) during the sleep restricted night. High sleep efficiency is equivalent to a low proportion of arousal time during the sleep period. Unexpectedly, the correlations and trends were in the direction that people who had higher sleep efficiency and shorter sleep onset latencies had more BMs. These findings may indicate that, paradoxically, high sleep efficiency and, perhaps, short sleep onset latency are related to greater vulnerability to sleep restriction. While intriguing, these findings will need to be confirmed in a larger group.

AS-12-1

SLEEP AND CIRCADIAN GENES: PREDICTORS FOR RESPONSE TO SLEEP RESTRICTION

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Sleep loss causes sleepiness and fatigue, as well as errors and accidents that are due to its adverse neurobehavioral effects on alertness, cognitive functions and mood. Recent evidence, however, indicates that healthy adults show significant, trait-like (phenotypic) differences in the extent to which they experience such neurobehavioral deficits when exposed to either acute total sleep deprivation or chronic sleep restriction. Thus far, such differences have not been explained by individuals' baseline functioning or by a number of other potential predictors including prior sleep history, circadian chronotype, and demographic factors. Data collected in carefully controlled laboratory experiments suggest that common genetic variations involved in sleep-wake and circadian rhythm regulation–including those found in the human leukocyte antigen (HLA) DQB1*0602 gene, the PERIOD 3 (PER3) gene, and the CLOCK gene–may underlie these large phenotypic differences in neurobehavioral vulnerability to chronic sleep restriction in healthy adults and may thus serve as putative biomarkers. Determination of biomarkers of individual differences to sleep loss will help identify those individuals who are most in need of prevention of sleep debt and in need of countermeasures for sleep loss; further our understanding and management of vulnerability to excessive sleepiness due to common sleep and medical disorders; and help inform public policies pertaining to the need for adequate sleep.

AS-12-2

THE PER3 VNTR AND SLEEP AND CIRCADIAN INTERACTION IN HUMANS AND ANIMAL MODELS

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Sleep and circadian systems are independent but interact to modulate their function. This is demonstrated in everyday life by jet lag and experimentally in forced desynchrony protocols. A distinct set of interacting clock genes forms the molecular basis for circadian rhythmicity, but much less is known concerning the genetic basis for sleep. However, there is growing evidence showing that a number of clock genes also have significant roles in the regulation of sleep architecture and homeostasis. *Period3* (*Per3*) plays a redundant role within the mouse central circadian clock, but a variable number tandem repeat (VNTR) polymorphism within human *PER3* is associated with diurnal preference, sleep homeostasis, cognitive vulnerability to sleep loss, and fMRI-assessed brain activity in response to sleep loss. We have investigated subjects genotyped for this polymorphism in sleep manipulation and forced desynchrony protocols. We have made multiple measures of circadian markers, sleep, cognition, and peripheral gene expression. We have also measured sleep, circadian activity rhythms, and gene expression in animal models either lacking PER3, or with the human VNTR polymorphism knocked-in. From these experiments, we further demonstrate the important interaction between sleep and circadian systems, and confirm the role for PER3 within this interaction.

AS-13-3

TIME TRENDS IN SLEEP DISTURBANCE AND DURATION – AN INTERNATIONAL REVIEW

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Background: Despite the enormous growth of sleep research over the past four decades, little is known about secular trends in sleep disturbance. Concerns over decreasing sleep durations, technology that may limiot sleep and the "24/7" lifestyle dominate the public, and to soem extent scientific discourse as progressively more research points to sleep disturbance as a health risk factor.
Methods: This presentation will cover(i) The background and development of these ideas(ii) Recent data on time trends in a number of aspects of sleep – adolescent sleep duration and insomnia(iii) Present the results of a systematic review of all published studies evaluating temporal trends in adult sleep duration.
Results: Self-reported adult average sleep duration had increased in 7 countries and had decreased in 6 countries. Inconsistent results were found for the United States and Sweden.
Conclusion: Data from less biased nationally representative studies does not support the thesis that sleep durations are decreasing globally. Measurement and reporting issues for future use will be identified.

AS-14-1

MRI STRUCTURAL AND SPECTROSCOPIC MARKERS OF DISTURBED SLEEP IN POSTTRAUMATIC STRESS DISORDER

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High field strength MR structural and spectroscopic imaging techniques now have the sensitivity to detect markers associated with sleep quality. This presentation will provide an overview of sleep and imaging for the symposium, "Advances in Neuroimaging of insomnia." This presentation will present data linking sleep quality in subjects with Posttraumatic Stress Disorder to the volume of CA3/dentate gyrus hippocampal subfield, and to concentrations of GABA, glutamate, and N-acetylaspartate in cortical brain regions. These findings indicate that poor sleep quality is associated with volume loss of the CA3/dentate subfields and low concentrations of GABA. The discussion will highlight converging evidence that impaired sleep may adversely affect adult neurogenesis.

AS-14-3

IMAGING IN PRIMARY INSOMNIA: STRUCTURE, FUNCTION, SLEEP, WAKE

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Primary insomnia is a prevalent sleep disorder that frequently and significantly impairs waking function. Insomnia confers significant risk the development of a new onset or recurrent major depressive disorder, as well as other psychiatric disorders, such as anxiety and substance abuse disorders. Complaints regarding daytime function across both cognitive and affective domains are common in insomnia, such as tiredness, difficulty concentrating, and impairments in affective function, such as low mood, and difficulty with interpersonal relationships. Yet, our understanding of the neural mechanisms that contribute to such complaints is not well understood. Using Positron Emission Topography studies, we have previously found higher global cerebral glucose metabolism during NREM sleep in wake-promoting regions, as well as reduced glucose metabolism during wakefulness in both cortical and subcortical regions in primary insomniacs compared to good sleeper controls. We will present findings from both structural and functional magnetic resonance imaging studies focusing on the neural circuitry underlying emotion regulation in individuals with primary insomnia. Such research into sleep disturbances, their consequences for waking function, and their distinct neuroanatomic basis can provide important insights regarding the potent risk relationship between primary insomnia and mood disorders.

AS-14-6

STRUCTURAL AND FUNCTIONAL NEUROIMAGING STUDIES IN PRIMARY INSOMNIA AND GOOD SLEEPER CONTROLS

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Primary insomnia afflicts approximately 3–5% of the adult population and is characterized by problems to fall asleep, to maintain sleep or the experience of non-restorative sleep. Additionally, patients with insomnia suffer from daytime consequences like tiredness or deficits in concentration or attention. In recent years several studies using neuroimaging methods have been published investigating primary insomnia. Own work is focussing on structural and functional neuroimaging studies with MR. In a pilot study with 8 patients we were able to demonstrate reduced bilateral hippocampal volumes in chronic insomnia compared to good sleepers. Another functional study revealed that the alpha rhythm is instigated by the same neuronal centers in insomnia and good sleepers. Ongoing work includes a structural approach and several paradigms looking at emotions and attentional bias in insomnia. 24 patients and 30 good sleepers were included in these studies. These new results will be presented at the meeting.

AS-15-1

NEW WAYS TO UNDERSTAND INSOMNIA: BRAIN IMAGING AND WEB-BASED PHENOTYPING

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Affecting about 10 percent of the population, insomnia is the most common health complaint in general practice. While insomnia has serious consequences, e.g. being the major risk factor for the development of psychiatric disorders, our understanding of its brain mechanisms is very limited. Investigations into the causes and consequences of insomnia have to a large extent applied theoretical frameworks and methods that are rooted in psychology. The present lecture provides examples that illustrate the value of application of the arsenal of brain imaging tools that have been developed in human cognitive neuroscience, to tackle the underlying mechanisms of insomnia. While some deviations recover after therapy, others do not, in the very same patients assessed on the same day. The unchanging abnormalities may be heritable traits involved in the risk of developing insomnia. For example, while attenuated prefrontal fMRI BOLD activation during word fluency recovered, attenuated activation of the head of the caudate nucleus during a planning task did not. Also, abnormal intracortical excitability demonstrated using transcranial magnetic stimulation did not recover after treatment. Voxel-based morphometry showed a lower volume of gray matter in areas that are part of the default mode network including the orbitofrontal cortex, where volume showed a strong negative correlation with insomnia severity. This area seems involved in disturbed hedonic evaluation, which we indeed found to be compromized in insomniacs. Concertedly, we found new angles on mechanisms of vulnerability. We now look for volunteers for extensive web-based characterization of phenotypes of good and poor sleepers on www.sleepregistry.eu.

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AS-15-2

PHENOTYPING COGNITIVE FACTORS ANDCORTICAL AROUSAL IN PSYCHOPHYSIOLOGICALINSOMNIA

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Although insomnia is very common, exactly how it develops and what are its crucial maintaining factors remain unclear. There is some evidence for phenotypical features that are behavioural (e.g. conditioned arousal, sleep-incompatible behaviour), and cognitive (e.g. sleep preoccupation, dysfunctional beliefs). However, the insomnia phenotype lacks objective markers, not least for the central phenomena of cognitive arousal. This paper reviews a range of cognitive perspectives on insomnia (e.g. dysfunctional thinking, performance anxiety, cortical arousal, sleep misperception, automaticity, attentional processing). Emphasis is placed upon models that yield testable hypotheses about putative cognitive processes in its aetiology and perpetuation. Experimental studies that have adapted methods from other fields of adult psychopathology research are highlighted because they yield valuable conceptual insights and offer novel measurement paradigms. An argument is made that because sleep normalcy is a relatively automatic process, it is vulnerable to inhibition (in insomnia) by selective attention upon sleep and by direct attempts to control its expression. Computerized tests of information-processing bias may offer one objective means of appraising mental processes in insomnia. Studying the interplay between subjective experience, cognitive performance and cortical arousal in insomnia may be a fruitful line of future research.

AS-16-1

NIGHTLY HYPOXEMIA IN THE ELDERLY AND ITS POSSIBLE LINK TO DEMENTIA

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Hypoxemia in elderly persons is a known phenomenon based on physiologic and pathophysiologic developments with growing age. However the prevalence of especially nightly hypoxemia and its influence on frailty and cognitive impairment of geriatric patients might be underestimated. Recently a Norwegian study showed that more than 30% of all elderly inpatient patients had a nightly hypoxemia with a SaO2 <90% more than 30% of total sleep time.
The studies on sleep disordered breathing and brain damage through episodes of short intermittent hypoxia have highlighted the topic to some account and nurtured speculations on a link between dementia and hypoxemia in elderly patients with cognitive impairment.
In a multicenter international study in Asia and Europe running since November 2010 we study the correlation between the prevalence for cognitive impairment assessed through the Mini Mental Status Exam and various other cognitive function tests and the prevalence of nightly hypoxemia measured via continuous pulse oximetry in elderly hospitalized patients aged over 75 years.

AS-16-2

FRAILTY AND INTERMITTENT HYOPEMIA IN A SAMPLE OF OLDER SUBJECTS

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Background: Frailty and sleep apnea are common entities in the elderly. Frailty causes dependency and need of care. The prevention of frailty is a major topic in geriatrics. However, the relationship between sleep apnea and frailty is hardly studied.
Methods: In a prospective pilot study, we examined the relationship between the presence of at least one of the five Frailty criteria proposed by Fried and sleep apnea. Patients were eligible, if they able to communicate and had no dementia. Sleep apnea was diagnosed by overnight pulse oximetry. Sleepiness was obtained by the questionnaire of Siegrist and the Pittsburgh Sleep Quality Index [PSQI].
Results: 42 patients with a mean age of 82 ± 7 years were enrolled. Fifteen (36%) patients were male, 27 (64%) were female. Twenty-eight (67%) patients had at least one frailty criterion. Patients with Frailty criteria had significantly more often daytime sleepiness (1/14 vs. 17/28, $p < 0.001$), had a significantly higher incidence of severe sleep apnea with an oxigen desaturation index >30/h ($p < 0.04$) and had a lower mean nocturnal oxygen saturation (95 ± 2% vs. 91 ± 4%, $p < 0.02$).
Conclusion: Our small pilot study shows an association between the presence of at least one frailty criterion, daytime sleepiness and severe sleep apnea. Given the high frequency of both phenomena and regarding the clinical relevance of frailty, prospective studies are warranted to proof of a causal relationship between sleep apnea and Frailty.

AS-17-1

EVALUATION OF THE HUMAN CIRCADIAN CLOCK USING HAIR FOLLICLE CELLS

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Circadian behavioral and physiological rhythms are driven by autonomous oscillation of clock gene expression. Thus, a clear understanding of the circadian core clock requires a thorough examination of the rhythmic expression of clock genes. Although more than ten years have past since the first mammalian clock gene was identified, there are still only a handful of reports on in vivo observation of circadian expression of human clock genes. The lack of an established method for evaluating circadian clock gene expression has markedly impeded the progress for studying human circadian rhythms. Here we report a convenient and less invasive method for detecting human clock gene expression using biopsy samples of hair follicle cells from the head or chin. We show that the circadian phase of clock gene expression in hair follicle cells reflects that of individual behavioral rhythms, demonstrating that this strategy is appropriate for evaluating the human peripheral circadian clock. Furthermore, using this method, we indicate that rotating shift workers suffer from a serious time lag between circadian gene expression rhythms and lifestyle. Researchers in the field of circadian rhythms can easily adopt our experimental strategy using hair follicle cells, without specialized experimental techniques. Qualitative evaluation of clock gene expression in hair follicle cells, therefore, may be an effective approach for studying the human circadian clock even in the clinical setting.

AS-17-2

LIGHT EXERTS POWERFUL NON-VISUAL EFFECTS IN HUMANS

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Environmental conditions such as light, sound, temperature, etc. play an important role in the control of sleep and wakefulness. Light is certainly the most regularly occurring stimulus in the environment. The challenge of a daily change of the lightdark cycle has profound impact on a wide range of biological functions and behavior. In humans, light is intuitively linked with an alert or wakeful state. On the other hand, closing the eyelids or dimming or turning off the lights has a very powerful soporific effect. Compared to the effects of light on human circadian rhythms, little attention has been paid to its acute alerting action. The influence of illuminance level, exposure duration, timing and wavelength of light needed to evoke alerting responses in humans, as well as their temporal relationship to light-induced changes in endocrinological and electrophysiological sequelae of alertness, clock gene expression, sleep and cognition will be summarized. Furthermore, our new data on low intensity blue-enriched and backlit LED screen light will be presented, which give evidence for light impacting on higher cognitive function, such as declarative memory and for individual differences in the response to short-wavelength light. We hope that our results will help to create optimized lighting conditions for work places and homes.

AS-18-1

SLEEP PHENOTYPING VALIDATES NEW MOUSE MODELS OF AFFECTIVE DISORDERS

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Impaired sleep is a key premorbid symptom that is often accompanied by affective disorders, e.g., major depression. However, its mechanism is rather complex, and differentiating its causalities from those of depression undergoes hardships. Depressed patients demonstrate characteristic changes in sleep architecture even before symptoms fully develop. Therefore, EEG activity must embrace a specific facet that possibly serves as a susceptibility marker for depression. In our institute, several animal models have been generated to investigate stress-related disorders. Monitoring EEGs in those animals can be used to select the most appropriate study model. Upon my presentation, sleep phenotypes in three different lines of mouse models will be compared; a conditional mouse mutant that chronically overexpresses corticotropin-releasing hormone (CRH) in the entire central nervous system (CRH-COE-Nes) or only in the forebrain including limbic structures (CRH-COE-Cam), a humanized mouse mutant in which the murine P2RX7 gene was substituted by the disease-associated variants of human P2RX7, and a bi-directionally bred mouse model of trait anxiety showing high and low anxiety-related behavior. All these mouse lines demonstrated sleep alterations, particularly fragmented sleep episodes and enhanced REM sleep. Sleep analysis highlighted significance of CRH-COE-Cam and heterozygous P2RX7 mutant mice that failed to show any particular changes in behavior. Measuring sleep is an only behavioral test applicable similarly both in humans and animals and can be a powerful tool to detect genetic influences on psychiatric diseases. Sleep phenotyping is thus requisite to validate new animal models of depression and supports discovery of close correlations between sleep and mental dysregulation.

AS-18-2

NEUROBIOLOGICAL MECHANISMS OF THERAPEUTIC SLEEP DEPRIVATION IN DEPRESSION

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Sleep deprivation (SD) is powerful antidepressant treatment which shows antidepressent responses within hours in 40 to 60 % of depressed patients. In more than 80% of the responders to SD a relapse into depression occurred after the recovery night. In addition, SD serves as an excellent tool to examine the neurobiological disturbance of depression and may profoundly contribute to the development of new specific and more rapidly acting antidepressant strategies.The reason why sleep deprivation works and relapses occur is still unclear. A key to solve this problem is to include the current knowledge about the neurobiological disturbance of depression into research with a focus on neurobiological aspects of sleep and SD (sleep EEG, neuroendocrinology, neurochemistry, chronobiology). Based on findings from these different areas different strategies to stabilize the antidepressant effect of SD have been applied. The lecture addresses these above mentioned topics including own studies in which neurobiological mechanisms of SD have been examined and an augmentation and stabilization of the effects of sleep deprivation has been performed by different neurochemical approaches.

AS-19-1

ETHNIC DISPARITIES IN CPAP USAGE: QUANTITATIVE EFFECTS OF SOCIOECONOMIC STATUS, HEALTH LITERACY AND SELF-EFFICACY

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We performed a prospective study of patients referred for CPAP treatment, quantitatively investigating usage, socioeconomic status, health literacy and self-efficacy, and gathering qualitative data through focus groups.

Consecutive CPAP-naive patients ≥18 years of age referred for treatment were included. After one month of CPAP, objective use was compared by ethnicity, Epworth Sleepiness Scale, Self-Efficacy Measure for Sleep Apnea, Rapid Estimate of Adult Literacy in Medicine, the area-based New Zealand Deprivation Index, New Zealand Individual Deprivation Index, educational history, income and employment data. Multivariate logistic regression was undertaken using univariate predictors of CPAP compliance ≥4 hours per night, as well as ethnicity (Maori/non-Maori). A sub-set of patients attended standardised ethnic-based focus groups, where they were encouraged to share their experiences with CPAP.

Usage data were available for 126 patients (mean ± SD apnea-hypopnea index 57.8 ± 38.8 events/hour). Maori (n = 25) used CPAP less than non-Maori (median 4.68 IQR 2.24 hours/night versus median 5.33 IQR 2.61 hours/night; p = 0.05), and were over-represented in areas of low socioeconomic status (p = 0.05). There were no significant relationships between use and subjective sleepiness, self-efficacy or health literacy. After controlling for ethnicity, not completing higher education and high individual deprivation were significant independent

predictors of not reaching ≥ 4 hours/night compliance (odds ratio 0.25, 95% CI 0.08–0.83, p = 0.02; odds ratio 0.10, 95% CI 0.02–0.86, p = 0.04 respectively). Focus groups of Maori, Pacific and European patients emphasised the importance of role models.
The disparity in CPAP usage and compliance demonstrated between Maori and non-Maori can be explained in part by lower education levels and socioeconomic status. An intervention to address the disparity should encompass these factors, as well as drawing on suggestions from patients of different backgrounds.

AS-19-2

THE IMPACT OF SLEEP CONSULTATION PRIOR TO A DIAGNOSTIC POLYSOMNOGRAM ON CPAP ADHERENCE

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Background: Polysomnograms (PSGs) are routinely ordered by non-sleep specialists. However, it is unknown whether a sleep specialist consultation prior to a diagnostic PSG influences adherence to continuous positive airway pressure (CPAP) therapy.
Methods: CPAP was set up at home and objective adherence was remotely monitored during the first 30 days of therapy. Physicians who ordered PSGs were divided into 2 groups: sleep specialists and non-sleep specialists. This study was done at the University of Chicago Sleep Disorders Center and included 403 patients with obstructive sleep apnea who had CPAP adherence data available.
Results: Mean (± standard deviation) age was 52.5 ± 14 years; 47% were men and 54% were African American. Mean daily CPAP use was greater in patients who were referred by sleep specialists (n = 105; 279 ± 179 min/day) compared to patients referred by non-sleep specialists (n = 298; 219 ± 152 min/day, p = 0.005). In the linear regression model adjusting for several covariates, only two predictors were significantly associated with CPAP adherence. A sleep specialist consultation prior to the diagnostic PSG was associated with 58.2 minutes more per day (p = 0.002) and African American race was associated with 56.0 minutes less per day (p = 0.002) of CPAP use.
Conclusions: In this cohort study, CPAP adherence was significantly higher with a sleep specialist consultation prior to the diagnostic PSG. In addition, African American race was associated with worse adherence to therapy. A better understanding of predictors of CPAP adherence may be useful in identifying patients that may benefit from a sleep specialist consultation prior to ordering a diagnostic PSG.

AS-20-1

SLEEP BRUXISM FROM BENCHSIDE TO CHAIRSIDE

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Sleep bruxism is the third most common parasomnia, with a reported prevalence in childhood of 14–46% to 6–8% in the adult population. Various risk factors have been associated to sleep bruxism, such as other parasomnias (i.e., sleep walking), some medical/psychological conditions (i.e., sleep-disordered breathing, ADHD, headaches), various medications (i.e., methylphenidate, SSRIs), and concomitant oral habits. Persistent sleep bruxism is often associated with orofacial pain, headache, dental injury and bed partner complaints. Relatively recent studies in animal models and in humans have shown that sleep bruxism is centrally generated, in association with cortical arousal, increased cardiovascular activity and increased respiratory amplitude. The animal models allows for a controlled manipulation of stress, catecholamine concentrations and muscle activity. However, the complete pathophysiology and causes are still unknown; thus multidisciplinary research spanning from bench to bedside is relevant to help open new prevention/treatment avenues and managing concomitant orofacial pain. The intention of this symposium is to present the status of the current multidisciplinary knowledge on sleep bruxism and to highlight the future research needs. The targeted audiences are physicians and dentists.

AS-20-2

SLEEP BRUXISM: FROM HUMAN RESEARCH TO CLINICAL PERSPECTIVE

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Sleep bruxism (SB) is a sleep-related motor disorder reported by 14–38% of pediatric and 6–8% of adult populations. SB episodes are characterized by tonic or phasic activities (rhythmic masticatory muscle activity) of the masseter and temporalis muscles that can be observed on electromyographic recordings performed during sleep. SB has been frequently associated with other disorsers, such as other parasomnias (i.e., sleep walking), sleep-disordered breathing (i.e., snoring and obstructive sleep apnea), some medical/psychological conditions (i.e., ADHD, headaches), orofacial pain, temporomandibular disorders, various medications (i.e., methylphenidate, SSRIs), and other concomitant oral habits (i.e., wake-time tooth clenching). Although the etiology of SB remains unknown, its physiopathology during sleep is partly explained by a re-activation of cerebral and autonomic nervous systems occurring during periods of sleep instability (a process called sleep arousal). In facts, recent polysomnographic studies in humans have shown that SB is more likely centrally generated, and often associated with increased in sympathetic tone, blood pressure and respiratory amplitude. Moreover, genetic predisposing factors and psychosocial components (such as anxiety and stress sensitivity) seem to play a role in the mechanisms that regulate the occurrence of SB. Probably, SB genesis could not be explained by a single cause and causative factors are most likely variable between patients. Thus, further research in experimental and clinical settings is needed to elucidate the etiologic and risk factors of SB, and its possible impact on the overall health of SB patients.

AS-20-5

SLEEP BRUXISM: TRANSFER KNOWLEDGE BETWEEN HUMAN RESEARCH AND BASIC SCIENCE

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There are various oromotor events during sleep. Sleep bruxism (SB) patients exhibit the increased number of oromotor events during sleep compared to normal subjects, and a frequent occurrence of rhythmic masticatory muscle activity is characteristic to SB patients. Polysomnographic studies in humans have revealed that SB is centrally generated in association with sleep states, cortical arousal fluctuation and increased

cardiovascular activity. However, neurophysiological mechanisms underlying the jaw motor activation in SB patients are still unknown. For studying such mechanisms, animal models with oromotor activity similar to SB are indispensable. Ideally, they should present physiological and pathological signs that are observed for SB in humans. Initial study done in the naturally sleeping animals for developing animal models has provided several findings regarding: 1) the differential modulation of motor activities in masticatory and neck muscles; 2) the association between jaw muscle activity and arousal/autonomic activities; 3) the effects of pharmacologic agents on sleep and jaw muscle activity; and 4) the characteristics of jaw muscle EMG bursts in association with jaw movement kinesiology. These findings, combined with the results from human studies, suggest that jaw motor activity during sleep reflects a variety of interactions between trigeminal motor and sleep regulatory systems and can not be recognized as a consequence of a single neural process. Further efforts are needed to develop adequate animal model relevant to translational research that addresses clinical and biological questions.

AS-21-1

DECOUPLING OF SLEEPINESS FROM SLEEP TIME AND INTENSITY DURING CHRONIC SLEEP RESTRICTION: THE ROLE OF ADENOSINE AND NOREPINEPHRINE SYSTEM

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The sleep responses to chronic sleep restriction (CSR) are fundamentally different from those to short-term total sleep deprivation. Specifically, when CSR continues for several consecutive days, animals fail to express homeostatic increases in sleep time and sleep intensity. These allostatic responses of sleep to CSR have been shown in both humans and rats. Here, we measured: 1) sleep latency to assess sleepiness during CSR, and 2) brain adenosine receptor and adrenergic receptor mRNA levels to determine neurochemical mechanisms underlying different sleep responses to CSR. Rats underwent 18h sleep deprivation (SD) and 6h sleep opportunity (SO) each day for 5 days, followed by 3 days of full recovery sleep (R1-R3). The 6h SO was given during the first half of the 12h light period. Another group of rats underwent the same protocol but their brains were collected at the end of each SD period to measure receptor mRNA levels. After 18h SD on the first sleep restriction (SR) day, the total sleep time and NREM delta power were significantly increased during the 6h SO, compared to the corresponding baseline level. However, those compensatory increases were absent from SR days 2 to 5. However, sleep latencies during 6h SO were significantly reduced to 3 min or less from SR1 through SR4, compared to 9.1 min on baseline day. Throughout the 5 days of SR and recovery day 1, adenosine A1 receptor (A1R) mRNA level was increased in the basal forebrain while adenosine A2a receptor (A2aR) was decreased in the frontal cortex. Beta-adrenergic receptor mRNA levels were significantly decreased in the anterior cingulate cortex only on SR1. Rats exposed to chronic sleep restriction do not sleep longer or deeper even though they continue to experience elevated sleepiness. We propose that there are at least two different sleep regulatory systems in the brain: one mediating sleepiness and the other mediating sleep amount. Our findings suggest that changes in the basal forebrain A1R and the cortical A2aR tone may mediate sleepiness, whereas the cortical beta-adrenergic receptor tone may mediate sleep time and intensity.

AS-21-2

TIME-OF-DAY MODULATION OF SLEEP HOMEOSTASIS AND ADAPTATION IN A RAT MODEL OF CHRONIC SLEEP RESTRICTION

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Chronic sleep restriction (CSR) is a common condition in modern societies. It impairs cognitive performance, and is associated with increased risks for various health problems, such as cardiovascular disease, diabetes and obesity. To understand the neurobehavioural impacts of CSR, we studied changes in sleep patterns during and following CSR, using a rat model of CSR ('3/1 model'). In this model, cycles of 3 h of sleep deprivation (SD) and 1 h of sleep opportunity (SO) are continuously imposed for 4 days (i.e., totaling 18 h of SD and 6 h of SO per day), followed by 2 recovery days. Sleep propensity is known to be modulated by both circadian and homeostatic processes, and this model permits analysis of time-of-day effects on responses to CSR. The 3/1 model is also consistent with the polyphasic sleep/wake cycles of rats. EEG and EMG were recorded in adult male rats before, during, and following the 4-day 3/1 CSR starting at lights on under a 12/12 h light/dark (L/D) cycle. During CSR, total sleep time was reduced by ~60%. During the SO periods, increases (above baseline levels) in both non-rapid eye movement sleep (NREMS) and REMS were sustained over the 4 days, while initial increases in NREMS EEG delta power (a measure of sleep intensity/drive) gradually declined. Normal daily rhythms in NREMS and REMS amounts persisted during SO, whereas daily rhythms in NREMS delta power were reduced in amplitude. Despite significant cumulative sleep loss, compensatory responses during the post-CSR recovery period were modest, and gated by time of day. Specifically, NREMS rebound was delayed until the late D phase on the first, as well as the second, recovery day, while REMS rebound occurred in the early L, as well as the late D, phase of the first recovery day; NREMS delta power was below baseline levels during the L phase of both recovery days. The amounts of NREMS, REMS, and EEG delta energy lost during CSR had not been recovered at the end of the second recovery day. These results suggest that the 4-day 3/1 CSR protocol may trigger both homeostatic and other regulatory (allostatic?) processes that are modulated by time of day.

AS-22-1

REMOTE CONTROL OF SLEEP-WAKE STATES USING VIRAL VECTORS

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Over the past 10 years, researchers have developed an impressive armamentarium of molecular and electro-physiological techniques for probing the neural circuitry subserving sleep-wake regulation. While these tools and techniques have provided significant insight into the CNS circuitry and neurotransmitter systems regulating sleep, each has non-trivial limitations.

For example, both pharmacological and global knockout approaches have limited temporal and spatial resolution, whereas lesion approaches can produce collateral damage to adjacent brain structures that may in turn produce effects on sleep behavior and the cortical electroencephalogram beyond those due to the lesion of the target site. Importantly, however, these technical and interpretational concerns are largely

obviated in newer conditional genomics models. The newer conditional technologies encompass a wide range of approaches, from conditional deletion of genes based on the Cre/loxP technology to RNA interference to the modulation of neuronal activity using genetically engineered optical switches to the in vivo reversible silencing and activation of neurons in freely behaving animals. In this symposium, we will highlight some of these more recent and advanced molecular biological techniques for investigation of mechanisms of sleep-wake regulation, with a particular emphasis on the use of viral vectors for genetic manipulation of the circuitry governing sleep-wake regulation.

AS-22-2

THE ROLE OF ADENOSINE A_{2A} RECEPTORS IN THE NUCLEUS ACCUMBENS FOR SLEEP-WAKE REGULATION

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Adenosine promotes sleep through the activation of A_{2A} receptors. A_{2A} receptors are densely expressed on striatopallidal neurons of the basal ganglia, where dopamine D_2 receptors are co-expressed with A_{2A} receptors and contribute to the control of locomotion, motivation, and addiction, all activities that require wakefulness. Abilities to maintain arousal are compromised under low dopamine conditions such as Parkinson's disease, but the extent to which A_{2A} receptors in the basal ganglia contribute to the regulation of wakefulness is not known. We generated striatopallidal-specific A_{2A} receptor knockout mice, based on the Cre/lox technology, and focal A_{2A} receptor knockdown rats, by using local infection with adeno-associated virus carrying short-hairpin RNA of A_{2A} receptors to silence the expression of A_{2A} receptors. By using these powerful tools for site-specific gene manipulations, we investigated the role of A_{2A} receptors in the basal ganglia for wakefulness in response to arousing stimuli, such as caffeine and light transition. We found that the deletion of the A_{2A} receptors selectively in the nucleus accumbens shell results in abrogation of the effect of caffeine on wakefulness, but did not change the amount of basal wakefulness during the sleep period. However, enhanced wakefulness can be observed in the waking period when A_{2A} receptors are focally removed from the nucleus accumbens. These observations demonstrate that A_{2A} receptors in the nucleus accumbens are required for the arousal effect of caffeine by activating pathways that have traditionally been associated with locomotion and motivational behaviors in the basal ganglia. We therefore propose that the adenosine/A_{2A} system in the nucleus accumbens acts as an accessory nucleus to a putative flip-flop arrangement between arousal-promoting regions and sleep-promoting neurons of the preoptic area for sleep/wake regulation.

AS-22-3

OREXIN/HYPOCRETIN NEURONS SPECIFIC CONTROL OF GENE EXPRESSION REVEALS ITS PHYSIOLOGICAL ROLE IN VIVO

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Orexin/hypocretin is a neuropeptide produced in neurons which are sparsely distributed in the lateral hypothalamic area (orexin neurons). Although specific ablation of orexin neurons results in sleep disorder narcolepsy, its physiological role on the regulation of sleep/wakefulness has not been completely understood. To reveal this, we generated transgenic mice in which orexin neurons specifically express tetracycline transactivator protein (tTA) (orexin-tTA mice). These mice enable to control the expression of specific gene in the orexin neurons in vivo since tTA induces gene expression to bind tetracycline response element (TetO). To confirm specific regulation of gene expression in the orexin neurons by tTA, orexin-tTA mice were bred with TetO red fluorescent protein (RFP) mice. In orexin-tTA; TetO RFP double transgenic mice brain, 85% of orexin-immunoreactive (ir) neurons expressed RFP. No ectopic expression of RFP other than orexin-ir neurons was observed throughout the brain. This result suggested that orexin-tTA mice enable to control the expression of gene in the orexin neurons just to breed with various TetO mice. Additionally gene expression could be temporally controlled since tTA lost its function to induce gene expression in the presence of doxycycline (DOX). Therefore, application of DOX in chow inhibits gene expression induced by tTA, but remove DOX from chow induces gene expression. These results suggest that orexin-tTA mice are useful tool to study its physiological role in vivo.

AS-23-1

ADENOSINE, HOMEOSTASIS AND BRAIN ENERGY

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Adenosine is a ubiquitous nucleoside that links the two central processes controlling sleep homeostasis and brain cellular energy metabolism. Recent research from our group has provided extensive evidence on the somnogenic role of extracellular adenosine on the wakefulness active neurons of the basal forebrain. Compared to sleep, extracellular levels of adenosine in the basal forebrain are higher during wakefulness, and increase further with prolonged wakefulness. Acting via A1 receptors, adenosine inhibits cortically projecting and wakefulness active cholinergic neurons, as well as GABAergic and other noncholinergic neurons, and thus induces a homeostatic sleep response. Moreover, the action of adenosine on the A1 adenosine receptor activates a second messenger pathway leading to a positive feedback regulation of the A1 receptor, and increasing the sensitivity of wakefulness active neurons to the inhibitory effects of adenosine. More recent work from our laboratory shows that a delayed increase in extracellular adenosine and its receptor also occurs in cortex. Thus adenosine serves as an inhibitory neuromodulator and promotes homeostatic sleep response in brain.
The changes in the levels of adenosine largely reflect the breakdown of the cellular high energy molecule, adenosine triphosphate, when energy consumption associated with cellular activity is increased, as during wakefulness. Thus, our theory about how adenosine functions during sleep and wakefulness derives from the fact that it is a byproduct of energy metabolism, and its negative feedback on cellular activity serves as a homeostatic regulator of energy in the brain. This is in accord with the hypothesis that energy restoration is one of the functions of sleep. In this talk I will present data in support of an interrelationship between adenosine and its roles in sleep and brain energy homeostasis.

AS-23-2

SLEEP IS FOR A SURGE IN BRAIN ENERGY

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An often postulated function of sleep is that it restores energy expended by the brain during active waking. While the brain comprises only 2% of the body weight, it receives 15% of cardiac output and uses 20% of total body oxygen consumption and 25% of total body glucose utilization. The extensive energy needs of the brain are met by continual supply of blood oxygen and glucose, because the brain is unique in that it cannot store large amounts of energy–yielding lipids or glycogen. Consequently, adenosine triphosphate (ATP), derived from the metabolism of blood glucose and oxygen, is the primary currency of energy in brain. This leads to the important question – Does sleep restore or regulate brain ATP levels, which have been depleted during wakefulness? No direct metrics exist about changing levels of brain ATP during sleep and waking, therefore we propose here a series of experiments to address this fundamental, but unanswered question of the interrelationship between sleep–wakefulness and brain energy balance. Data will be presented in support of the hypothesis that the states of sleep and wakefulness are closely interrelated with brain energy status. The ATP levels in wake-active brain regions will show a surge during sleep that is prevented if sleep is prevented. Here we will present data to show that while sleep–wake state changes regulate the intra– and extra–cellular levels of the regional ATP, and of its metabolite, adenosine, these compounds, in turn, regulate sleep and wakefulness. The data from our experiments also strive to understand the feedback regulatory role of ATP and adenosine in sleep – wake–regulation. The knowledge of the molecular and biochemical processes occurring during sleep–wakefulness that contribute to ATP regulation, and the relationship of ATP levels with the cellular catabolic/anabolic activity, will provide insight into the restorative role of sleep.

AS-24-1

PREOPTIC HYPOTHALAMIC NEURONS ARE ACTIVATED BY HOMEOSTATIC SLEEP PRESSURE

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The preoptic hypothalamus (POH) is a functionally important sleep regulatory region of the brain, as evidenced by results of lesion, stimulation and unit recording studies. Within the POH of rats, the ventrolateral preoptic nucleus (VLPO) and the median preoptic nucleus (MnPN) contain numerous sleep-active neurons, confirmed by unit recording and by sleep-related c-Fos protein expression. While the relationship of neuronal activity in these nuclei to alterations in wake and sleep is established, effects of changing levels of homeostatic sleep pressure on MnPN and VLPO neurons is unknown. We have shown that Fos+ cell counts in the MnPN are elevated after 2 hours of sleep deprivation (SD) compared to 2 hours of spontaneous sleep-waking and 2 hours of recovery sleep (RS). We have also recorded MnPN single unit activity sequentially across periods of baseline sleep-wake, SD and RS. Activity of MnPN units increases progressively during SD such that after 2 hours, waking discharge rates are approximately double baseline waking rates. During early RS, discharge rates are >60% higher than rates during baseline sleep, but return to baseline levels after 90 min of RS. In the VLPO, Fos+ cell counts are significantly elevated after periods of RS compared to SD. Waking discharge of VLPO neurons increase moderately during SD, but VLPO units display sustained increases in discharge during RS compared to baseline sleep. These findings demonstrate that activity of MnPN and VLPO neurons reflects changes in homeostatic sleep pressure. Injections of A2A adenosine receptor antagonist into the subarachnoid space rostroventral to the POH promotes sleep and activates c-Fos expression in MnPN and VLPO neurons. Hence, increases in extracellular adenosine levels in and adjacent to the POH is one mechanism by which sustained waking can alter MnPN and VLPO neuronal activity.

AS-24-2

OPTOGENETIC MANIPULATION OF THE ACTIVITY OF OREXIN NEURONS CONTROLS SLEEP/WAKEFULNESS STATE IN MICE

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Orexin/hypocretin is a neuropeptide produced in the neurons, which are sparsely distributed in the lateral hypothalamic area. The mice lacking prepro-orexin gene or orexin-producing neurons (orexin neurons) show narcolepsy-like phenotypes, a fragmentation of sleep/wakefulness and sudden attack of muscle weakness, cataplexy. Although these facts suggest that the orexin neurons play critical role in the regulation of sleep/wakefulness, it is not clear that how the activity of orexin neurons maintain wakefulness. To study this *in vivo*, a hot technology optogenetics was incorporated. Optogenetics enables to control the activity of neurons by illuminating light. A light-activated neuronal silencer, halorhodopsin or arcaerhodopsin-3, is expressed in the orexin neurons in the transgenic mice. Slice patch clamp recordings of orexin neurons demonstrated that photic illumination silenced orexin neuron. In the light period, acute silencing of orexin neurons *in vivo* synchronized the electroencephalogram and reduced in amplitude of the electromyogram. These are characteristic in slow wave sleep (SWS). This result indicates that activation of orexin neurons is necessary for keeping wakefulness during the light period. Acute photic inhibition of orexin neurons reduced discharge rate of serotonergic neurons in the dorsal raphe (DR) nucleus. Taken together, this study revealed that optogenetics modulation of orexin neuronal activity enabled us to control the transition from wakefulness to SWS in mice. Furthermore, the silencing of orexin neurons and transition to SWS was accompanied by a reduction of the activity of serotonergic neurons in the DR.

AS-24-3

ACTIVATION OF CORTICAL INTERNEURONS DURING SLOW WAVE SLEEP: AN ANATOMICAL LINK TO SLEEP HOMEOSTASIS?

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The Two Process model of homeostatic sleep regulation posits that the timing of sleep results from an interaction between a circadian process (Process C) and a homeostatically-regulated sleep process (Process S). Whereas Process C is linked to neural systems that generate circadian rhythms, the neural basis of Process S is currently unknown. We have identified a population of GABAergic cells in the cerebral cortex that

express neuronal nitric oxide synthase (nNOS) and also express the transcription factor FOS specifically during sleep in three different species. FOS expression in cortical nNOS neurons varies across the diurnal cycle in conjunction with the natural occurrence of sleep; sleep deprivation (SD) experiments further demonstrate that the extent of activation of these cells is proportional to homeostatic sleep drive. Cortical nNOS neurons receive inputs from subcortical sleep-related neurotransmitter systems such as serotonergic and cholinergic neurons. nNOS cells are unique among cortical GABAergic interneurons because they have intracortical efferent projections. nNOS knockout (KO) mice exhibit disrupted sleep architecture and are sleepier than WT mice yet have an impaired ability to respond to SD. Cortical nNOS neurons express the receptor NK1, which enables identification of the sleep-active neurons (SANs) in nNOS KO mice; SANs are activated by SD in the absence of nNOS. Since cortical nNOS/NK1 neurons receive monoaminergic and cholinergic inputs, are active during sleep in proportion to homeostatic sleep drive, and project intracortically, we propose that cortical nNOS/NK1 neurons are critical integrators in the neuronal network that links state-dependent afferent inputs to the generation of cortical slow wave activity and the homeostatic response to SD. Supported by NIH R01 HL059658.

AS-25-1

HOW CHOLINERGIC, GABAERGIC AND GLUTAMATERGIC BASAL FOREBRAIN NEURONS REGULATE SLEEP-WAKE STATES

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Using juxtacellular recording and labeling with Neurobiotin (Nb) of neurons in naturally sleeping-waking, head-fixed rats, we have identified and characterized the discharge properties of cholinergic, GABAergic and glutamatergic basal forebrain neurons across the sleep-wake cycle (Lee et al., JN, 2005; Hassani et al., JN, 2009). We distinguished four pairs or sets of functionally distinct cell groups, each comprised of similarly discharging glutamatergic and GABAergic cells together with cholinergic cells in one group that discharged maximally in W, SWS and/or PS in association with either EEG activity or EMG activity. They represent: 1) W/PS-max active cells (47%), which include cholinergic cells, whose discharge is positively correlated with EEG gamma activity, 2) SWS-max active cells (20%), whose discharge is negatively correlated with EEG gamma activity, 3) W-max active cells (8%), whose discharge is positively correlated with EMG and 4) PS-max active cells (23%), whose discharge is negatively correlated with EMG. Together with our findings from neuroanatomical studies, we conclude that the EEG related W/PS-max and SWS-max cell set/pairs project to the cortex and reciprocally modulate EEG gamma activity, whereas the EMG related W-max and PS-max cell pairs project to the hypothalamus, brainstem or spinal cord and reciprocally modulate muscle tone across the sleep-wake cycle. Following from these findings and conclusions, we created a computational model with inhibitory interconnections between reciprocally related EEG or EMG cell set/pairs and excitatory coupling between similarly related EEG and EMG cell set/pairs. This basal forebrain network has the capacity to generate oscillatory discharge profiles of the intrinsic neurons, cyclic modulation of cortical activation and muscle tone and the cyclic succession of the three states of W, SWS and PS (Cordova et al., SfN Abstracts, 2010).

AS-25-2

ROLES OF PREOPTIC AND ADJACENT BASAL FOREBRAIN NEURONS IN THE CONTROL OF SLEEP-WAKING SWITCH

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The preoptic area (POA) and adjacent basal forebrain (BFB) play an important role in the control of sleep and wakefulness. According to a prevailing current hypothesis, the sleep process starts and ends with the beginning or cessation, respectively, of firing of POA/BFB sleep-promoting neurons. Using the c-fos immunostaining method, two clusters of neurons that exhibit Fos protein expression after sustained sleep, but not after waking, were reported in the rat, first in the ventrolateral preoptic area (VLPO), then in the median preoptic nucleus (MnPO), and have been proposed to be the principal sleep-promoting cell groups within the POA/BFB. However, the sleep/waking-related neuronal activity of the POA/BFB neurons can be known only by recording their unit activity during the sleep-waking cycle. Using extracellular single unit recordings in unanesthetized, head-restrained mice, we therefore recorded a large number (>1500) of single units in the POA/BFB and determined their activity profiles during all sleep-waking states and at state transitions in an attempt to identify sleep-promoting and waking-promoting neurons and determine their anatomical distribution. In order to elucidate the mechanisms of sleep-waking switch, we also recorded a large number of single units in the posterior hypothalamus ($n > 500$) and mesopontine structures ($n > 1500$) deeply involved in the regulation of sleep and wakefulness. Our study showed that sleep-promoting neurons are found throughout the POA/BFB, rather than in specific sites within the POA/BFB and that contrary to the current hypothesis, the sleep process does not start with the activation of forebrain sleep-promoting neurons, but with a cascade of disfacilitation of forebrain and brainstem waking-promoting neurons.

AS-25-3

HOW PROJECTION AND INTER-NEURONS IN THE THALAMUS AND CORTEX MODULATE EEG ACTIVITY ACROSS SLEEP-WAKE STATES

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During slow-wave sleep the field potentials reveal large amplitude slow-waves and during waking state and REM sleep cortical field potentials show activated pattern, composed of fast and low amplitude oscillations. Cortical field potential recordings reflect intracellular activities of neuronal populations. The objective of the present study was to understand how neuronal activities contribute to the generation of field potentials. During slow-wave sleep the membrane potential of cortical neurons undergoes large amplitude fluctuations. The hyperpolarizing phase of membrane potential correspond to depth-positive local field potential components. The depth-negative components of field potentials as well as during waking state and REM sleep the membrane potential of majority of cortical neurons is depolarized and the neurons fire action potentials. During depolarizing components of all these states, the fast-spiking (inhibitory) neurons fired at higher frequencies than other neurons. Conductance measurements demonstrate that inhibitory activities dominate active cortical states. In quiet wakefulness, due to intense firing of inhibitory interneurons, a half of cortical pyramidal neurons is relatively hyperpolarized and these neurons either do not fire action

potentials or fire at very low rates. Intracellular activities of thalamocortical neurons were less investigated during natural states of vigilance. Our current study demonstrates that thalamus contributes to the generation of cortical slow oscillation, although cortical networks are able to produce slow oscillation without any other structure.

AS-26-1

TREATMENT OPTIONS FOR MILD TO MODERATE SLEEP APNEA PATIENTS

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Obstructive Sleep Apnea (OSA) primary health consequences include sleepiness and serious neurocognitive and cardiovascular sequelae. The primary mechanisms by which OSA triggers cardiovascular disease include intermittent hypoxia, generation of negative intrathoracic pressure during occluded breaths and arousals from sleep. Cardiovascular sequelae may include pulmonary and systemic hypertension, congestive heart failure, arrhythmia, myocardial infarction, and stroke. Still, controversy remains as to how much impact the severity of OSA has on cardiovascular consequences, independent of other confounding factors such as obesity, gender and age. Busselton Health Study reported an increase in all-cause mortality amongst moderate to severe OSA patients, while the Wisconsin Sleep Cohort Study reported an increase in all-cause mortality only in untreated severe OSA patients. The effect of CPAP or mandibular advancement splints (MAS) treatment in objective cardiovascular measurements in patients with mild OSA is less clear. Studies evaluating milder OSA cases and cardiovascular consequences will be discussed. Barnes et al. have identified four of 24 mild OSA patients who became normotensive under CPAP therapy, but did not find differences derived from 24 hour blood pressure recordings after CPAP or placebo compared with baseline. While in another study, MAS improved the nocturnal diastolic blood pressure and increased the proportion of subjects with a normal night-time dip in blood pressure only in the MAS group when compared to CPAP. Compliance and complexities of treatment are especially important in milder cases, where subjective improvement may be small and not be perceived as important by the patients. OSA seems to progress from snoring to sleep apnea. Even simple snoring could cause local nervous lesions in the upper airway, and this trauma could be responsible for the progressive nature of the disease. OSA treatment should be considered for primary and secondary cardiovascular prevention, even in milder OSA.

AS-27-1

CENTRAL ROLE OF SLEEP DISORDERS IN MENTAL DISORDERS / DISEASES

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The number of permanently increasing sleep disturbed and neurological patients is alarming in the industrial countries, caused in eastern and western social structures: specially the number of patients with Insomnia, OSAS and with Stroke, TIA, AD and Dementia is increasing. Mostly the causes of the disorders and/or diseases are unkown. Both sleep disorders and neurological diseases leads to a lot of physical, (neuro)cognitive, emotional and social changes and comorbidities. Possibility there is a strong relationship between both kinds of diseases – some sleep disorders could be a predictor for special acute and chronic neurological diseases and could be used as prognosis for it. Particularly the degree of severity of the disease and the length of the therapy having been carried out till now could play an important role in this.Altogether, in Western Europe already suffer more than 10 percent of the population from Sleep-Awake-Disturbances which has to be treated urgently; 800,000 from Sleep Apnea Syndromes and 25,000 from Narcolepsy.Not diagnosed and untreatedly among others these diseases cause on the one hand frequently subjective sorrow with the persons affected and on the other hand accident danger frequently also increased one due to the increased daytime sleepiness or doziness in the traffic and at work.The aim of this symposium is to analyse the physical, cognitive and emotional impairments as well as the quality of life before and after any therapeutical measures from peoples who suffer from sleep disorders or neurological diseases. The necessary therapy time and the degree of severity shall be analysed too. Although the therapeutical effect of some of the therapeutical interventions is confessed, greater, particularly systematic examinations are almost completely missing, however. It comes added to that that in the existing examinations the case numbers are frequently very low and do not withstand a statistical proof.

AS-27-2

POSSIBLE MECHANISM OF CYTOMORPHOLOGICAL AND APOPTOTIC CHANGES IN RAT BRAIN NEURONS INDUCED BY RAPID EYE MOVEMENT SLEEP DEPRIVATION

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Rapid eye movement sleep (REMS) is a complex but unique phenomenon expressed at least in higher vertebrates, including humans. It is present throughout life although its quantity varies with progress in age and maturity and its duration varies with depth of sleep. Its proportion varies in species and it is affected in most of the diseases. Its role has been implicated with almost all psycho-somatic and patho-physiological processes and in severe cases its loss may cause death. As a unified hypothesis it has been proposed that "REMS maintains brain excitability and it serves as House Keeping Function of the Brain" (Mallick and Singh 2011). I will present evidence showing REMS deprivation (REMSD) modulates neuronal cytomorphology and biochemical properties suggesting apoptotic changes and noradrenaline (NA) is a key factor in mediating such effects in rats.

Studies on male wistar rats revealed that REMSD by classical flower pot method caused changes in neuronal size in different brain areas and these changes could be prevented by alpha-adrenergic antagonist, prazosin. The REMSD on one hand caused fragmentation of cellular structural proteins leading to apoptotic changes in neurons, on the other hand, it induced loss of synaptic boutons. As mechanism of action we have found in vivo that experimentally non-cessation of NA-ergic REM-OFF neurons in the locus coeruleus, which is likely to increase NA-level in the brain, induced REMS loss and in vitro, NA indeed affected neuronal membrane properties, oxidation-reduction levels, calcium influx, growth and development and all these effects are dependent on duration of REMSD and NA concentration.

The findings advance our knowledge on the functions of REMS, REMSD associated changes in neuronal properties, its possible mechanism of action, which help us better understand and attempt to counter REMS loss associated disorders.

Acknowledgement: My students for carrying out the experiments. Funding from Indian agencies CSIR, DBT, DST, ICMR and UGC.

Mallick and Singh, Sleep Med Rev, 2011.

AS-27-3

LINKS BETWEEN RBD, RLS, PLM AND M. PARKINSON & LINKS BETWEEN OSAS AND DEMENTIA, DEPRESSION, ANXIETY

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Abstract not arrived.

AS-28-1

LARGE-SCALE FUNCTIONAL BRAIN NETWORKS IN HUMAN SLEEP; INSIGHTS FROM EEG/FMRI STUDIES

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Ultraslow spontaneous fluctuations of the blood oxygen level dependent (BOLD) signal as measured with fMRI show temporal correlations in functionally related networks. Previous EEG/fMRI studies have examined these resting networks during sleep and reported that, in general, functional connectivity was maintained in light sleep. These results are largely in line with EEG studies, which reported increased neocortical connectivity (EEG synchronization) in specific frequency bands during sleep. The breakdown in functional connectivity in deep NREM sleep is in accord with the fading of consciousness and deepening of sleep, but the preservation or even increase in functional connectivity in light NREM sleep stages appears more puzzling and counterintuitive. We applied graph theoretical analysis on wavelet correlations of extracted BOLD signal time-courses of atlas-defined cortical and subcortical regions in wakefulness, light sleep stages and slow wave sleep, and we confirmed the widespread increase in cortico-cortical connectivity in light sleep stages and a strong reduction of cortico-cortical connectivity in slow wave sleep. Moreover, thalamo-cortical correlation values sharply decreased in light sleep stage 1 and were partially restored in deeper sleep stages. There was also a significant effect of sleep on network topology, in particular on local clustering values, which were lowest in light sleep when compared to values of randomly rewired networks. This randomization process can be contrasted with network reconfiguration in different states of unconsciousness. A network approach to the sleeping brain may be helpful for our understanding of potential brain plasticity/maintenance functions of sleep.

AS-28-2

SLEEP SHAPES SMALL-WORLD PROPERTIES OF SUBSEQUENT SPONTANEOUS WAKING BRAIN ACTIVITY

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The role of sleep for waking brain activity remains poorly understood. As a model for investigating this role, we studied sleep deprivation and its effects on brain function, described in terms of functional network organization measured with high-density EEG. We found that sleep deprivation selectively affects the network parameters of frontal regions. After sleep deprivation, local connectivity was lower for the alpha frequency band and pathlength was higher in the theta band compared to after normal sleep. These changes could not be explained by power differences. Thus, frontal connectivity was decreased locally after sleep deprivation, indexed by both reduced local integration, and reduced global integration of the frontal cluster. A homeostatic restorative function of sleep would therefore be most prominent for the frontal regions and its connections. It remains to be investigated how task-related neural network activity responds to sleep deprivation: the findings fit well with the notion that specifically functions associated with the frontal cortex suffer from sleep deprivation, such as executive control and higher-order cognitive processes.

AS-29-1

GIFT OF SLEEP: HOW TODAY'S EXPERIENCES BECOME TOMORROW'S MEMORIES

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Sleep in mammals is not a homogenous behavioral state, rather it is a continuum of mixed states that differ in their physiology, chemistry, and phenomenological experiences. Like sleep, long-term memory formation is also not a single step, rather it is a multistep process. Over the last four decades, an impressive number of studies have shown that sleep confers a beneficial effect on learning and memory. There is now strong evidence in both humans and animals to support the hypothesis that separate sleep states are differentially involved in different steps of memory consolidation. This presentation will explain the cellular and molecular mechanisms, as well as the beneficial effects, of each sleep stage in the memory consolidation process.

AS-29-2

THETA WAVE PHASE SPECIFIC HIPPOCAMPAL REACTIVATION DURING REM SLEEP INFLUENCES SYNAPTIC PLASTICITY AND LEARNING

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Hippocampal place cell activity encodes one of the associative memory functions of the hippocampus necessary for learning and consolidation to the neocortex. During exploration, place cells fire primarily at the

peaks of the ongoing hippocampal theta EEG activity (4–9 Hz) associated with potentiating synapses between cells which underlies long term memory. During times of learning in wakefulness theta activity is essential for memory formation. REM sleep (REMS) also shows sustained theta activity in the hippocampus and associated structures. We found that hippocampal place cells encoding a recently learned environment reactivate during REMS theta at primarily the peaks of the theta waves. Cellular measures also indicate strengthened synapses, consistent with the proposed REMS memory consolidation process. However, place cells encoding familiar, already consolidated environments reactivate primarily at the troughs of REMS theta, which is associated with weakening previously potentiated synapses of those consolidated memories in the temporary memory assembly place of the hippocampus. Cellular and place field activity measures show synaptic weakening after REMS theta trough activity episodes, as would be expected for clearing unnecessary memory networks during REMS. Further, auditory stimuli such as loud clicks increase REMS duration and/or the density of REM phasic activity, including P waves. We found that auditory stimuli delivered during REMS following learning increased the efficiency of the memory consolidation process, rescued the detrimental effects of short term REMS deprivation on learning, and influenced REMS reactivation profiles of hippocampal cells during theta. These results further reveal the physiological mechanisms underlying REMS memory consolidation.

AS-29-3

PONTINE-WAVE ASSOCIATED SYNCHRONIZATION BETWEEN HIPPOCAMPAL AND AMYGDALA THETA WAVES: A PHYSIOLOGICAL PROCESS FOR SLEEP-DEPENDENT MEMORY PROCESSING

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The pontine reticular formation (PRF) nuclei are involved in the generation of hippocampal theta wave, which is recorded during particular behavioral activities and REM sleep. A group of PRF neurons begins to fire and/or increase their discharge rate coincident with ponto-geniculo-occipital (PGO) wave in cats during REM sleep. In rats, a PGO-like phasic potential called pontine (P) wave can be recorded in the subcoeruleus region (SubC), which has mutual connections with the other PRF nuclei. We have shown a close time-relationship between theta and P waves. Theta wave appears not only in the hippocampus but also in the amygdala. One of the intriguing features of amygdala theta wave is the synchronization with hippocampal theta. We examined correlations between the dynamics of the two theta and P waves and found that frequency of both hippocampal and amygdala theta waves increased with an increase in P wave, synchronization between hippocampal and amygdala theta waves was enhanced in association with increased P wave density, lesion of the SubC decreased the theta frequency and degraded theta synchronization. These indicate that SubC enhances synchronization between hippocampal and amygdala theta waves.
The immediate early gene leading to the formation of LTP is highly expressed in the hippocampus and amygdala during REM sleep just after a learning task. This supports the hypothesis that REM sleep serves to consolidate memories. The function of synchronization of hippocampal-amygdala theta wave is not yet clear, but the theta activity is considered to be important for the synaptic plasticity in the hippocampus and amygdala. Theta-frequency stimulation facilitates synaptic plasticity, such as LTP in the hippocampus and long-term depression in the amygdala. Recently, it was found that activation of the SubC enhances memory consolidation and increases synaptic plasticity-related gene expression in the hippocampus and amygdala. These suggest that the close time relation between theta wave dynamics and P wave density contributes to memory functions during REM sleep.

AS-30-0

UNDERSTANDING THE MECHANISMS FOR THE SUDDEN INFANT DEATH SYNDROME: WHAT WE CAN LEARN FROM INFANT SLEEP STUDIES

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During infancy sleep is at a life time maximum and the development of sleep is one of the major physiological processes which occurs during the first year of life. Sleep has a marked effect on cardio-respiratory physiology and control in adults. During infancy cardio-respiratory control also undergoes significant maturation, and until this is mature the cardio-respiratory system is unstable, and this is particularly so during sleep. Sudden Infant Death Syndrome (SIDS) is the sudden death of an infant less than 1 year of age that remains unexplained after a complete autopsy, death scene investigation, and a review of the clinical history, and is presumed to occur during sleep. Although the underlying mechanisms involved in SIDS remain unclear, impaired cardiovascular control during sleep together with an impairment in arousal from sleep are thought to be a likely mechanisms. In support of this hypothesis, future SIDS victims have been found to have altered or impaired cardiovascular control and reduced arousability in the weeks to months before death. In addition, the major risk factors for SIDS such as the prone sleeping position, maternal smoking and prematurity all have significant negative effects on both cardiovascular control and arousability from sleep. Polysomnography studies in infants, both at low and high risk for SIDS, have provided important insights into the mechanisms underlying SIDS and can provide important information to further reduce the occurrence of SIDS. This symposium will focus on the studies which have examined deficits in cardiovascular control and arousal from sleep.

AS-30-1

CARDIOVASCULAR CONTROL AND THE RISK FACTORS FOR SIDS

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Sudden Infant Death Syndrome (SIDS) is the most common cause of death in infants aged 1–12 months in developed countries and is believed to occur during sleep. Epidemiological studies have identified that prone sleeping is one of the major risk factors for SIDS and that SIDS peaks between 2–3 months of age. Despite the identification of major risk factors, the actual underlying mechanism(s) involved in SIDS remain unclear. However, it has been suggested that the fatal event may occur due to an impaired ability to mount an appropriate compensatory response to a profound loss of blood pressure. Thus, understanding the development of cardiovascular control during sleep in infancy may provide vital clues into the pathology of SIDS. Until recently, there has been limited information regarding cardiovascular control in healthy full-term infants. The paucity of cardiovascular data has been largely

due to the inability to measure blood pressure continuously and non-invasively in infants. However, advances in blood pressure measurement, has allowed the recent validation of a new non-invasive beat-beat measurement in infants. Using these techniques in longitudinal studies, we have identified that within the first 6 months of life, blood pressure dips at 2–3 months postnatal age, when the risk of SIDS is greatest. Importantly, we have identified that prone sleeping, which is the major SIDS risk factor, reduces blood pressure, impairs the response to a cardiovascular challenge, and reduces baroreflex sensitivity and these effects are most marked during quiet sleep at 2–3 months. In summary, these studies provide evidence that impaired cardiovascular control during sleep in the prone position may dampen protective responses to hypotensive events and play a vital role in pathogenesis of SIDS.

AS-30-2

THE IMPORTANCE OF AROUSAL FROM SLEEP IN SIDS

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Sudden Infant Death Syndrome (SIDS) is one of the leading causes of infant mortality in western countries and is commonly thought to occur during sleep. Although the exact underlying mechanism(s) remain to be elucidated, there is compelling evidence for the involvement of an impaired ability to arouse from sleep in response to a life threatening challenge. In infants, arousal is a hierarchical response, whereby full cortical arousal and awakening is preceded by a stereotypical sequence of sub-cortical events. When compared with age-matched controls, a decrease in cortical arousal frequency has been identified in infants who subsequently died of SIDS. These findings suggest that future SIDS victims may have subtle pre-existing abnormalities in their arousal pathways inhibiting progression from sub-cortical activation to cortical arousal. Previous studies identified that infant arousability from sleep is reduced by major risk factors for SIDS, including the prone position and maternal smoking, and increased by protective factors. More recently, however, studies have focused on the progression from sub-cortical activation to full cortical arousal. Our studies showed that this arousal process in otherwise healthy, term infants is modified by exposure to prone sleeping and maternal smoking, particularly at 2 to 3 months, the peak risk age for SIDS. Furthermore, we have found that factors that have been suggested to protect against SIDS, swaddling and pacifier use, also modify both total arousability and the arousal process itself; however, the effects of swaddling were dependent on the infants previous experience with the technique. An inhibited progression of sub-cortical activation to full cortical arousal may prove to be a clinically significant marker of infants who have an increased likelihood of succumbing to SIDS. Our findings highlight the importance of continued education of the known risk factors for SIDS for both parents and additional caregivers, to avoid complacency.

AS-31-1

RE EMERGENCE OF THE PREOPTIC AREA IN SLEEP REGULATION

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Over the last 80 years the basic mechanisms of sleep-wakefulness have been studied with an interdisciplinary approach embracing neurophysiology, neuroanatomy and neurochemistry. The existence of a sleep-promoting area in the brain was first implied from the post-mortem findings in Encephalitis lethargica patients by von Economo in 1930. The patients having lesion in the anterior hypothalamic preoptic area (POA) had insomnia. On the other hand hypersomnolence was correlated with lesion in the posterior hypothalamus. Later in 1946, Nauta showed lesions of the POA resulted in decrease in sleep and disruption of sleep cycle. In 1962, electrical stimulation of basal forebrain and the POA by Sterman and Clemente showed drowsiness followed by behavioural and electroencephalographic sleep. In the intervening years, the role of the POA in sleep regulation was eclipsed by the rising popularity of ascending reticular activating system hypothesis. During 1965–85 the chemical signatures of ARAS were discovered. However over last 25 years, in our laboratory, the role of POA in sleep regulation has been confirmed by several lines of animal experiments including stimulation, neurotoxic lesion, single unit recording, neural transplantation, and functional magnetic resonance imaging. More recently sleep active neurons have been found to be concentrated exclusively in the ventrolateral POA (VLPOA) and median POA (MnPOA). The importance of these cell groups is evident from c-fos expression particularly during sleep and not during wake. The results of few studies suggest that small lesions in the VLPOA and MnPOA effectively suppress sleep. Compared to VLPOA a number of studies employing variety of techniques have shown that, the medial POA is equally important if not less in regulating sleep. Together these findings suggest that the sleep promoting areas within the POA are multiple and intermingled. The POA also takes part in homeostatic control of sleep-wakefulness at adverse environmental temperature and situation.

AS-31-2

SLEEP TO SURVIVAL: EMERGING ROLE OF THE PREOPTIC AREA NETWORKING

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Preoptic area (POA) harbors neurons involved in varied functions including sleep initiation and maintenance, thermoregulation, male sexual behavior, maternal behavior etc. Some of these vital functions are closely interrelated that alteration in one behavior gets reflected in up or down regulation of the other function for energy homeostasis. It has been challenging to examine the neuronal networking involved in central processing and control of these functions, especially when it involves understanding the mechanism for integration of functionality in the in-vivo systems. On the basis of modern and classical techniques in animal models, roles of various nuclei in the preoptic area are redefined for regulation of sleep. The original studies demonstrated the role of medial preoptic neurons in promotion of sleep. The presence of abundant warm sensitive neurons in this area were functionally correlated with the generation of slow wave sleep as the brain temperature

showed significant alteration with respect to change in the vigilant state. In the late nineties, after identification of neuropeptide orexin/hypocretin, regulation of sleep-wakefulness was restructured via the lateral-POA. The modulation of arousal states and sleep by various established neurotransmitters were routed through orexin/hypocretin. The optogenetic methods provided important insights into the state dependent variation in the neuronal activity in the POA. The ventrolateral-POA and the median preoptic nuclei for sleep initiation also gained momentum. However, the medial-POA continued to be important for maintenance of sleep. The strong inputs from the adjoining nuclei in the basal forebrain, like septum needs attention for a comprehensive understanding of neuronal networking in the multimodal POA. In the current decade, wherein sleep disturbances are more frequently encountered that are causing serious health implications, the study of regulation of sleep deserves a new prospective.

AS-31-3

SLEEP IS AUTO-REGULATED: BASAL FORE-BRAIN AREAS MODIFY SLEEP AS PER HOMEOSTATIC NEEDS

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Sleep is an auto-regulatory global phenomenon as almost all the brain segments have an inherent tendency for sleep-wake oscillation. This tendency is derived from a collective response of the several hundreds of neurons with oscillating membrane potential. In an intact animal, the prior activity in the network determines the probability of its entering the sleep-like state or awake-like state. Normal alteration and expression of sleep-wakefulness are influenced by several factors including external input and internal feedback. There are several internal signals, including sleep-inducing substances, which are sleep facilitating. Basal fore-brain and hypothalamus should be considered as part of the neural mechanism through which many of these internal signals act. There is enough evidence to suggest that the basal fore-brain and the hypothalamus integrate sleep with body temperature, hunger, thirst, circadian cycles, neuroendocrine outputs, autonomic responses and stereotyped behaviors as per homeostatic needs.

AS-32-1

SPIKE TIMING OF PEDUNCULOPONTINE NEURONS DURING SLOW OSCILLATIONS AND THEIR INVOLVEMENT IN THE MODULATION OF PHASIC EVENTS DURING SLEEP

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The pedunculopontine nucleus (PPN) constitutes one of the main components of the reticular activating system. Along with other neuronal systems in the brainstem and midbrain, it influences the occurrence of specific brain states and contributes to their cyclic alternation. The PPN is composed of three main types of neurons, cholinergic, GABAergic and glutamatergic, but it is the cholinergic population that has been traditionally associated with its function as part of the reticular activating system. Recent results show that specific firing patterns of different PPN neuronal subtypes are distinctively correlated with discrete components of the cortical slow oscillations that occur during sleep and anesthesia. Thus, subtypes of cholinergic neurons show distinct discharge properties, express different molecular markers and are distinctly modulated by their afferents. Similarly, GABAergic and glutamatergic neurons are composed of subsets of functionally distinct neurons with distinct dynamics across brain states. The analysis of these neuronal populations at the single cell level has revealed evidence of a local synaptic network primarily maintained by cholinergic neurons. The activation of such a network produces phasic increases in cortical fast-frequency oscillations that are constrained to the temporal dynamics of the slow oscillations. These results, along with recent evidence revealing similar mechanisms in other subcortical structures, suggest that the orchestrated activation of midbrain/brainstem networks during the slow oscillations that are characteristic of sleep and anesthesia, plays a role in shaping global neuronal activity, possibly by modulating the phasic events occurring during slow wave activity.

AS-32-2

NORADRENERGIC NEURONS OF THE LOCUS COERULEUS ARE PHASE-LOCKED TO CORTICAL UP-DOWN STATES DURING SLEEP

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Slow wave, or non rapid eye movement sleep (nREM) is known to be beneficial for memory in humans and other species, although the underlying mechanisms are just beginning to be understood. NREM sleep is characterized by periodic changes of cortical excitability, reflected in the EEG as high-amplitude slow oscillations (UP/DOWN states). Discovery of a learning-dependent increase in activity of the noradrenergic nucleus Locus Coeruleus (LC) during slow wave sleep prompted us to investigate the timing of LC spikes as a function of sleep-associated cortical oscillations. We monitored these slow oscillations, along with extracellularly recorded unit activity of LC neurons and neurons of the prefrontal cortex, in non-anesthetized freely sleeping rats. Spike-triggered averaging of EEG, together with phase-locking analysis, confirmed that cortical neurons fired around the peak of the slow oscillation. These analyses further revealed preferential firing of LC neurons along the ascending edge of the slow oscillation, correlating with Down-to-Up state transition. LC neurons were locked best when spikes were shifted forward ~50 ms in time with respect to the EEG slow oscillation. This precise timing of LC activity with the transitional state of cortical excitability provides neuromodulatory input which could facilitate the transition by making cortical neurons more excitable. Moreover, plasticity processes ocurring during this phase of sleep would be reinforced by release of noradrenaline by the LC neurons.

AS-33-1

AWAKE AT NIGHT – HOW EXTREME DOES SLEEPINESS GET?

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Night work is associated with an increased accident risk often attributed to sleepiness. This attribution is based on inference in the sense that sleepiness normally results from activity at the circadian through or from reduced sleep or, frequently, from both. Rarely, however, is sleepiness actually measured in relation to accidents, near accidents, or corresponding situations. Here we present data showing that physiological

indications of sleepiness during night work in general, as well as subjective reports of sleepiness. Sleep intrusions is seen during work at night and subjective reports reach high levels. In a series of studies of driving on rural roads and motorways we have described the levels of sleepiness reached and related this to measures such as unintentional line crossings and driving interrupted because of dangerous sleepiness. The results indicate that shortly before driving is interrupted reported sleepiness is increased to very high levels (corresponding to those seen just before driving off the road in a simulator) and sleepiness intrusions in the EEG and EOG increase., as well as blink duration.

AS-33-2

RECOVERY SLEEP AND NAPPING AS COUNTERMEASURES TO FATIGUE: BENEFITS AND CONSEQUENCES IN INDUSTRIAL SETTINGS

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Sleep plays an essential role in recovery from work-related fatigue. The management of sleep is linked to practical strategies for occupational safety and health. Recently, much attention has been directed toward the effects of chronic sleep loss and the subsequent recovery process. This research interest may be inspired by the effects of long working times on health and safety among daytime workers.

A great deal of previous research has focused on alertness and performance in response to manipulated sleep times (e.g., Van Dongen et al., 2003). However, very little is known about the influences of daytime activities during the period of sleep restriction on subsequent sleep and daytime function the next day. Examining the interaction between sleep and social (i.e., work) or individual (i.e., leisure) activity is crucial to understanding fatigue recovery among workers. In short, the recovery power of sleep may change based on the type of daytime activities, even though the same sleep times are provided (Kubo et al., 2008).

Also, since shift workers take a daytime sleep after night shift at the expense of individual time, their daytime activity would be limited compared to daytime workers. According to previous research (Sasaki et al. 1992, Takeyama et al., 2005), night-shift napping is expected as an effective strategy for enhancing the quality of daytime activities after night shift in addition to reducing fatigue and sleepiness during night shift.

Taken together, fruitful time for social or individual activity is considered to be a key factor to high quality of sleep for facilitating fatigue recovery among workers. The presentation will highlight findings as to fatigue recovery among workers in terms of the interaction between sleep and daytime activities.

AS-33-3

THE EFFECTIVENESS OF A RESTART BREAK TO SUSTAIN PERFORMANCE ACROSS CONSECUTIVE WORK SHIFTS DEPENDS ON THE CIRCADIAN TIMING OF THE SHIFTS

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U.S. truck drivers are allowed to accumulate 60 h/70 h on duty in a work period of 7/8 consecutive days, and to begin another work period after a 34 h restart break. We investigated the effectiveness of this break for sustaining performance in daytime and nighttime schedules. N = 27 healthy subjects (22–39 y; 14 f) participated in a 14-day in-residence laboratory study, which included a 5-day work period, a 34 h restart break, and another 5-day work period. 14 subjects were randomized to a daytime condition, involving nocturnal sleep (22:00–08:00) daily during the two 5-day work periods and the restart. 13 subjects were randomized to a nighttime condition, involving nocturnal wake and diurnal sleep (10:00–20:00) daily during the two 5-day work periods, while reverting to diurnal wake and nocturnal sleep during the restart. Performance on cognitive tasks and on a high-fidelity driving simulator was tested four times per day, except during the restart. Mixed-effects ANOVA revealed significant interactions of work period (before versus after the restart) by condition (daytime versus nighttime) for lapses (RTs > 500 ms) on a psychomotor vigilance test (PVT; $F = 20.1$, $p < 0.001$), for ability to orient a map in a cardinal direction decision task (CDDT; $F = 17.8$, $p < 0.001$), and for lane deviation on the driving simulator ($F = 9.2$, $p = 0.003$). In the daytime condition, performance after the restart was the same or better than before the restart. In the nighttime condition, performance after the restart was degraded (PVT lapses) or showed less improvement from practice than in the daytime condition (CDDT, driving) relative to before the restart. Thus, the 34 h restart break was adequate to sustain performance in subjects scheduled to daytime shifts, but not in subjects scheduled to nighttime shifts. This stresses the importance of circadian effects on sleep and performance for effective hours-of-service regulations.

Poster Presentations

Poster presentations 1

PO-1-001

BIDIRECTIONAL ASSOCIATIONS BETWEEN SLEEP PROBLEMS AND BEHAVIOURAL RISK FACTORS

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Objective: It has been hypothesized that sleep problems may induce adverse health behaviours and health behaviours may negatively affect sleep. The aim of this study was to examine whether there are bidirectional associations between sleep problems and behavioural risk factors.
Method: The data were derived from the Helsinki Health Study prospective cohort study. The baseline data were collected in 2000–2002 (n = 8960, response rate 67%) among 40–60-year old employees of the City Helsinki and follow up data in 2007 (n = 7332, response rate 83%). Logistic regression analysis was used to examine associations among sleep problems and behavioural risk factors, including heavy and binge drinking, smoking, leisure-time physical inactivity, unhealthy food habits and obesity (BMI > 30 kg/m^2).
Results: At baseline, 17% of men and 21% of women reported frequent sleep problems. At follow-up, these figures were 20% for men and 27% for women. Among women, frequent sleep problems at baseline predicted heavy drinking (OR 1.30; CI 1.02–1.66), physical inactivity (OR 1.37; 95% CI 1.16–1.63) and obesity (OR 1.28; 95% CI 1.01–1.63) at follow-up after adjusting for baseline behavioural risk factors, occupational class and sleep duration. Additionally, among women heavy drinking (OR 1.56; 95% CI 1.26–1.92), binge drinking (OR 1.29; 95% CI 1.09–1.53), physical inactivity (OR 1.17; 95% CI 1.00–1.39) and obesity (OR 1.31; 95% CI 1.09–1.58) reported at baseline predicted subsequent sleep problems at follow-up. Obesity at baseline was associated with frequent sleep problems at follow-up also in men (OR 1.66; 95% CI 1.09–2.55).
Conclusion: Sleep problems are associated with subsequent behavioural risk factors and also behavioural risk factors are associated with subsequent sleep problems in women.

PO-1-002 / AS-15 Presenter

POOR SLEEP AND EEG SLEEP SPINDLE ACTIVITY IN CHILDREN AND ADULTS WITH AUTISM

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Introduction: Autism is characterized with poor sleep maintenance. EEG sleep spindles represent a sleep protective process by which access of inputs to the brain is diminished via a thalamo-cortical loop inhibition. In typically developed individuals, sleep spindle density decreases with age. In adults with an Autism Spectrum Disorder (ASD) the density of left central (C3) sleep spindles, not left prefrontal (Fp1), is significantly lower than controls (Limoges et al., 2005). The goals of the present study were to: 1) See whether SS density is also low in children with ASD; 2) Compare the results in children and adults.
Methods: Twenty-eight individuals with ASD (15 adults: 14M, 1F, 22.3 ± 3.6 yrs; 13 boys, 10.7 ± 1.9 yrs) and 29 controls (16 adults: 15M, 1F, 24.4 ± 4.0 yrs; 13 boys, 9.8 ± 2.2 yrs) were recorded for two consecutive nights. Sleep stages were determined for night 2 according to Rechtschaffen and Kales (1968) using 20 sec. epochs. Stage 2 sleep spindles were visually identified at the Fp1 and C3 electrodes. Results were compared using t-tests ($p < .05$).
Results: Children and adults with ASD showed longer sleep latencies and more awakenings than controls. Sleep spindle density was not different between ASD and control children; adults with ASD had significantly less spindles than controls, at C3 only. Children with ASD had significantly more sleep spindles than adults with ASD at Fp1 and C3 while the control children had significantly more spindles that adult controls at Fp1.
Discussion: These results could suggest that sleep protective mechanisms are intact in children with ASD but other EEG markers (K-complexes and EEG power) and more recording sites should be investigated. Moreover, other age-dependant sources of poor sleep could affect children with autism, including an impaired circadian timing system and behavioral issues. The present EEG results also show an atypical cortical maturation way along the antero-posterior axis in autistics that will require further investigation using a full EEG montage.

PO-1-003 / AS-27 Presenter

RESIDUAL SLEEP DISTURBANCES AFTER REMISSION OF MAJOR DEPRESSIVE DISORDER – A 4-YEAR NATURALISTIC FOLLOW-UP STUDY

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Objectives: A substantial portion of depressed patients continued to experience residual symptoms despite optimized antidepressant

treatment. The aim of the current study was to investigate the prevalence, clinical, psychosocial as well as quality of life correlates of residual sleep disturbances in a cohort of psychiatric outpatients with MDD.
Methods: A total of 421 depressed outpatients were assessed in 2006 and 2010, which consisted of a standardized diagnostic psychiatric interview and a packet of self-reported questionnaires, including a general sleep questionnaire, Hospital Anxiety and Depression Scale (HADS), NEO-Five Factor Inventory (NEO-FRI), and Short-Form-12 Health Survey (SF-12v2).
Results: A total of 371 patients (mean age: 44.6 ± 10.4 years, female: 81.8%; response rate 88.5%) completed the reassessments, in which 41% were classified as remitted cases. One-year prevalence of frequent insomnia at baseline and follow-up was 38.0% and 19.3%, respectively. One-year prevalence of frequent nightmares at baseline and follow-up was 24.0% and 9.3%, respectively. Remitted participants with residual insomnia were more likely to be divorced ($p < .05$), and scored higher on anxiety subscale ($p < .05$). Additionally, remitted participants with residual nightmares were younger ($p < .05$), and scored higher on neuroticism ($p < .05$) and anxiety subscale ($p < .01$). Residual insomnia was associated with lower physical functioning ($p < .05$) and role-emotional ($p < .01$); residual nightmares was associated with bodily pain ($p < .05$) and lower vitality ($p < .05$). Suicidal ideation was significantly associated with residual nightmares (OR = 8.40, 95% C.I. 1.79–39.33) after controlling for potential confounding factors.
Conclusion: Residual sleep disturbances were associated with a constellation of psychosocial factors, impaired quality of life and suicidal ideation in remitted depressed patients. Future prospective studies should be conducted to examine the prognostic significance of residual sleep disturbances in relation to the recurrence of depression.

PO-1-004 / AS-14 Presenter

GRAY MATTER CHANGES IN BRAINS OF PRIMARY INSOMNIA

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Introduction & Objective: To investigate differences in brain gray matter concentrations (GMC) in patients with primary insomnia (psychophysiological insomnia, PI) and good sleepers (GS).
Methods: The study consisted of 27 female PI and 27 GS matched for age (mean age, 47.5 years). All subjects underwent night polysomnography to exclude other sleep disorders and then optimized voxel-based morphometry, an automated processing technique for MRI was applied.
Results: On visual inspection of brain MRIs, there were no structural abnormalities. Compared to GS, GMCs of PI were significantly decreased in the superior and inferior frontal gyri, superior temporal gyrus, and postcentral gyrus in right hemisphere middle and inferior frontal gyri and postcentral gyrus in left hemisphere (uncorrected $P < 0.001$). Gray matter volume was not different between PI and GS. Also there were no brain areas showing increased GMCs in PI than GS.
Conclusions: These findings suggest that attention and affective disturbances and executive dysfunction frequently found in PI patients might be related to morphological differences in the brain gray matter areas.

PO-1-005 / AS-1 Presenter

NIGHT-TO-NIGHT SLEEP VARIABILITY IN INSOMNIA PATIENTS PARTICIPATING IN GROUP CBTI

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INTRO: Regularizing sleep-wake times is a target for cognitive-behavioral therapy for insomnia (CBT-I), yet little is known about determinants of variability in sleep behaviors and insomnia symptoms.
METHODS: 455 participants (57.6% female; M = 48.12 ± 14.38 years) participated in a 7-session CBTI group. Participants completed the Beck Depression Inventory (BDI), the Morningness-Eveningness Composite Scale (MECS), and one week of sleep diaries at baseline and end of treatment. Participants were categorized into Evening and Non-evening chronotypes based on the 20th percentile MECS score. The weekly means of successive squared differences of bed time, lights out, wake time, out of bed, and time in bed were computed, converted to z-scores and averaged, yielding behavioral composite scores (BCS). The same procedure was used to derive an insomnia composite score (ICS) based on variability of sleep onset latency, time awake after sleep onset, and total sleep time.
RESULTS: Pre- to post-treatment reductions were found on all BCS and ICS variables ($p < 0.01$). Multiple regressions with age as a covariate were employed to examine the effects of depression and chronotype on BCS and ICS. For BCS, the model (Adjusted $R^2 = .19$) had significant effects for depression ($B = .30$, $p < .001$), chronotype ($B = .27$, $p < .001$) and their interaction ($B = .02$, $p = .003$). Among those with higher depression severity (BDI > 14), evening chronotypes exhibited significantly greater variability in sleep behaviors than non-evening chronotypes ($t = -2.44$, $p = 0.03$). Among those with low depressive symptoms, there was no significant difference in BCS. For ICS, the model (Adjusted $R^2 = .03$) had a significant effect for depression ($B = .12$, $p = .001$), but not chronotype or interaction.
CONCLUSION: Elevations in depressive symptoms and evening chronotype status is associated with high levels of sleep variability, suggesting that regularizing sleep may be an especially important treatment target. In addition, elevations in depressive symptoms predicted more variable insomnia symptoms, which stabilized following group CBTI.

PO-1-006

WITHDRAWN

PO-1-007

THE DAYTIME IMPACT OF DSM-V INSOMNIA DISORDER: COMPARATIVE ANALYSIS OF INSOMNIA SUBTYPE FROM THE GREAT BRITISH SLEEP SURVEY (N = 11,129)

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The DSM-V work group for sleep-wake disorders propose moving away from the notion of primary and secondary insomnia, and instead advocate the view that, whenever present, insomnia disorder (ID) should be coded and treated as a substantive psychiatric disorder in its own right, regardless of the presence of co-morbid illness. Here, we report data from the Great British Sleep Survey (GBSS) on the daytime impact of DSM-V defined ID and its diagnostic subtypes. The GBSS is an online population survey, based upon proposed DSM-V criteria, covering both night-time and daytime symptoms, physical- and mental-health, and symptoms of additional sleep disorders. We compared those with ID and those with NO-ID, in terms of daytime impact in the following areas: energy, concentration, relationships, ability to stay awake, mood and ability to get through work. ID subtypes (difficulty initiating sleep {DIS}; difficulty maintaining sleep {DMS}; early morning awakening {EMA}; mixed; non-restorative sleep {NRS}) and ID presentations (ID and poor mental health; ID and poor physical health; ID and additional sleep-related symptoms; ID on its own) were also compared in terms daytime impact. A total of 11,129 surveys (72% female; mean age = 39 yrs) were completed in a 12-month period. Using DSM-V criteria, 5,713 participants screened as having a possible ID. The ID group, compared with the NO-ID group, reported significantly greater impairments in all six areas of impact (Cohen's d > .70). In terms of ID subtypes, EMA and mixed groups reported significantly greater impairment in all areas of functioning compared with DIS, DMS, and NRS. The ID and poor mental health group were found to be consistently more impaired in five out of six areas of daytime dysfunction (excluding ability to stay awake) relative to ID on its own, ID and poor physical health, and ID in addition to other sleep-disordered symptoms. The GBSS provides some of the first data on the proposed new DSM-V ID criteria, revealing differential subtype profiles in terms of daytime impact, which may shed light on differing underlying pathogenic mechanisms.

PO-1-008 / AS-1 Presenter

EFFECTS OF COGNITIVE BEHAVIORAL THERAPY ON PATIENTS WITH PHARMACOLOGICAL TREATMENT-RESISTANT INSOMNIA

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This study examined whether cognitive behavioral therapy (CBT-I) improves insomnia symptom and whether CBT-I contribute to the reduction of the dose of hypnotics medication among patients with pharmacological treatment-resistant chronic insomnia. Sixty three insomniac outpatients with pharmacological treatment-resistant chronic insomnia (42 Female (67%), Mean age: 46.5 ± 15.5 years, self-reported morbidity of the disorder: 7.5 years; mean duration of hypnotics medication: 3.9 years, mean score of the PSQI was 13.1 ± 3.0) were assigned to a biweekly six-session CBT-I (n = 34) or to treatment as usual by sleep disorder specialist physicians (TAU; n = 29). CBT-I included psychoeducation, sleep hygiene, relaxation, stimulus control, sleep restriction, contingency management, and coping for worry. Subjective measures including the following variables were evaluated at the baseline and at the end of the treatment; the Pittsburgh Sleep Quality Index (PSQI), the Athens Insomnia Scale (AIS; a cut-off score is 6), and the Self-rating Depression Scale (SDS). Descriptive variables (e.g., gender) and the scores of these subjective measures did not differ between CBT-I group and TAU group at the baseline. The scores of the PSQI and the AIS decreased significantly at the end of the treatment in both groups and between groups at the end of the treatment. Significant decrease in the score of the SDS was observed only in CBT-I group. The rates of change after the treatment of CBT-I were larger than that of TAU. As for daily lormetazepam equivalent dose of hypnotics. the doses of hypnotics decreased significantly in CBT-I compared to those in TAU group at the end of the treatment. In addition, 24 participants (71%) in CBT-I group and 7 (24%) in TAU group had the AIS score of 6 points or lower at the end of treatment. Our result strongly supported the assumption that CBT-I improves the nocturnal and daytime symptoms of pharmacological treatment-resistant chronic insomnia, and that the treatment is helpful for the discontinuation or reduction of the medication usage.

PO-1-009

BRIEF BEHAVIORAL THERAPY FOR REFRACTORY INSOMNIA IN RESIDUAL DEPRESSION: ASSESSOR-BLIND, RANDOMIZED CONTROLLED TRIAL

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Objective: Insomnia often persists despite pharmacotherapy in depression and represents an obstacle to its full remission. This study aimed to investigate the added value of brief Behavioural Therapy for insomnia (bBTi) over treatment as usual (TAU) for residual depression and refractory insomnia.
Method: Thirty-seven outpatients (average age of 50.5 years) were randomly assigned to TAU alone or TAU plus bBTi, consisting of 4 weekly 1-hour individual sessions. The Insomnia Severity Index (ISI) scores (primary outcome), sleep parameters, the Hamilton Rating Scale for Depression (HAMD) scores assessed by blind raters, and remission rates for both insomnia and depression were collected at 4- and 8-week follow-ups.
Results: bBTi plus TAU resulted in significantly lower ISI scores than TAU alone at 8 weeks (P < .0005). The sleep efficiency for the combination was also significantly better than that for TAU alone (P = .015). Significant differences were observed in favour of the combination group on both the total HAMD scores (P = .013) and the HAMD scores

after removing the three sleep items (P = .008). The combination treatment produced higher rates of remission than TAU alone, both in terms of insomnia (50% vs 0%) with a number-needed-to-treat (NNT) of 2 (95% confidence intervals, 1 to 4), and in terms of depression (50% vs 6%) with an NNT of 2 (1 to 5).
Conclusions: In patients with residual depression and treatment refractory insomnia, adding bBTi to usual clinical care produced statistically significant and clinically substantive added benefits.
Reference:
Watanabe N, Furukawa TA, Shimodera S, Morokuma I, Katsuki F, Fujita H, Sasaki M, Kawamura C, Perlis ML. Brief behavioral therapy for refractory insomnia in residual depression: an assessor-blind, randomized controlled trial. J Clin Psychiatry. 2011. Online ahead of print.

PO-1-010

EFFICACY OF CO-MORBID COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA COMBINED WITH DEPRESSION PREVENTION PROGRAM IN PATIENTS WITH REMIT DEPRESSION

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Backgrounds: The rate of patients having sleep problems is approximately 27–65% in remit depression. Insomnia deteriorates the efficacy of therapy for depression and increases the risk for relapse. We carried out the depression prevention program (DPP) from 1994 in our hospital. DPP is group psychotherapy which is combination of cognitive behavioral therapy and social learning theory for remit depressed patients. A course is consisted of 8 sessions held weekly, which takes 60–90 min per session. According to our previous study, DPP had significant effects on residual depressive symptoms, but did not have enough effects for insomnia. Therefore, we put focus on clarifying the efficacy of co-morbid cognitive behavioral therapy for insomnia (CBT-I) combined with DPP for insomnia and other symptoms in remit depressive patients.
Subjects and Methods:
1) Subjects:
   a) DPP + CBT-I group 8 (M/F 4/4, mean age 43.1 ± 12.1y) and DPP group 16 (M/F 8/8, mean age 44.6 ± 11.9y)
   b) Inclusion criteria: 1) Depressive episode or Recurrent depressive disorder in ICD-10 2) Less than 15 points in HAMD-24 (the Hamilton Rating Scale for Depression-24) before DPP.
2) Measurements:
   a) HAMD-24
   b) Profile of Mood States (POMS)
   c) Automatic Thoughts Questionnaire Revised (ATQ-R)
   d) Pittsburgh Sleep Quality Index (PSQI)

These items were assessed before and after DPP.
Results:
1) There was no difference in HAMD total score between DDP and DPP + CBT-I group before first session (Two-sided Mann-Whitney's U test).
2) In both of DPP and DPP + CBT-I group, HAMD total score and ATQ-R score significantly decreased after treatment of either DPP or DPP + CBT-I ($P < 0.05$; two-sided Wilcoxon's signed rank test).
3) Compared with DDP group, the sub score of early morning awakening in HAMD tended to decrease more in DPP + CBT-I group ($P < 0.1$; ANOVA).
4) Compared with DDP group, the sub score of general somatic symptoms in HAMD was significantly lower in DPP + CBT-I group (P = 0.035; ANOVA).

Conclusions: From our results, it was suggested that addition of CBT-I to DPP was effective for not only insomnia but also general somatic symptoms in remit depressed patients.

PO-1-011

SELF-HELP TREATMENT FOR INSOMNIA SYMPTOMS ASSOCIATED WITH CHRONIC CONDITIONS IN OLDER ADULTS: A RANDOMISED CONTROLLED TRIAL

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Introduction: While the benefits of self-management approaches to chronic conditions are widely recognised, self-help CBT-I strategies have not been evaluated for use among older people with comorbid insomnia symptoms. In a randomised controlled trial patients with DSM-IV insomnia symptoms associated with long-term health problems received either treatment as usual (TAU) or self-help CBT-I. The self-help comprised six consecutive booklets, mailed at weekly intervals, providing structured advice on self-monitoring, sleep hygiene, sleep restriction, stimulus control procedures, and cognitive strategies. In addition, a telephone helpline was provided to support the implementation of the self-help advice. Outcomes (PSQI, Insomnia Severity Index, the Fatigue Severity Scale, and medication use) were assessed at baseline, on completion of the self-help programme (post-treatment), and then 3 and 6 months later.
Results: 193 patients (aged 55–87) were randomly allocated to the intervention (n = 98) or TAU (n = 95) groups. In models controlling for age, gender and baseline values patients in the self-help arm showed: significantly improved sleep quality, and significantly reduced insomnia symptom severity at post-treatment, 3 and 6 month follow-ups (all $p < 0.001$); and significantly reduced sleep medication use at the post-treatment follow-up ($p < 0.05$). Effect sizes were low, and treatment had no effect on levels of daytime fatigue. Most treated patients (73%) said they would recommend the self-help programme to others.
Conclusion: Self-help CBT-I offers a practical, low-cost, first-line response to insomnia symptoms associated with chronic disease in primary care settings. Among these patients, however, symptoms of daytime fatigue appear to be more closely associated with disease processes than to sleep quality.

PO-1-012

SUBJECTIVE SLEEP QUALITY, DEPRESSION AND ANXIETY IN AUSTRALIAN ADOLESCENTS

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Introduction: Poor sleep is widely observed in adolescence and is a common symptom of psychological disturbances. This study examined the relationship between depression and anxiety symptoms, and subjective sleep quality in an adolescent sample.

Method: 213 (38 boys) 12 to 18 year olds in Australian secondary colleges completed the Centre for Epidemiological Studies Depression Scale (CES-D), the Spence Children's Anxiety Scale (SCAS), and the Pittsburgh Sleep Quality Index (PSQI). Questionnaires produced Total Scores with cut offs reflecting overall high or low levels of depression, anxiety and sleep quality. The PSQI also assessed sleep disturbance, onset latency (SOL), total sleep time (TST) and daytime dysfunction.
Results: The groups average total PSQI score (7.58) indicated substantially disturbed sleep with 37.5% of participants reporting poor sleep quality. Average TST was 7.58 (SD = 3.7) hrs and SOL 30 (SD = 20.2) min. SCAS and CES-D scores were significantly correlated with total PSQI score ($p < 0.01$), TST ($p < 0.01$) and sleep disturbance ($p < 0.01$). Adolescents scoring above CES-D clinical cut off, indicating possible major depression (n = 55), reported significantly less TST, higher sleep disturbance and daytime dysfunction, lower sleep quality and longer SOL compared to those below the cut off. Sleep disturbance was higher with increasing symptoms, i.e. those with comorbid anxiety and depressive symptoms reporting the highest sleep disturbance compared to those who scored highly on either alone. Interestingly, regression analyses indicated sleep disturbance was more strongly associated with scores of depression than anxiety.
Conclusion: Poor sleep is common and highly correlated with anxiety and depressive symptoms in adolescents, and was more strongly associated with depression than anxiety symptoms.

PO-1-013

EVENING STATE ANXIETY AND AUTONOMIC MODULATION OF HEART AMONG GOOD SLEEPERS AND CHRONIC PRIMARY INSOMNIA

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Introduction & Objectives: Physiologic hyperactivation is a correlate of anxiety. Insomnia is associated with both of this factors. The question remains as whether anxiety is the mediator of physiological hyperactivation in insomniacs. In this study we assessed the relationship between evening anxiety state and autonomic arousal in subjects with insomnia compared to good sleepers. Materials & Methods We studied 19 subjects with a diagnosis of chronic primary insomnia (15w; 44y sd = 8) and 10 good sleepers (6w; 41y sd = 8). All subjects were free of any medical or psychiatric co-morbidity and other sleep disorders. Subjects underwent 2 week sleep diary and 2 night of polysomnographic recording including non-invasive beat-to-beat BP recordings. Analysis was made with variables evaluated and recording on pre-sleep wakefulness and during subsequent sleep. Mean heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were calculated for both state. An estimate of nocturnal dipping was provided by the delta (d) between wake and sleep. Anxiety was measured by the STATE anxiety inventory (STAI), administrated immediately before sleep. Pearson correlation coefficients were calculated between STAI and autonomic cardiovascular variables.
Results: Insomniacs STAI was negatively correlate with sleep HR (-0.48, $p < 0.05$). No difference for wake HR, SBP, DBP; night HR, SBP, DBP and for dHR, dSBP and dDBP. Control good sleeper STAI was positively correlate with wake HR ($+0.85$, $p < 0.01$) and negatively correlate with dHR (-0.66, $p < 0.05$). No significative difference was found for night HR, SBP and DBP; night HR, SBP, DBP and dSBP and dDBP.
Conclusion: Our results showed different pattern of activation in the two groups about response to evening anxiety state. Anxious good sleeper show an activation response in evening and an effective recovery after a night normal sleep. Anxious insomniac wasn't correlated with evening activation but they're was with decrease HR activation during night, which may suggesting somatisation mechanisms for insomniac who doesn't auto-report anxiety.

PO-1-014

THE COURSE OF INSOMNIA AND HEALTH-RELATED QUALITY OF LIFE OVER TWO YEARS: A LONGITUDINAL STUDY IN THE GENERAL POPULATION IN JAPAN

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Objectives: Only a few reports are available about the longitudinal course of insomnia in the general population. This study was designed to investigate the two years natural course of insomnia symptom and QOL on the rural cohort.
Methods: The Ethics Committee of Tottori University approved this study, and all participants provided written informed consent. Two-point epidemiological surveys with a two-year interval were performed on the same adult cohort in a rural town in Japan. 1,577 people both surveys (responder rate: 56%, 683 males, mean age [SD]: 58.6 [16.1]) answered the questionnaires consisted of demographic variables, the Japanese version of the Pittsburgh Sleep Quality Index (PSQI), the standardized 8-items Short Form Health Survey of the Medical Outcomes Study (SF-8), twelve-item version of the Center for Epidemiological Studies Depression Scale (CES-D). Responders with PSQI scores of 5.5 or higher were considered as insomniacs.
Results: The prevalence rates of chronic insomnia (PSQI score >5.5 at both surveys) were 18.7%, and morbidity of insomnia was significantly associated with existence of depression at either survey, PCS and MCS deterioration at both surveys. There were no significant differences over the course of two year in CES-D, PCS and MCS scores among chronic insomnia as a whole, although there was a significant but small increase in PSQI total score. On the other hand, chronic insomnia with mild to moderate severity ($5.5 < PSQI < 8.5$ at the baseline) of showed significant deterioration in PSQI total score and MCS at the follow up, whereas there was no significant deterioration among those with severe disturbance ($PSQI > 8.5$).
Conclusions: This investigation showed that chronic insomnia is a prevalent condition. Appropriate treatment is necessary for not only sever insomnia but also mild to moderate insomnia, since the insomnia symptoms and QOL become worse even among the mild to moderate insomnia over the two years course.

PO-1-015 / AS-15 Presenter

EFFICACY OF INTERNET AND GROUP ADMINISTERED COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA IN ADOLESCENTS; A PILOT STUDY

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Introduction: Literature shows a high prevalence of insomnia in adolescents. Cognitive behavioral therapy for insomnia (CBT-I) is proven effective in adults. Adolescents however are not inclined to seek help for their sleep problems. Therefore we developed a CBT-I protocol for adolescents of 6 weekly consults administered through an internet-site (N = 13) and compared results to CBT-I in a group setting (N = 7). We expected shorter sleep onset latency (SOL), less wake after sleep onset (WASO), longer total sleep time (TST) and higher sleep efficiency (SE) after treatment for both groups.
Methods: Subjects were recruited through the media. After screening with online questionnaires and an interview for further diagnosis subjects without other primary psychological or medical disorders interfering with sleep were included in the trial. A baseline measurement with wrist-actigraphy for a 7 day period was obtained registering SOL, WASO, TST and SE, followed by the CBT-I treatment. Directly after the last consult follow up measurements were obtained for another 7 consecutive days.
Results: Mixed model analysis showed a significant decrease of SOL after treatment for both groups ($F(1, 186.79) = 35.76$, $p < .01$) although at baseline SOL in the internet condition was significantly lower compared to the group condition ($F(1, 25.92) = 27.92$, $p < .01$). There was also a significant improvement of SE for both groups ($F(1, 178.85) = 24.89$, $p < .01$) with a significant interaction for treatment and condition showing more improvement for the group condition ($F(1, 180.27) = 6.84$, $p < .05$). There was no significant effect on WASO and TST for either group.
Conclusion: Internet and group administered CBT-I is effective for improvement of sleep in adolescents. SOL decreased and SE improved. TST did not show an increase which we attribute to restriction of time in bed that still is applied after the last consult. Differences in SOL before treatment could be caused by holidays during baseline for the internet condition. Further studies with a larger sample, a waiting list control group and long term follow up are needed.

PO-1-016 / AS-1 Presenter

THE CLINICAL TRIAL OF GROUP COGNITIVE BEHAVIOR THERAPY FOR PRIMARY INSOMNIA IN OUTPATIENTS

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Psychophysiological insomnia (PPI), as defined in ICSD-II is the almost the same as primary insomnia as defined in DSM-IV-TR. It is well known that cognitive behavior therapy (CBT) for insomnia is useful for PPI patients. Therefore we conducted group CBT for primary insomnia outpatients and investigated its clinical efficacy. Nineteen patients (10 of them woman) suffering from primary insomnia were enrolled to CBT. The mean patient age was 62.4 years, and the mean duration of insomnia was 8.8 years. Each received group combined CBT treatments that consisted of stimulus control, sleep reduction, cognitive therapy and sleep hygiene education 60–90 min sessions twice in a month. As booster sessions, the author gave consultations to each subject, and supervised the contents of the CBT. Just before the CBT, and after its completion, we conducted sleep measurements that involved 1) subjective evaluation of sleep: sleep logs, Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS), the Pittsburgh Sleep Quality Index (PSQI), 2) objective evaluation of sleep: actigraphy, 3) dissociation between subjective and objective evaluation of sleep. Just after the CBT, we found 1) decrease of dissociation between subjective and objective evaluation of sleep, 2) improvement of patients` incorrect cognition about sleep (DBAS), and 3) improvement in both the subjective and objective evaluation of sleep. Result1) was especially noteworthy because the primary aim of CBT was to change patients` incorrect cognition about sleep. The author defined result1) as the primary outcome of the study. The present results suggest that group CBT for primary insomnia is able to modify incorrect cognition about sleep.

PO-1-017

INTERNET ADDICTION AND ITS RELATION TO SLEEP AND DEPRESSION IN KOREAN ADOLESCENTS

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Introduction: Internet-addiction came into common use not only in clinical setting but also in everyday life. The objectives of this study were to investigate the characteristics of internet addiction and its association with sleep pattern and depression in Korean adolescence.
Methods: Subjects were 799 middle and high school students in Seoul, Korea. We administered a self reported questionnaire including sociodemographic data, Korean versions of Young's Internet Addiction Scale (YIAS), Pittsburgh Sleep Quality Index (PSQI), the Center for Epidemiologic Studies for Depression Scale (CES-D) and questions about internet using patterns. Data of 696 subjects were included in analysis.
Results: Of the 696 participants, 2.0% (n = 14) were internet-addicted (IA), 27.7% (n = 193) were over-using (OU) and 70.3% (n = 489) were not-addicted (NA). Comparing variables among IA, OU and NA groups, computer using time not for study (96.36 ± 63.31 min. vs. 134.92 ± 86.79 min. vs. 213.57 ± 136.87 min., $F = 34.287$, $p < 0.001$) and portable device using time not for study (84.22 ± 79.11 min. vs. 96.97 ± 91.89 min. vs. 152.31 ± 93.64 min., $F = 5.400$, $p = 0.005$) were different among groups. PSQI (5.26 ± 2.97 vs. 6.08 ± 2.97 vs. 7.50 ± 4.41, $F = 8.218$, $p < 0.001$) and CES-D scores (15.40 ± 8.08 vs. 19.05 ± 8.42 vs. 30.43 ± 13.43, $F = 32.692$, $p < 0.001$) were also different among groups. YIAS score were correlated with computer using time not for study ($r = 0.356$, $p < 0.001$) and portable device using time not for study ($r = 0.136$, $p < 0.001$). PSQI score ($r = 0.237$, $p < 0.001$) and CES-D score ($r = 0.332$, $p < 0.001$). YIAS score and PSQI score ($r = 0.131$, $p = 0.001$), YIAS and CES-D score ($r = 0.265$, $p < 0.001$), PSQI score and CES-D score ($r = 0.357$, $p < 0.001$) were correlated each other.
Conclusion: These results suggested that adolescents' internet-addiction was correlated with not only computer and portable device using time not for study but also depression and sleep-related problems. We should pay attention to depression and sleep-related problems, when evaluating internet-addiction in adolescents.

PO-1-018 / AS-4 Presenter

SLEEP DISTURBANCE AND ATTENTION DEFICIT/HYPERACTIVITY SYMPTOMS IN YOUNG ADULTS

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We aimed to determine the prevalence of sleep disturbance and symptoms of attention deficit/ hyperkinetic disorder in young adults and their relationship. Students, attending the Faculty of Psychology from two major cities, received a battery of tests containing the Sleep Disorders Questionnaire, the Sleep Timing Questionnaire, the Sleep Condition Index, as well as the Adult ADHD Self-Report Scale 1.1 and the Barkley Adult ADHD Rating Scale IV. To date, most of the respondents were females (N = 121, 85%), aged 21.1 ± 3.8 years. Preliminary data show that 13% (N = 18) of the surveyed complained of chronic insomnia and 20–29% were likely of having adult ADHD. Chronic insomnia was significantly more severe (p = 0.007) and more frequently reported (28%; p = 0.003) by those with symptoms of ADHD. As both insomnia and ADHD symptoms seem to be common among young adults, we are to further investigate them through clinical interview, as well as actigraphy.

PO-1-019

PERSONALITY AND MOOD CHARACTERISTICS IN PATIENTS WITH PSYCHOPHYSIOLOGICAL INSOMNIA

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Purpose: To investigate the mood status in patients with PPI who were underwent polysomnography (PSG) to exclude the co morbidity of other sleep disorders.
Methods: we recruited 185 patients (M : F = 71:114, mean age 56.8 yr) who visited our sleep center complaining sleep onset or maintenance insomnia. By detail history taking, overnight PSG, we excluded the patients who had obstructive sleep apnea syndrome (OSA), restless leg syndrome (RLS), periodic leg movement disorder (PLMD) or other problems that disturb sleep. The patients diagnosed as depression were also excluded. Included PPI patients completed the Insomnia Severity Index (ISI), Beck depression inventory (BDI), Beck anxiety inventory (BAI), Minnesota Multiphasic Personality Inventory (MMPI), Pittsburgh Sleep Quality Index (PSQI), and Profiles of Mood States (POMS).
Results: Mean duration of insomnia was 10.5 yrs and they had taken more than one kind of hypnotics. Seventy-nine patients (42.7%) underwent PSG, which showed alterations of sleep architecture (increased light sleep and decreased deep sleep) and increased REM latency (125.6 min). Sleep fragmentation was noted as increased arousal index (18.9 ± 9.6/hour), waking after sleep onset (23.1 ± 18.4%), and decreased sleep efficiency (77.6 ± 13.5%). BDI (15.5 ± 13.2) and BAI (13.4 ± 9.4) showed the abnormally high scores in PPI patients and were correlated with ISI (p = 0.018 in BDI; p = 0.02 in BAI) significantly. PPI patients complaint of poor sleep qualities (PSQI score 17.5 ± 7.6) although. PSQI score was not correlated with ISI. MMPI was obtained from 105 out of 185 patients (56.5%). Absolutely high scores were observed in personality with hypochondriasis (57.9 ± 10.3), depression (61.5 ± 11.2), hysteria (57.9 ± 10.1) and pyscoasthenia (56.7 ± 9.9) in the patients.
Conclusion: PPI patients showed sleep fragmentation although they had no definite sleep disorders. Depression and anxiety level were high and well associated with insomnia severity. It seems that certain personality predisposed to the patients with PPI.

PO-1-020

INSOMNIA AND HEALTH-RELATED QUALITY OF LIFE IN HOSPITALIZED DIABETIC PATIENTS

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Background: Some epidemiological studies reported that approximately 40% of diabetic patients suffered from insomnia. This study reports the relationship between insomnia and health-related quality of life (QOL) in hospitalized diabetic patients.
Method: Data were obtained from 39 diabetic patients who admitted to our hospital to receive diabetes treatment (26 males, aged 57.3 ± 16.4 years, and 13 females, aged 61.4 ± 15.6 years). Pittsburg Sleep Quality Index (PSQI) and the Japanese version of the Insomnia Severity Index (ISI-J) were used to evaluate their sleep. Japanese version of SF36 v2 was used to evaluate health-related QOL. The patients were asked to answer the questionnaires based on their conditions prior to admission to the hospital. The t- test and the Mann-Whitney U-test were used for comparing two groups with significance level of 0.05.
Result: Mean PSQI global score was 6.7 ± 4.2. The histogram of PSQI global score exhibited a bimodal distribution. Nineteen patients (50%) had PSQI global score of 6 points or higher, a level in which individual is considered to be a poor sleeper. The group had lower SF36 subscale scores in Bodily Pain (P = 0.017). Mean ISI-J score was 9.6 ± 6.1. Eighteen patients (46.2%) had total ISI-J score of 10 points or higher, a level in which individual is considered suffering from insomnia. Insomnia group had lower Mental Component Summary, Bodily Pain, Vitality, and Mental Health scales (P = 0.006, 0.047, 0.013, 0.034, respectively). 41.0% of the patients had difficulty initiating sleep (DIS), 43.6% had difficulty maintaining sleep (DMS) and 33.3% had non-restorative sleep. The DIS group had lower Mental Component Summary and Vitality scale (P = 0.014, 0.049, respectively). The DMS group had lower Mental Component Summary, Bodily Pain, Vitality, Social Functioning and Mental Health scales (P = 0.001, 0.026, 0.004, 0.026, 0.005, respectively).
Conclusion: The study suggests that hospitalized diabetic patients who suffer from insomnia, especially with DMS, have poor mental health.

PO-1-021

RELATIONSHIP BETWEEN INSOMNIA AND FUTURE DEVELOPMENT OF DEPRESSION

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Objective: We conducted to examine the relationship between insomnia and future incidence of depression through a 2-year cohort study of male Japanese workers.
Method: A self-completed questionnaire survey was conducted in conjunction with annual health checkups for male employees at a synthetic

fiber manufacturing plant. The questionnaire survey of job stress, sleep conditions, and depression was conducted in 2007 and 2009. Sleep quality and depression were examined with the Athens Insomnia Scale (AIS-5) and the Job Stress Questionnaire, respectively. Sleep quality was surveyed utilizing the AIS, an instrument for assessing insomnia that is used worldwide.

Results: Of the 158 respondents over the 2-year, 108 without depression at baseline were analyzed (mean age 38.2 ± 12.8 year; range 20–63 years). The incidence of new depression was 10.2% (11 of the 108 subjects) over the 2-year. None of the subjects without insomnia in 2007 suffered symptoms of depression in 2009, while 15.7% of the subjects with insomnia did so. In the subjects having insomnia with AIS-5 scores of 3 or more, 20.0% experienced depression in 2009. Logistic regression analysis showed a significant association between depression and the AIS score (OR 1.40; 95% CI 1.09–1.81, $p < 0.05$). The total AIS scores were also associated with increased scores for qualitative workload ($p < 0.05$), and decreased scores for appropriateness of work ($p < 0.01$).

Conclusions: Insomnia can be a risk factor for developing depression or, at least, an important marker for the later development of depression and workers' mental health. Measures to counter insomnia will serve to reduce the incidence of depression.

PO-1-022

SLEEP COMPLAINTS AMONG FINNISH ADOLESCENTS WITH MAJOR DEPRESSIVE DISORDER

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BACKGROUND: Studies assessing the prevalence and nature of sleep disturbances in adolescents diagnosed with major depressive disorder (MDD) are significantly few in number.[1] Whether depressed adolescents manifest different clinical features according to the absence or presence, and according to the nature of the sleep disturbances remains poorly understood. In particular, to our knowledge, depressed adolescents have not been previously studied separately from prepubertal children despite the fact that the association between sleep problems and depression may change when children mature into adolescence and adulthood.[2]

AIM OF THE STUDY: The aim of our study was to 1) examine the prevalence rates of different sleep disturbances in a sample of Finnish adolescents with MDD, 2) examine whether the adolescents without and with sleep disturbances differ in severity of depression and the presence of comorbid psychiatric disorders, 3) examine whether the different sleep disturbances in adolescents can be associated with different symptom profiles of depression.

METHODS: A total of 169 Finnish adolescents (age 13–19; mean 16,5 years old; 17% boys) diagnosed with MDD (as defined by DSM-IV criteria) were included in the study. Their sleep complaints were assessed with self-rating scales and interviews as a part of their clinical assessment.

RESULTS: In our preliminary analysis, the prevalence rate of subjective sleep complaints in Finnish adolescents with MDD was high: 74% of the depressed adolescents experienced significantly disturbed sleep, while the minority (13%) did not have any sleep problems. The most common type of insomnia was initial insomnia (41%), while middle (26%) and late-night (10%) insomnia were less frequent. 30% of the adolescents reported having much more nightmares than usual.

CONCLUSIONS: These findings suggest a need for the assessment of and attention to sleep problems among depressed adolescents in research and clinical settings.

1. Ivanenko et al. Sleep Med Rev 2005;9:115–29.
2. Knowles et al. Neuropsychopharmacology 1990;3:251–9.

PO-1-023

HYPERAROUSAL AMONG CHRONIC INSOMNIA PATIENTS AND INDIVIDUALS PRONE TO STRESS-RELATED SLEEP DISTURBANCES

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Many physiological and behavioral/psychological factors have been shown to be associated with chronic insomnia. However, the roles that the factors play along the development of chronic insomnia are still unclear. Previous studies have demonstrated that patients with insomnia showed increased levels of arousal in autonomic nervous system (e.g. heart rate, metabolic rate, cortisol level), central nervous system (e.g. EEG, event-related potential [ERP]), and subjective ratings of arousal level. However, it is not clear if the hyperarousal is a predisposing condition that exists before the development of persistent insomnia or a perpetuating factor that developed after a longer term of insomnia. The present study aims to clarify the role of hyperarousal in the development of insomnia. The study included 9 chronic insomnia patients, 14 non-insomniac subjects with high vulnerability to stress-related transient sleep disturbance as measured by the Ford Insomnia Response to Stress Test (FIRST), and 13 good sleepers with low vulnerability. Their ERP to tones during NREM sleep, R-R interval of EKGs and subjective arousal on the Pre-Sleep Arousal Scale (PSAS) were measured. In addition to a baseline condition, a stress-eliciting condition by anticipating giving a speech was introduced for the two non-insomniac groups. The results showed that chronic insomnia patients manifested higher level of arousal in ERP latency and R-R interval than the other two groups under no stress elicitation. However, while under stress condition, high vulnerable group showed increased level of subjective cognitive arousal similar to insomnia group that is higher than low vulnerable group. The findings suggest that the hyperarousal may be more a product of long-term experiences of poor sleep rather than a predisposing trait. The psychological reactivity to stress, however, may prone individuals to react to stress and that may prolong the sleep disturbance into a chronic condition.

PO-1-024

INSOMNIA AND QUALITY OF LIFE OF PATIENTS WITH DEMENTIA IN LONG-TERM CARE FACILITIES

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Quality of life (QOL) is an important target of dementia care and insomnia is very frequent symptoms among dementia patients. However, there have been few studies on the relationship of insomnia

to QOL of dementia patients in long-term care facilities. We performed a questionnaire survey of QOL assessment and clinical characteristics in elderly patients with dementia in Japan, using QOL questionnaire for dementia (QOL-D). Insomnia is significantly correlated with low QOL scores in the field of negative affect&actions and restlessness, but not correlated with QOL scores in the fields of positive affect, communication ability, attachment to others and sponteneity. Logistic regression analysis revealed that insomnia is significantly related with low QOL scores in the fields of negative affect&actions and restlessnee, independently of age, sex, cognitive function and activity of daily livings. QOL of dementia patients might be influenced by insomnia. We should more attention to insomnia among dementia.

PO-1-025

THE RELATIONSHIP BETWEEN SLEEP PATTERNS AND MENTAL HEALTH IN ELDERLY PEOPLE SUFFERING MINOR DEPRESSION

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Depression is increasing in Japan prompting the need to find ways to prevent and combat depression. We have created a program to combat and prevent depression as well as a program to improve sleep patterns using physical exercise. Our studies indicate that exercise reduces depression symptoms and improves sleep patterns in community-dwelling elderly (CDE) people. Exacerbation of depression symptoms worsens sleep patterns, while poor sleep patterns worsen symptoms of depression. This condition results in a vicious cycle of worsening depression and sleep patterns. Our hypothesis is that exercise is a way to break this cycle. To test our hypothesis, we did research among CDE people who have the highest number of sleep related complaints and exhibit higher depression rates.

PURPOSE: This study explored the relationship between sleep patterns and mental health in elderly people suffering minor depression.

METHODS: This was a cross-sectional study. Subjects were elderly people diagnosed with symptoms of minor depression by a psychiatrist (n = 20, 76 ± 4 yr: mean±SD male = 1, Female = 19). The Pittsburgh Sleep Quality Index (PSQI-J) measured sleep quality. The Profile of Mood States (POMS) was the mental health index. Correlation analysis was used for statistical analysis.

RESULTS: The average PSQI-J score was 7.6 points. 65% of participants had sleep disorders. There is a significant relationship between the PSQI-J scores and the Tension-Anxiety, Depression-Dejection, and Anger-Hostility scores through correlation analysis ($r = 0.545$, $P < 0.05$, $r = 0.634$ $P < 0.01$, $r = 0.558$ $P < 0.05$).

CONCLUSION: People with sleep related problems had higher levels of depression. This doesn't necessarily indicate a causal relationship, however this does lend credence to studies showing that poor sleep patterns are a risk factor leading to depression. This study intimates that exercise is effective in breaking the vicious cycle of depression and poor sleep patterns.

PO-1-026

ASSOCIATION BETWEEN DEPRESSION SYMPTOMS AND INSOMNIA IN SMALL OFFICES

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Background of the study: The prevalence of depression is increasing in the Methods.

Subjects: Small-to-medium-sized business offices with 50 or less employees joining local chambers of commerce within an area of 600,000 people under the district K public health center.

Survey method: Questionnaires were mailed to 700 offices by random sampling requesting a response by mail.

Contents: Sixteen items concerning depression symptoms.

Analysis: Statistics software SPSS 17.0J for Windows was used to analyze and compare values by descriptive statistics and the Wilcoxon rank-sum test. workplace every year. Ethical consideration. Each registrant of chambers of commerce was asked to participate in the study after an explanation of the purpose of the study in writing. Submission of a completed questionnaire was considered acceptance of study participation. Submitted data were handled appropriately and used with the promise of them being used only for study purposes so that individual subjects could not be identified.

Conflicts of interest: None.

Results: Three hundred and thirteen offices submitted effective responses, of which 39.6% were manufacturers, 16.9% were builders, 12.5% service industry, and 8.3% transportation industry. There was a positive correlation between insomnia and depression symptoms: people with a sense of responsibility are likely to have depression ($P < 0.01$); depression can develop in about 1 out of 15 persons during life ($P < 0.05$); it is difficult to recover from depression once it develops ($P < 0.01$); people with depression should change jobs or resign because they do not fit in the current workplace ($P < 0.01$); I want them to work a little harder because we are busy ($P < 0.05$); it is difficult to visit psychiatric clinics ($P < 0.01$).

PO-1-027

ANALYSIS OF GENETIC EXPRESSION IN THE SOFT PALATE OF PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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To evaluate the biomolecular characteristics of the tissue where airway obstruction actually occurs, the genetic expression was investigated in the soft palate of patients with obstructive sleep apnea (OSA). The soft palate mucosa was obtained during uvulopalatal flap surgery. Three patients with apnea/hypopnea index (AHI) over 60 were enrolled for an OSA group, and 3 simple snoring patients with AHI less than 5 for a control group. After total RNA was extracted and amplified into microarray, gene expression levels were calculated, and relative signal intensities for each gene were evaluated. Of the 45,034 genes analyzed, 232 genes were statistically different between the OSA group and simple snoring group and genes involved in metabolism were the most common. Our results suggest that there may be changes of gene expression in soft palate as OSA proceeds.

PO-1-028 / AS-12 Presenter

A GENOME-WIDE LINKAGE STUDY IN OBSTRUCTIVE SLEEP APNEA PHENOTYPES AND SUB-PHENOTYPES

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Background: Familial aggregation of obstructive sleep apnea (OSA) has been identified in several populations. Whilst the few OSA genome-wide linkage studies conducted have demonstrated suggestive linkage regions, they have failed to show significant linkage. The aim was to conduct a genome-wide linkage study in a well-characterized population to further investigate OSA susceptibility genes.
Methods: Subjects were from the Iceland Sleep Apnea Cohort Study. OSA diagnosis was defined from overnight polysomnography. Linkage analysis was conducted for OSA phenotypes using 4–6 meiotic clustering (MC) for dichotomous outcomes, and quantitative trait loci (QTL) analysis for the apnea-hypopnea index (AHI) and oxygen desaturation index (ODI). Parametric and non-parametric analyses were performed using an affected-only approach. Fine mapping of linkage regions was conducted via the 300 K Illumina Bead Chip.
Results: There were 2,250 OSA subjects included. Eleven linkage peaks were observed (2q36, 5p14, 7p14, 7p21, 10q26, 11p14, 11q13, 11q25, 12q24, 18q12, 19p13). The highest LOD scores were demonstrated for 5p14 and 11q25. The linkage peak at 5p14 was found in subjects with AHI and/or ODI more than or equal to 5, and in subjects with AHI and/or ODI more than or equal to 15. The linkage peak at 11q25 was shared between OSA and obese OSA phenotypes. Most linkage peaks were confined to obese OSA phenotypes (2q36, 7p21, 10q26, 11p14). QTL analysis yielded one linkage peak for AHI (3q29) and four for ODI (2p14, 4q13, 4q31 10p15). Fine mapping of these linkage regions did not detect any significant associations with OSA phenotypes.
Conclusions: Several peaks for suggestive linkage regions were identified, with most limited to obese OSA phenotypes, some of which contain known obesity genes. None of the linkage peaks identified in this study reached genome-wide significance. These findings suggest there may not be any common variants with large effects which contribute to OSA risk, however further investigation is required.

PO-1-029

THE INFLUENCE OF AGE ON AROUSAL DENSITY FOR OBSTRUCTIVE SLEEP APNEA SYNDROME

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Objectives: Obstructive sleep apnea syndrome (OSAS) is a common syndrome afflicting millions. OSAS is a sleep breathing disorder characterized by recurrent airflow obstruction caused by total or partial collapse of the upper airway. Cardiovascular and neuropsychological morbidity has been demonstrated in untreated sleep apnea. At present polysomnography (PSG) remains the golden standard for the diagnosis of OSAS. The arousals are transient and generally do not result in behavioral awakening, and recur in some conditions as often as once per minute. EEG arousal is the important parameter of sleep fragmentation. Previous study reported respiratory effort decreases with increasing age. The objective of this study was to evaluate the effect of age on arousal for OSAS.
Methods: Five-hundred forty-two male patients with a diagnosis of OSAS by standard PSG were recruited from China Medical University Hospital Centre and obtained the EEG arousal index (ArI). The presence of OSAS was defined as AHI > 5/h. This study divided subjects into groups based on age > 40, 40 ≦ age < 60 and age ≧ 60. To avoid the effect of the severity of OSAS, this study also separated patients into three levels of severity of OSAS included the AHI < 15, 15 ≦ AHI < 30, and AHI ≧ 30, respectively.
Results: When the severity of OSAS is AHI < 15, the ArI between different age groups is not significant (age < 40: 18.4 ± 10.3, 40 ≦ age < 60: 23.7 ± 14.3, age ≧ 60: 19.4 ± 7.8, NS). Moreover, when the severity of OSAS is 15 ≦ AHI < 30 and AHI ≧ 30, the ArI between different age groups is still not significant (15 ≦ AHI < 30, age < 40: 25.2 ± 10.4, 40 ≦ age < 60: 28.2 ± 10.4, age ≧ 60: 33.6 ± 15.3, NS; AHI ≧ 30, age < 40: 43.8 ± 22.7, 40 ≦ age < 60: 47.4 ± 19.6, age ≧ 60: 46.2 ± 23.2, NS).
Conclusions: This study evaluated the influence of age on arousal in male patients with OSAS. The results revealed the aging has no effect on arousal density and the arousal density increased as the severity of OSAS increased.

PO-1-030

FREQUENTLY USED SLEEP QUESTIONNAIRES IN GENETIC AND EPIDEMIOLOGICAL RESEARCH FOR OBSTRUCTIVE SLEEP APNEA: A REVIEW

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Background: Many sleep questionnaires are utilized by the epidemiological and genetic research communities. This paper will review and compare sleep-related questions and answers commonly used in epidemiological studies, with a particular emphasis on the utility of the response options available.
Methods: A literature search was conducted to identify sleep questionnaires meeting the inclusion criteria. Questionnaires were limited to the English language and had to include questions specific to snoring or stop breathing during sleep. Questionnaires also had to demonstrate a citation count > 10 through Web of Science. Questions and answers from eligible questionnaires were compared.
Results: There were fourteen questionnaires meeting the inclusion criteria for final review. These questionnaires were very heterogeneous, with only some (n = 6) allowing a *don't know* alternative. Altogether six specified the time period referred to as *past month*, one referred to *last three months* and the remaining questionnaires had no specific timeframe. The response alternatives to specific questions were Yes or No (n = 5), wording only like *never*, *seldom*, *often* (n = 4), or a frequency scale indicating times per week (n = 8).
Conclusions: There is a need for improved standardized instruments not only to capture relevant sleep information but also to allow greater comparability between studies.

PO-1-031

THE PREVALENCE OF SLEEP APNEA IN POMERANIA / GERMANY – PRELIMINARY RESULTS FROM THE SHIP-TREND STUDY

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The SHIP-TREND study (Study of Health in Pomerania) is the first German population based study which implemented attended cardiorespiratory polysomnography (PSG) with a one night recording as one of the key parameters. The method in the main focus of this epidemiological study is a full body MRI to evaluate the health status of the pomeranian population. A high cardiovascular risk, specifically arterial hypertension, has been reported earlier for this region of Germany.
As one part of the SHIP- Trend study cardiorespiratory PSG is offered to all subjects between 20 and 79 years of age when they are drawn to participate. As part of the sleep study module subjects completed the Insomnia Severity Index (ISI scale), Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), and Restless- Legs Syndrome Diagnostic Index (RLS-DI). Additionally all participants answered some specific questions about sleep duration and quality.
Until December 2010 2769 volunteers entered the study and 966 of them underwent PSG. In a preliminary analysis 805 subjects were analyzed (370 female, 435 male). The mean age was 53 years. 208 of 805 subjects (25.8%) showed an apnea-hypopnea index (AHI) greater than 15 per hour sleep. There was a significant difference in gender related prevalence of obstructive and central apnoeas. Mean AHI in women was 7.6 per hour sleep and in men 15.1 per hour sleep. Independent of gender the AHI increases with BMI and age significantly.
Prevalence of obstructive sleep apnea in pomeranian population is high. PSG was done only in those subjects who agreed to participate in this module. Men showed more nocturnal breathing events than women. We detected in both groups a progression of breathing events with age. In the influence of concomitant disorders has to be analyzed.

PO-1-032 / AS-2 Presenter

ASSOCIATION BETWEEN SYMPTOMS OF SLEEP-DISORDERED BREATHING AND DAYTIME SLEEPINESS WITH SCHOOL-AGED CHILDREN IN JAPAN: A LARGE-SCALE CROSS-SECTIONAL SURVEY

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Objective: Children with sleep-disordered breathing (SDB) have been shown to be vulnerable to significant daytime sleepiness and consecutive cognitive impairment and behavioral symptoms. This study aimed to investigate the prevalence rate of SDB-related symptoms in the Japanese school-aged children, and confirm the association between SDB-related symptoms and daytime sleepiness.
Subjects & Methods: Cross-sectional survey was performed for 6 to 15 year-old-children (n = 25,211, average age = 10.8 ± 2.5) in 148 elementary schools and 71 junior high schools in 10 areas across the country. Parents answered a newly prepared questionnaire based on A Brief Screening Questionnaire for Infant Sleep Problems (Sadeh et al.) and Children's Sleep Habits Questionnaire (Owens et al.). This questionnaire consisted of thirty-one items to evaluate sleep habits and sleep problems including four items to detect SDB (snoring, SN; snorts and gasps, SG; stop breathing, SB) and daytime sleepiness.
Result: Among 25,211 children whose parents completed questionnaire, the prevalence rate of SN, SG, SB and daytime sleepiness with the frequency of five or more times a week were 378(1.4%), 47(0.18%), 52(0.2%) and 226(0.89%), respectively. The prevalence rate of daytime sleepiness in children with SN, SG and SB was 5.0%, 14.8% and 21.2%. The prevalence rate of daytime sleepiness in children with all the three SDB-related symptoms was 26.0%. Logistic regression analysis revealed that SN (OR = 3.824, 95% CI 2.038 to 7.176) and "SG or SB" (OR = 13.378, 95% CI 6.002 to 29.816) significantly correlated with the presence of daytime sleepiness even after adjusting age, gender and total sleep time.
Conclusion: This large-scale cross-sectional survey has revealed the prevalence rate of SDB-related symptoms among the Japanese school-aged children and that they could be independent risk factors of severe daytime sleepiness in these children.

PO-1-033

PREVALENCE OF RESTLESS LEG SYNDROME AMONG ADOLESCENT CHILDREN IN THE TUCSON CHILDRENS ASSESSMENT OF SLEEP APNEA STUDY TUCASA

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Introduction: Restless Leg Syndrome (RLS) and its association with sleep problems in normal children has been understudied. This analysis aims to describe the prevalence of RLS, and its association with sleep problems, in the adolescent age group.
Methods: TuCASA study is a prospective, cohort study that initially enrolled Hispanic and Caucasian children between the ages of 6 and 11 years (Time 1) and subsequently re-studied them about 5 years later at approximately 10–18 years of age (Time 2). At both time points, in-home polysomnography as well as comprehensive sleep habits surveys were completed. RLS was present if the subject met 4 essential adult RLS criteria described by Allen (2003). Habitual snoring (SN), excessive daytime sleepiness (EDS), difficulty initiating or maintaining sleep (DIMS), and learning problems (LP) were present if symptoms were present frequently or almost always. Enuresis (EN), sleep terrors (TR), sleep walking (SW) and sleep talking (ST) were also assessed.
Results: Assessments were obtained in 348 children (49% girls; 36% Hispanic) at both time points with a mean interval between assessments of 4.6 years. The prevalence of RLS was 4.3%. RLS was associated with the presence of EDS ($p < 0.006$), DIMS ($p < 0.013$), and SN ($p < 0.029$). There was no significant association between RLS and gender or ethnicity. There was no association between RLS and LP, EN, SW, or ST, however, in general we lacked the power to demonstrate a statistically relevant result.
Conclusions: The prevalence of RLS in a community based sample of adolescents is approximately 4.3%. RLS in adolescents is associated with EDS, DIMS, and habitual snoring. The prevalence of RLS was

higher in girls than boys (5.3% vs 3.4%) but this difference was not statistically significant. HL 62373

PO-1-034 / AS-9 Presenter

THE ROLE OF OBESITY, DIFFERENT FAT COMPARTMENTS AND SLEEP APNEA SEVERITY IN CIRCULATING LEPTIN LEVELS: THE ISAC STUDY

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Aim: To assess the relative role of OSA and obesity on leptin levels.
Methods: 452 untreated OSA patients in the Icelandic Sleep Apnea Cohort (ISAC) study were assessed. They underwent a sleep study, magnetic resonance imaging of the abdomen to measure visceral and subcutaneous fat volume and fasting morning leptin levels were measured in serum.
Results: BMI, subcutaneous and total fat volume were more highly correlated with leptin levels than visceral fat volume (bootstrapped analysis, $r = 0.58–0.67$ vs. $r = 0.24$, $p < 0.001$). A multiple linear regression model with quadratics and interactions was used to assess the effects of obesity and OSA severity on leptin levels adjusting for gender (main effects only). The model involving BMI, AHI and gender explained 60.6% of the variance in leptin levels. Terms involving BMI explained 38.7%, gender 21.2% but AHI had no significant effect. The same was found for hypoxia severity. No interaction was found between different measures of OSA severity and BMI on leptin levels. The presence of hypertension had, however, a significant effect on the interaction between AHI and BMI ($p = 0.04$). For subjects without hypertension ($n = 249$), there was a significant but minor effect of OSA severity (explaining 2.1–3.2%) and an interaction between OSA severity and BMI (explaining 1.5–1.7%). For nonhypertensive subjects, the effect of increased OSA severity was the greatest for nonobese subjects and smaller for obese subjects. However, these associations where not found for hypertensive subjects ($n = 199$).
Conclusion: OSA severity does not affect leptin levels, except in nonobese nonhypertensive OSA subjects. Total fat and subcutaneous fat volume is more important in determining leptin levels than visceral fat volume.

PO-1-035

MORBIDITY PRIOR AND AFTER A DIAGNOSIS OF SLEEP DISORDERED BREATHING. A CONTROLLED NATIONAL STUDY

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Sleep disordered breathing (SDB) causes significant burden. Former studies have focused on cardiovascular diseases (CVD) after diagnose of sleep apnea (SA) or obesity hypoventilation syndrome (OHS) but the overall morbidity prior to a SDB diagnose is incompletely evaluated. Using data from the Danish National Patient Registry (1998–2006), we identified all national patients with a diagnosis of SA (19438), or OHS (755). For every patient, we randomly selected 4 age-, sex- and socio-economic-matched citizens from the Danish Civil Registration System Statistics. We further extracted information from the Danish Ministry of Health, Danish Medicines Agency, and National Health Security. Pts with SA and OHS presented increased morbidity (p lt 0.01) up to more than eight years prior to a SDB diagnose of SA the most common contacts were diseases of the endocrine, nutritional and metabolic diseases ((Odds Ratio (OR) SA/OHS 4.5/4.8), nervous system: OR 4.4/5.5), respiratory system (OR: 2.9/4.0), skin and subcutaneous tissue (OR 2.5/1–3), infections (OR 1.8/3.0), CVD (OR 1.7/1.3), genito-urinary system (OR 1.3), ear-nose and throat (OR 1.3), psychiatric diseases (OR 1.1/1.4). After a SDB diagnose, patients also presented significant morbidities and mortality. CPAP treatment reduced mortality 6.6% versus 5.5 in SA pts, 4.0% in control subjects.
Conclusion: Patients with SDB shows significant morbidities several years prior to a diagnose of SA or OHS. As early detection of SA/OHS is important for improving prognosis, SDB should be considered in patients with endocrine, nutritional, metabolic, neurological, and pulmonary and CVD disorders.

PO-1-036

ASSOCIATION OF WORSE GLYCEMIC CONTROL AND HYPOXEMIA IN MIDDLE-AGED CHINESE PATIENTS WITH TYPE II DIABETES AND OBSTRUCTIVE SLEEP APNEA

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Introduction: Accumulating data suggest that obstructive sleep apnea (OSA) is highly associated with glucose dysmetabolism, but the association between OSA and glycemic control in established diabetes is not well understood. This study investigated the relationship between OSA and glucose control in type II diabetic Chinese patients.
Methods: Patients with type II diabetes and age <65 were recruited from our outpatient clinic. They were all invited to undergo overnight in-laboratory polysomnography. Clinical data and fasting biochemical markers were collected on waking the next morning. HbA1C was measured as the glycemic control index.
Results: 112 diabetic patients were evaluated. Their mean (±SD) age was 53.0 ± 6.7 years, body mass index (BMI) was 27.2 ± 4.5 kg/m^2, HbA1C was 8.6 ± 1.5% and median (±interquartile range) apnea hypopnea index was 6.1 (1.7, 19.8) events/hour. When they were divided into 3 groups according to HbA1C level (Group 1: <8% (n = 38),Group 2: 8–8.9% (n = 32), Group 3: >= 9% (n = 42)), there was no significant difference in age, BMI, Epworth sleepiness scale, blood pressure, smoking and drinking history. However, minimum oxygen saturation was significantly lower in group 3 ($p = 0.006$) compared to groups 1 and 2, after adjusting for gender, duration of diabetes and number of diabetic drugs.
Conclusion: In this clinic-based population, hypoxemia is significantly associated with worse glycemic control in middle-aged Chinese patients with type II diabetes and OSA.

PO-1-037

QUALITY OF LIFE IN SLEEP APNEA COMPARED TO CONTROLS

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Introduction: The quality of life is intrinsically linked to sleep quality. Patients suffering from obstructive sleep apnea (OSA) have disturbed sleep which may in some patients lead to severe impairment. The aim of this study was to measure health-related quality of life with standardized measurements in a large group of OSA patients and compares the results to the general population.
Material and Methods: The OSA subjects (n = 822) were a part of the Icelandic Sleep Apnea Cohort. They were newly diagnosed with moderate or severe OSA (665 males, 157 females). The control subjects (n = 742) were randomly chosen Icelanders (394 males, 348 females) who participated in another epidemiological study (www.boldcopd.org). To measure Quality of life, SF-12 was administered to controls and OSA patients before CPAP treatment was started. A 2 year follow-up is ongoing.
Results: The mean ± SD unadjusted SF-12 Physical Component Summary Score (PCS) was 40.3 ± 10.9 for OSA patients but 50.7 ± 8.0 for controls. The mean ± SD SF-12 Mental Health Component Summary Score (MCS) was 48.3 ± 10.9 for OSA patients compared 51.4 ± 4.8 for controls. Multiple linear regression analysis for the pooled material of OSA and controls showed that PCS was strongly related to presence of OSA, male gender, age and obesity (R2 adjusted = 33.5%) while much less of the variation in MCS could be explained (R2 adjusted = 5.4%). OSA severity by itself was, however, neither related to PCS nor MCS. Altogether 497 OSA patients have been evaluated in the two year follow-up (80% of invited). Of these, 179 were no longer CPAP users. Preliminary results among CPAP users show that CPAP use is associated with an increase in PCS by 3.3 ± 9.4 (compared to 2.1 ± 10 among non-users). MSC increased by 3.1 ± 10.4 among CPAP users (compared to1.7 ± 11.3 among non-users).
Conclusion: OSA patients report severely impaired quality life compared to controls, especially in the physical component.

PO-1-038

GENDER DIFFERENCES IN THE RELATIONSHIPS BETWEEN POLYSOMNOGRAPHY AND PHYSICAL FACTORS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA-HYPOPNEA SYNDROME

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Purpose: To determine whether apnea severity between men and women is related to physical characteristics such as body mass index (BMI), neck circumference (NC) and age.
Material and Method: A total of 1094 patients with obstructive sleep apnea-hypopnea syndrome (OSAHS) were referred to our sleep clinic. Each patient's BMI, NC and age were recorded during one month period in April, 2011. Polysomnography (PSG) was performed on all patients who attended our clinic. Sixty eight patients presented by the other hospital were excluded from the study. The patients were divided according to sex and age (over or below 60 y.o.). Apnea-hypopnea index (AHI) and lowest SpO_2 were included in the results of PSG. The patients who indicated the lowest SpO_2 below 50% were excluded for the analysis. Physical characteristics measured were BMI and NC.
Result: The patients were divided into male <60 y.o., male.≧60 y.o., female <60 y.o. and female.≧60 y.o. Their number was 756, 194, 32 and 44 respectively. BMI and NC correlated with AHI significantly in each of the 4 subgroups. In males, BMI and NC correlated with the lowest SpO_2 negatively irrespective of age, but not in females.
Conclusion: These results suggest that obesity and neck circumference are not related to severe hypoxemia during sleep in females with OSAHS in Japan.

PO-1-039

ASSOCIATION BETWEEN SLEEP DISORDERED BREATHING (SDB) AND PSYCHOMOTOR VIGILANCE TASK (PVT) IN GENERAL POPULATION: A CROSS-SECTIONAL STUDY

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Introduction: Sleep disordered breathing (SDB) is known to be associated with increased risk of car accidents. To evaluate sleepiness associated with impaired performance, the multiple sleep latency test is considered a valuable objective measure, although it is too complex to be performed widely. The Epworth Sleepiness Scale (ESS) is commonly used to evaluate sleepiness because of its simplicity, but it does not necessarily correlate with objective measures. We hypothesized in patients with SDB, their performance is impaired regardless of their ESS scores, and it could be detected by psychomotor vigilance task (PVT).
Methods: 642 local residents aged 30–79 years from Toon City, Japan participated. They completed 10 minutes PVT in a morning at local health center and underwent SDB screening test at their home using single-channel airflow monitor on the subsequent night. SDB was indicated by the respiratory disturbance index (RDI); PVT variables included mean reciprocal of reaction time (RT)s, number of lapses, mean reciprocal of fastest 10% RTs, mean reciprocal of slowest 10% RTs, slope of linear regression line across the 10 minutes of the task fit to reciprocal of RTs, and number of false responses. Also, detailed questionnaire including ESS, sleep duration, and ethanol intake were obtained.
Results: A linear trend of the PVT variables with RDI levels showed significant negative association between RDI and mean of the slowest 10%, number of lapses, and the slope in participants aged <= 60, even after adjusted for age, sex, BMI, ethanol intake, and sleep duration. The ESS score did not differ significantly among each RDI levels.
Conclusion: Our finding indicated that in patients with SDB, the PVT may be useful in evaluating impaired vigilance which could not be detected by the ESS.

PO-1-040

LONGITUDINAL STUDY OF SLEEP BREATHING DISORDER (SBD) IN THE GENERAL POPULATION OF KOREA

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Objective: Evolution of SBD has been little documented in general population. Longitudinal information can be gathered by interviewing the same individuals at different times but it can also be obtained by measuring a population at different occasions. This study presents the results related to SBD in South Korea assessed in a 7-year interval.
Methods: The first study was carried on in 2001 with 3719 individuals aged 15 years or older representative of the general population of South Korea. The second study was performed in 2008 using a representative sample of 2537 individuals in the same age range. The methodology was the same for both studies. The participants were interviewed by telephone using the Sleep-EVAL system. The interviews covered sleep habits, sleep symptomatology, physical and psychiatric illnesses. DSM-IV sleep and psychiatric disorder diagnoses were also assessed.
Results:

1) MenIn 2001; 8.1% of the sample reported having snoring; the prevalence was increased to 13.7% in 2008. In 2001; 2.9% of the sample reported having OSAS; the prevalence was increased to 4.7% in 2008.
2) WomenIn 2001; 2.8% of the sample reported having snoring; the prevalence was increased to 6.2% in 2008. In 2001; 1.7% of the sample reported having OSAS; the prevalence was increased to 2.6% in 2008.

Conclusions: Overall, prevalence of SBD has increased over a 7-year period mainly in the young adult individuals. The increase of SBD is strongly correlated with weight gain among the young adult in korean population.

PO-1-041

A SURVEY ON THE MANAGEMENT OF SLEEP APNEA IN EUROPE

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Introduction: Even within Europe, the services provided for the investigation and management of sleep disordered breathing (SDB) vary from country to country. To study this variation a questionnaire-based study was initiated to investigate the status of diagnostic pathways and therapeutic methods currently used. In the management of SDB in Europe personal qualification requirements for physicians involved in the diagnosis and treatment of SDB are assessed and reimbursement of sleep medicine services in different European countries are specified.MethodsTwo questionnaires were sent to 39 physicians in 22 European countries. In order to standardize the answers, the questionnaires were accompanied by completed examples.ResultsSleep centers from 21 countries (38 physicians) participated. A broad consistency among countries with respect to the following was found: clinical pathways included referral to sleep physicians, sleep laboratories, requirement of an objective diagnosis (primarily by polysomnography), indications for positive airway pressure (PAP) therapy, application of standard PAP therapy (100% with an CPAP/APAP ratio of 2.24:1), and the need for some form of treatment follow-up study (90.5%). Differences between countries were apparent for reimbursement of the diagnostic procedures, reimbursement for follow-up studies, in the procedures for PAP titration which ranged from home APAP titration with portable sleep apnoea monitoring (38.1%) up to titration with hospital based attended polysomnography and APAP (85.7%), as well as the personal qualification requirements for sleep physicians.DiscussionManagement of OSA in different European countries is similar but there are differences in reimbursement rules, qualification of sleep specialists and procedures applied for titration of CPAP treatment. A European network can help to implement a better unified health-service for sleep medicine in sleep disordered breathing in order to standardize management in a cost-effective way. Key words: Public health services; sleep disordered breathing.

PO-1-042

SERUM FERRITIN LEVELS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNOEA (OSA), COMPARED TO THE GENERAL POPULATION. – AN EPIDEMIOLOGICAL CASE-CONTROL STUDY-

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Background: Ferritin is an intracellular iron storage protein but also a marker of acute and chronic inflammation. Previous studies have shown that subjects with sleep apnea (OSA) have higher levels of circulating pro-inflammatory cytokines but little is known about the association between ferritin, OSA and its comorbitities.
Objective: The aim of the study was to evaluate S-ferritin levels in OSA patients before and after CPAP treatment and compare it to S-ferritin levels in the general population. Also to study if there were correlation of S-ferritin levels to OSA comorbiditis.
Methods: The OSA subjects (n = 822) were a part of the Icelandic Sleep Apnea Cohort. They were newly diagnosed with moderate or severe OSA (665 males,157 females). The control subjects (n = 742) were randomly chosen Icelanders (394 males, 348 females) who participated in another epidemiological study (www.boldcopd.org). S-ferritin levels were measured, participants answeared a detailed questionnaire with questions about sleep, health and the Epworth Sleepiness scale. The OSA patients underwent a sleep study. The change with CPAP treatment was assessed after 2 years (n = 538).
Results: S-ferritin was significantly higher in OSA patients than controls, both in men ($p = 0.007$) and women ($p = 0.0006$) but after adjusting for body mass index (BMI), age, smoking status and co-morbidities, S-ferritin was only found to be significantly elevated in OSA women ($p = 0.032$). S-ferritin did not show any significant correlation with severity of OSA, daytime-sleepiness or level of CPAP usage at the two-year follow up.
Conclusions: Women with OSA had significantly higher S-ferritin levels than controls after adjusting for BMI, age, smoking status and co-morbidities.

PO-1-043

PREVALENCE OF HYPERTENSION IN INDONESIAN SLEEP APNEA PATIENTS

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Introduction: Sleep-disordered breathing (SDB) and sleep apnea have been linked to hypertension in many studies. Apnea and hypopnea cause temporary elevations in blood pressure in association with blood oxygen desaturation, arousal, and sympathetic activation and may cause elevated blood pressure during the daytime and, ultimately,sustained hypertension. There is no data on prevalence of hypertension in Indonesian Sleep Apnea patients. Should the diagnosis of apnea be actively sought with sleep studies in hypertensive populations?
Methodology: This is a cross-sectional study of more than 200 Indonesian patients attending a sleep clinic. All patients were diagnosed as Obstructive Sleep Apnea by undergoing attended in hospital overnight polysomnography. We analyzed data of hypertension, body mass index, diabetes, ischemic heart disease and stroke in these patients. Severity of Sleep Apnea and oxygen desaturations was examined in conjunction to hypertension.
Results: Patients age range from 21 to 79 years. All patients present with snoring, 40% present with snoring and hypertension. Most patients had moderate to severe Sleep Apnea with Apnea-Hypopnea Index of more than 15 per hour.
Conclusions: Prevalence of hypertension is very high in Indonesian Sleep Apnea patients. The presence of hypertension in snoring patients should alert physicians to investigate with sleep studies.

PO-1-044

ASSOCIATIONS BETWEEN SLEEP APNEA SYNDROME AND GASTROESOPHAGEAL REFLUX DISEASE (GERD)

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A link between obstructive sleep apnea syndrome (OSAS) and gastroesphageal reflux disease (GERD) has been suggested, with patients being predisposed to both conditions, with similar etiologic risk factors such as obesity and alcohol use. Although a high prevalence of GERD in patients with OSAS is noted even in Japan, no studies have shown a clear association and therefore a cause and effect relationship is not unknown. We aim to investigate the direct associations between GERD and OSAS in relatively large number of the patients. Eight hundreds thirty eight consecutive men who referred to the Sleep Center of Nihon University and Sleep Clinic of Kanamecyo Hospital were included in this study. Before diagnostic polysomnography (PSG), subjects completed a brief 12 item questionnaire that is called the frequency scale for the symptoms of GERD (FSSG) and is the sole tool used to diagnose GERD in this study. More than 8 of 48 points was evaluated positive (+) in GERD. A full night PSG was performed in all subjects. The patients with apnea-hypopnea index (AHI) > 5 received a diagnosis of OSAS. OSAS was found in 781 (93.1%) and GERD (+) (FSSG > 8) was detected in 316 (37.7%) out of 838 cases. GERD (+) group were significantly younger than GERD (-) group. On PSG data, although AHI was not different among groups, the lowest SpO2 was significantly lower in GERD (+) group than that in GERD (-) group. Subjects were divided to 5 groups according to AHI, non, mild, moderate, severe, and very severe OSAS and were examined the relationships between severity of SAS and GERD. FSSG and prevalence of GERD (+) were significantly increased as AHI was elevated. However FSSG was also significantly higher in obese subjects than in nonobese subjects. These results suggest that OSAS was clearly associated with occurrence of GERD although the influence of body habitus was not ruled out even in large scale study.

PO-1-045

PREVALENCE OF RISK FACTORS FOR UNDIAGNOSED OBSTRUCTIVE SLEEP APNOEA IS HIGH IN TRUCK DRIVERS ON UK ROADS

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Objectives: To determine the prevalence of symptoms and risk factors of obstructive sleep apnoea (OSA) in truck drivers at a UK large truck stop.
Methods: Over a 5 day period, truck drivers completed a short questionnaire at a major UK 'truck stop'. The questionnaire asked about OSA rist factors and symptoms, and included the Epworth Sleepiness Scale (ESS). Additionally, measurements of height, weight and collar size were taken. 148 truck drivers participated and within this random group the risk factors of OSA that were looked for were:men age over 40 y, obesity, parge neck circumference, smoking, high ESS and bed partner reporting snoring with witnessed apnoeas.
Results: Our sample were all men, with 82% aged over 40 y. 47% were obese (compared with 23% for UK men in general) and average neck circumference was 42 cm (compared with 38 cm for UK men in general – Martin et al 1997). 31% smoked (vs 21% for general population), and ESS averaged 2.1 points higher than expected for a healthy population (Johns et al 1997). Snoring was quite evident at 57% (compared wth 40% for men in general) and witnessed apnoeas were almost double (7%) compared with 3.8% given by Ohayon et al (1997) generally for men.
Conclusion: 8 key symptoms and risk factors of OSA have been found to be prevalent in a sample of truck drivers on UK roads, and to greater extent that for estimates in the general male population. Bed partners of truck drivers reporting witnessed apnoeas strongly suggests this group has a high potential for undiagnosed OSA. OSA sufferers are known to be at high risk of causing road traffic accidents. This, together with the large size of trucks, then the potential for serious road crashes is great. Truck drivers, especially those who are obese, ought to be a high priority population for OSA screening.

PO-1-046

WHICH FACTOR RELATES TO SUBJECTIVE SLEEPINESS IN JAPANESE SNORERS? A PROSPECTIVE STUDY BASED ON DATA COLLECTED FROM THE INTERNET

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Background: Subjective excessive daytime sleepiness (EDS) is very weakly associated with the severity of sleep disordered breathing. However, EDS has been reported to be associated with snoring variables as well as apnea/hypopnea index. We investigated EDS determinant in visitors of our homepage on snoring.
Methods: The subjects answered a questionnaire between December 1, 2009 and November 30, 2010. The inclusion criteria were habitual (greater than or equal to 3 nights a week) snorers and age greater than or equal to 20 years. The exclusion criteria were sedative hypnotic use, antiallergic agents use, and previous diagnosis of sleep apnea. Multiple regression analysis was performed using Epworth sleepiness scale (ESS) as the dependent variable.
Results: We included 1,425 subjects (956 men, 469 women) of average age, 39.2 years (20–79); BMI, 24.0 ± 4.0 (mean ± SD); daily time in bed, 6.4 ± 1.3 h; nocturia frequency, 0.3 ± 0.7 (0–5); and ESS, 8.1 ± 4.8. Among these, 733 (51%) had witnessed apnea, 1,148 (81%) had dry feeling in the pharynx at waking, 906 (64%) had night-time nasal obstruction, and 277 (19%) had hypertension. Subjects whose daily time in bed was less than 3 h or greater than or equal to 9 h were excluded, and multiple regression analysis was performed in the remaining 1,387 subjects (931 men, 456 women). Daily time in bed ($\beta = -0.162$), witnessed apnea frequency ($\beta = 0.116$), frequency of dry feeling in the pharynx at waking ($\beta = 0.099$), age ($\beta = -0.059$), and sex ($\beta = -0.059$) were significantly related to ESS ($R^2 = 0.065$; $P < 0.05$). Excluding the frequency of dry feeling in the pharynx at waking, significant factors in the multiple regression model were daily time in bed ($\beta = -0.163$), witnessed apnea frequency ($\beta = 0.125$), age ($\beta = -0.074$), frequency of night-time nasal obstruction ($\beta = 0.064$), and sex ($\beta = -0.064$) ($R^2 = 0.057$; $P < 0.05$).
Conclusions: EDS in Japanese snorers was related to less sleep time, witnessed apnea frequency, frequency of dry feeling in the pharynx at waking, less age, and female sex. Furthermore, nasal obstruction might be related to EDS.

PO-1-047

ASSOCIATION BETWEEN SNORING AND CAROTID ATHEROSCLEROSIS IN NON-OBESE WOMEN

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Background: Recent animal studies have suggested that snoring-induced vibration might have an impact on cardiovascular and subclinical atherosclerotic changes, due to increased local inflammatory responses and adjunct vessel damage in carotid arteries by transmission of vibration energy. The purpose of the present study was to examine whether snoring is associated with intima-media thickness (IMT) on carotid arteries, independent of obesity and sleep apnea.
Methods: Subjects were derived from the Korean Genome Epidemiology Study, an ongoing cohort study of Korean adults. The final sample comprised 1,096 men and 1,014 women who were free of known cardio/cerebrovascular disease, who did not take any medication due to hypertension, diabetes, and dyslipidemia, and who had a body mass index (BMI) less than 27.5 kg/m^2. IMT at the far and near wall of common carotid arteries was measured by B-mode ultrasonogram on both sides. Averaged mean and maximal values of IMT from the four segments were used for analysis. Individuals were grouped into habitual snorers (snoring ≧ 4 days/week), occasional snorers (<4 days/ week), and non-snorers. All participants were asked about a witnessed sleep apnea as follows: "Have you ever heard that you stopped breathing during sleep?"
Results: After adjusting for witnessed sleep apnea and other covariates, both occasional and habitual snorers had significantly higher mean and maximal values of carotid IMT than non-snorers in women ($p = 0.0156$ and $p = 0.0146$ for mean and maximal IMT, respectively), but not in men. In the multivariate logistic regression analyses, odds ratios (95% confidence interval) of mean carotid IMT greater than 0.8 mm were 2.60 (1.10–6.19) for habitual snorers, compared with non-snorers. Odds ratios for maximal carotid IMT greater than 1.0 mm were 1.94 (1.07–3.51) and 3.00 (1.50–6.02) for both occasional and habitual snorers, respectively.
Conclusions: The findings indicate that snoring is positively associated with the early process of atherosclerosis on carotid arteries in non-obese women, independent of sleep apnea.

PO-1-048 / AS-10 Presenter

THE EFFECTS OF BODY MASS INDEX (BMI) ON GENIOGLOSSUS MOTION IN AWAKE HEALTHY SUBJECTS

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Obstructive sleep apneoa (OSA) is a respiratory disorder characterized by the repetitive collapse of the upper airway during sleep and is commonly associated with obesity. EMG of the upper airway muscles is commonly studied to understand OSA. However, EMG cannot be translated into tissue motion and how upper airway patency is maintained in individuals remain unclear. By using a novel MR imaging technique (CSPAMM), we mapped the EMG of the tongue and showed that genioglossus moves anteriorly to dilate the upper airway during inspiration in awake healthy subjects [1]. The effects of BMI on genioglossus motion remains unclear and understanding this is important to elucidate the pathophysiology of OSA. 10 healthy subjects with normal (n = 7) and high BMI (n = 7) were recruited. CSPAMM was used to image respiratory-related tissue motion around the upper airway using a 3T scanner. Genioglossus motion was tracked during inspiration. Cross sectional area at the level of the soft palate (CSAsp) was also measured in 10 subjects (5 with normal BMI and 5 with high BMI). The BMI of the two groups of subjects is significantly different ($p < 0.05$). While the average genioglossus motion is anterior for the group with normal BMI, it is posterior for the high BMI group. The average anteroposterior motion of genioglossus for the normal and high BMI subjects is –0.26 mm and 1.22 mm respectively and is significantly higher in the high BMI group ($p < 0.05$). There is a linear relationship between

genioglossus motion and CSAsp (R = 0.78) such that posterior motion of genioglossus is greater for smaller CSAsp. This study shows that genioglossus is less effective in dilating the upper airway in healthy subjects with high BMI despite this cohort having a likely higher EMG in the muscle than the normal BMI group during inspiration. This study together with our work on genioglossus motion in OSA patients present a novel and potential assessment for OSA. [1. S. Cheng, J.E. Butler, S. Gandevia, L.E.Bilston, Movement of the human tongue during normal breathing in awake healthy subjects. Journal of Physiology (2008),586, pg. 4283–94.]

PO-1-049

THE ASSOCIATION OF OBSTRUCTIVE SLEEP APNEA WITH SINGLE NUCLEOTIDE POLYMORPHISMS LOCATED NEAR THE CDKN2A/2B LOCI ON CHROMOSOME 9P21

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Background: Genetic variants located near CDKN2A/2B loci are associated with insulin resistance and cardiovascular disease (CVD) risk. It is unknown whether these polymorphisms are independently associated with obstructive sleep apnea (OSA). The aim of this study was to investigate CDKN2A/2B variant associations with OSA risk and severity, adjusting for conventional confounders.
Methods: Four single nucleotide polymorphisms (SNPs) were genotyped and analyzed in an OSA case population (Western Australian Sleep Health Study) and compared with two general population control groups (Busselton Health Surveys). Sleep clinic cases were defined by AHI more than or equal to 5 from overnight polysomnography. Community controls included: (a) unselected participants and (b) those with low OSA probability as determined by sleep questionnaire. Subjects were assessed for hypertension, diabetes, CVD and metabolic syndrome. Sex-stratified generalized linear modelling characterized multivariate associations adjusted for age, body mass index (BMI), smoking and other co-morbidities.
Results: There were 973 cases, 4,772 unselected controls, and 1,526 controls with low OSA probability. Case-control analysis indicated significant interactions between diabetes and the rs10811661 and rs564398 SNPs on OSA risk in women. Within OSA cases, multivariate analyses indicated significant SNP associations with OSA and CVD associated phenotypes independently of BMI and other confounders (P less than 0.05). Variant rs10757278 was significantly associated with diabetes, and a SNP:diabetes interaction was significantly associated with loge(AHI) (P less than 0.05).
Conclusions: These results suggest pleiotropic loci near the CDKN2A/2B region are associated with OSA both in association with and independently of cardiovascular and metabolic factors. Replication analyses and functional genetic investigations are required to determine causality.

PO-1-050

INTERACTION BETWEEN CO_2 AND DORSOMEDIAL MEDULLARY 5-HT2 RECEPTOR ACTIVITY IN HYPOXIC VENTILATORY AIRWAY RESPONSES

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In obstructive sleep apnea (OSA) patients, it is suggested that the number and sensitivity of central 5-HT receptors are possibly increased during sleep due to an enhanced cortisol increase by 5-HT precursor ingestion. Genioglossus muscle contraction is mediated via 5-HT2 receptors in the nXII. 5-HT neurons in the nXII originate from the raphe nuclei (nR), related with CO_2 /pH-sensitive central chemoreceptors and wakefulness. Those in the solitary tract nucleus (nTS) also originate from the nR. In the present study, the influence of 5-HT2 receptors in the dorsomedial medulla oblongata (DMM), including the nXII and the nTS, on hypoxic ventilatory airway responses was investigated with and without hypercapnia.Adult male mice (C57BL/6N) were anesthetized intraperitoneally with sodium pentobarbital and locally with Xylocaine or Marcaine. Microdialysis probes were inserted into the DMM. The mice in the double-chamber plethysmograph were recovered from anesthesia, became acclimatized to the chamber, and were inhaled air for 25 min. They were then exposed to hypoxic gas (7% O_2 in N_2) or hypercapnic hypoxic gas (7% O_2 and 5% CO_2 in N_2) with and without a 5-HT2 receptor antagonist (10^{-5} M LY-53857). Under these conditions, two respiratory curves through the head and body chambers were recorded, and concomitantly, extracellular fluid was collected through the microdialysis probe in the DMM.5-HT release in the DMM was increased by hypoxia and hypercapnic hypoxia. 5-HT2 activity in the DMM elicited immediate airway dilation and immediate hyperventilation in hypoxia condition and enhanced polypnea, stable airway dilation, and no different ventilatory facilitation in hypercapnic hypoxia. Hypercapnia compensated for the hypoxic responses mediated via 5-HT2 receptors in the DMM. Maintenance of pCO_2 and/or CO_2 responsiveness is important for ventilatory airway control during sleep.

PO-1-051

BRAIN FUNCTIONS IN RESPONSE TO ORAL AND COGNITIVE TASKS ASSESSED BY NEAR-INFRARED SPECTROSCOPY IN OBSTRUCTIVE SLEEP APNEA SYNDROME

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Aim: Nocturnal respiratory disturbances and disrupted sleep architecture due to obstructive sleep apnea syndrome (OSAS) cause daytime sleepiness and cognitive deficits. The aim of this study was to evaluate the functional brain imaging of OSAS patients during oral and cognitive tasks.
Methods: Ten Japanese patients with OSAS (mean age: 52.5 years, mean AHI: 18.9) and ten normal subjects (mean age: 50.8 years) were examined. We recorded the activity of brain tissue in response to oral function tasks (mouth opening, tongue protrusion, phonation) and a cognitive function task (word fluency task) using near-infrared spectroscopy (ETG-4000 Optical Topography, Hitachi Medical, Tokyo, Japan). In the word fluency task, the subjects were requested to generate

as many words of which the initial syllables were /a/, /ka/, or /sa/ as they could. Fifty-two measurement points were placed on subjects' frontal and bilateral temporal regions. During measurements of the oral function tasks, the subjects repeated 30 s' rest and 10 s' tasks for 5 times. The cognitive activation consisted of a 30 s' pretask baseline, a 60 s' word fluency task, and a 60 s' posttask baseline.
Results: In response to the oral function tasks, an event-related increase in total hemoglobin (Hb) was evident, and all subjects showed significant ($p < 0.01$) changes in total Hb over the bilateral temporal cortex. No significant differences were observed between the two groups. During the word fluency task, clear oxy-Hb increases were observed in the lower frontal and anterior lower channels. The increases in the Hb during the word fluency task were significantly ($p < 0.05$) reduced in the patients compared to the controls.
Conclusion: The results may be related to prefrontal lobe dysfunction in OSAS patients.

PO-1-052

PREVALENCE OF PATENT FORAMEN OVALE AND ITS IMPACT ON OXYGEN DESATURATION IN OBSTRUCTIVE SLEEP APNEA

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A possible association between patent foramen ovale (PFO) and obstructive sleep apnea has been suggested (OSA), whereby right-to-left shunting may exacerbate the severity of nocturnal oxygen desaturation. However, the interaction between these two conditions has not been well characterised.
Methods: A case-control study was conducted to evaluate the epidemiological association between PFO and OSA. Subjects were recruited prospectively from a sleep laboratory population, and 102 OSA subjects (mean age 51.5 ± 13 years) were compared to 50 controls without OSA (mean age 49.9 ± 12.4). The presence and size of right-to-left shunting were determined by contrast transcranial Doppler ultrasonography with Valsalva provocation. Using the 21,749 obstructive breathing events recorded at polysomnography from the OSA group, a mixed-effects linear regression model was developed to evaluate the impact of right-to-left shunting on nocturnal oxygen desaturation ($deltaSpO_2$).
Results: A higher prevalence of PFO was present in the OSA group compared to the control group (47.1% versus 26.0%, OR 2.53, CI 1.20 to 5.31, $p = 0.014$). From the regression model, right-to-left shunt size did not exert a significant influence on the severity of $deltaSpO_2$ (coefficient 0.85, CI −0.62 to 2.32, $p = 0.254$); whereas sleep state, event type, sleep position, event duration, awake oxygen saturation, apnea-hypopnea index and body mass index were all independent predictors of $deltaSpO_2$.
Conclusion: A higher prevalence of PFO is found in OSA subjects. However, the degree of right-to-left shunting, characterised by Valsalva provocation, is not associated with an increased severity of nocturnal oxygen desaturation.

PO-1-053

ASSOCIATION BETWEEN OBSTRUCTIVE SLEEP APNEA AND ELEVATED LEVELS OF B-TYPE NATRIURETIC PEPTIDE IN A COMMUNITY BASED SAMPLE OF WOMEN

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Background: Obstructive sleep apnea (OSA) is associated with an increased risk of cardiovascular disease and mortality. One contributory factor may be hemodynamic stress due to the negative intrathoracic pressure during each apnea. Type-B Natriuretic Peptide (BNP) is secreted by the cardiac ventricles in response to volume expansion and pressure load and we hypothesized that there would be an association between indices of obstructive sleep apnea in the night and levels of BNP in the morning.
Methods: From a community-based sample, 349 women underwent full-night polysomnography, anthropometric measurements and answered a questionnaire about medical conditions and current medication. The morning following the polysomnography, blood samples were drawn for analysis of plasma BNP, C-reactive protein, creatinine and hemoglobin.
Results: There was an increase in mean BNP as the severity of sleep apnea increased, increasing from a mean value of 8.5 ng/L among women with an AHI of <5 to 18.0 ng/L in women with an AHI of >30. Elevated BNP levels (>20 ng/L) were found in 29.8% of the women, while 70.2% had normal levels. The odds ratio was 2.2 for elevated BNP levels for women with an AHI of 5-<15 in relation to women with an AHI of <5, 3.1 for women with an AHI of 15-<30 and 4.5 for women with an AHI of >30 after adjustment for age, BMI, systolic blood pressure, antihypertensive drugs and creatinine.
Conclusions: We conclude that there is a dose-response relationship between the severity of sleep apnea during the night in women and the levels of BNP in the morning.

PO-1-054

COMMON PRE-MOTOR DRIVE TO GENIOGLOSSUS AND TENSOR PALATINI MOTOR NEURONS

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Introduction: Upper Airway Muscles (UAM) are critical in maintaining airway patency, with deficits in the control of these muscles being implicated in airway collapse during sleep. Thus, it is important to understand motor control of UAMs. A powerful method of understanding pre-motor inputs to motor nuclei is to analyze the correlated activity of pairs of Motor Units (MU). We analyzed pairs of MUs from two UAMs, Genioglossus (GG) and Tensor Palatini (TP) during relaxed wakefulness and quantified the levels of Common Drive and MU synchronization in the frequency domain.
Methods: GG and TP EMG activities were recorded from 2 fine wire electrodes inserted bilaterally into each muscle. Sleep-wake state and respiratory activity were recorded. The discharge characteristics of MUs

were identified over 30 to 60 second epochs. Pairs of MUs recorded within the same epoch were identified and classified according to whether the two MUs: 1) came from the same or different muscles and; 2) had the same or different discharge patterns.
Results: 141 pairs of MUs were identified: 47 GG; 39 TP and 55 mixed. CD was quantified as the maximum coherence value from 0 to 5 Hz such that 0.60 to 1.00 indicated strong; 0.30 to 0.60 moderate and 0.30 to 0.00 weak CD. For both muscles, MU pairs with the same pattern and either an inspiratory or expiratory phasic component had strong CD (mean = .75). MU pairs that had the same pattern and a tonic component had moderate CD in both muscles (mean = .57). Pairs that had different patterns, but had a tonic component and were from the same muscle (e.g. Tonic & Inspiratory Tonic pairs), had moderate CD (mean = .39). However, MUs from different muscles where both units had a Tonic component had weak CD (mean = .20). Synchronization (maximum coherence from 10 to 30 Hz) was weak in all pair combinations in both muscles (range = .10 to .26).
Conclusions: Coherence analysis of MU pairs identified a strong phasic component in both GG and TP and inspiratory and expiratory MUs. Tonic MU pairs exhibited moderately strong CD, but the drive was idiosyncratic to each muscle.

PO-1-055

EFFECT OF DEEP SLEEP ON THE REGULATION OF THE REPRODUCTIVE FUNCTION-ASSESSMENT OF PLASMA KISSPEPTIN LEVELS IN OSAS-

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Secretion of gonadotropins, such as of the LH and FSH, is affected by the sex and age, and particularly in women, is closely correlated with the menstrual cycle. In healthy individuals, both males and females, gonadotropin secretion is slight before puberty and increases in the early stage of puberty, being known to reach high levels particularly during sleep. Recently, studies on kisspeptins, a kind of gonadotropin, have clarified that Kisspeptin-GPR54 signaling plays a crucial role in the regulation of gonadal function, and that kisspeptins strongly promote the secretion of LH and FSH.Meanwhile, plasma LH and total testosterone levels are reported to be low and the frequencies of erectile dysfunction (ED) and hyposexuality is known to be increased in patients with OSAS. On the assumption that positive feedback by kisspeptins is not relayed to the hypothalamus despite the low level of LH and total testosterone secretion in severe OSAS, we measured the plasma kisspeptin concentrations by RIA in patients with OSAS (122 males, 27 females) and a healthy control group without sleep disturbances (7 males, 7 females). The results revealed reduced plasma kisspeptin concentrations in the OSAS group as compared with those in the healthy control group in both sexes (OSAS group: 2.9 ± 0.1 pg/L for males, 3.5 ± 0.3 pg/L for females; Healthy control group: 4.2 ± 0.8 pg/L for males, 5.1 ± 0.7 pg/L for females). Furthermore, the plasma kisspeptin concentrations were significantly correlated with the percentage of slow-wave sleep ($p < 0.005$, $r = 0.451$).The above results suggest that the onset of gonadal dysfunction in patients with severe OSAS is likely mediated by the suppression of kisspeptin secretion induced by sleep disturbances.

PO-1-056

THE CARDIOVASCULAR RISKS ACCORDING TO THE FRAMINGHAM HEART STUDY IN PATIENTS WITH SLEEP APNEA

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Many recent reports suggest the relationship between sleep apnea and cardiovascular disease (CVD) and it is required to be clear the mechanism of these associations. This study was designed to estimate the CVD risks of sleep apnea patients according to the Framingham Risk Scores (FRSs) and evaluate the relationship between FRSs and sleep related variables.
Methods: Subjects were 429 male patients diagnosed with OSA at the Sleep Center, Tsuda Hospital in Japan (age 57.1 ± 12.2 years, BMI 25.8 ± 3.8, AHI 31.5 ± 20.9). The evaluated sleep related variables included AHI, arousal index, slow wave sleep% (%SWS), minimum and average SpO2, SpO2 less than 90% time, Epworth Sleepiness Scale (ESS). FRSs for general cardiovascular disease (GCD), stroke and coronary heart disease (CHD) were calculated based on blood pressure, medication history, diabetes mellitus, previous CVD, drinking, smoking, and lipid related measurements. Statistical analyses were performed with significance defined as a 2-tailed P value less than 0.05. Spearman rank correlations were applied between the FRSs and sleep related variables. One-way ANOVA tests compared continuous variables between the groups divided by AHI severity.
Results: From FRSs, probabilities of a GCD, stroke and CHD within 10 years were 16.7 ± 9.9%, 10.8 ± 7.0% and 12.4 ± 8.7% respectively. There is no significant correlations between FRSs and evaluated variables except between GCD risk score and%SWS ($p < 0.01$, $r = -0.223$). There was no significant difference between groups classified with AHI severity except BMI ($p < 0.01$). Some 35.1% subjects had higher CHD risk score than age-matched general population. Especially CHD risk score in age group 30 to 34, 85.7% subjects exceeded the average.
Conclusion: Lower SWS% subjects had higher cardiovascular risks in sleep apnea patients. More than 30% of subjects had high CHD risks compared with the age-matched control. As there is no significant cardiovascular risk differences in groups classified with AHI severity, considerations for the cardiovascular risk would be required for all sleep apnea patients.

PO-1-057

LIPOCALIN-TYPE PROSTAGLANDIN D SYNTHASE (L-PGDS) IS ASSOCIATED WITH OBSTRUCTIVE SLEEP APNEA

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Background: Obstructive sleep apnea (OSA) is associated with excessive daytime sleepiness, neurocognitive impairment, and cardiovascular

mortality. The prostaglandin D2 (PGD2) system is a physiological regulator of sleep. However, the relation between the PGD2 system and OSA is not exactly known.
Methods: Forty adult patients with suspected OSA were enrolled and underwent polysomnography. The median apnea-hypopnea index (AHI) was 26.7}17.5 events per hour. Urine samples were collected at night and the morning following overnight polysomnography, and urinary concentrations of lipocalin-type prostaglandin D synthase (L-PGDS) were measured. Additionally, in the OSA patients who were using continuous positive airway pressure (CPAP), urinary L-PGDS was also measured after 2 days of CPAP treatment.
Results: Morning urinary L-PGDS concentrations correlated positively with AHI ($r = 0.422$, $p = 0.008$), arousal index ($r = 0.328$, $p = 0.04$), plasma fibrinogen ($r = 0.484$, $p = 0.002$), and plasma noradrenaline ($r = 0.471$, $p = 0.002$). Morning urinary L-PGDS was higher in patients with severe OSA (n = 15, 939.9 ± 215.6 ng/mgCreatinine) than in patients with mild-to-moderate OSA (n = 21, 487.8 ± 68.7 ng/mgCreatinine, $p = 0.02$). After 2 days of CPAP treatment, urinary L-PGDS concentrations decreased significantly (n = 12, $p = 0.04$).
Conclusions: Through the data from urinary L-PGDS, OSA might have significant effects on the PGD2 system, which is thought to be a powerful sleep-related factor. The urinary L-PGDS may be a novel parameter that is useful for managing patients with OSA.

PO-1-058 / AS-20 Presenter

SLEEP BRUXISM, SLEEP APNEA AND CPAP COMPLIANCE: THE ICELANDIC SLEEP APNEA COHORT

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Objectives: To analyze the clinical characteristics of sleep bruxism (SB) among subjects with obstructive sleep apnea (OSA) and upper airway morphology based on MRI. Also the effect of CPAP treatment on subjects reporting bruxism.
Materials and Methods: The OSA subjects (n = 590) were newly diagnosed with moderate/severe OSA (479 males/111 females). SB was defined as yes to the question: Do you grind or clench your teeth during sleep. The prevalence of SB with CPAP treatment was assessed after 2 years (n = 538).
Results: Among OSA patients 18.8% reported SB. There was no gender difference. SB was more common in younger age groups ($p < 0.001$). Subjects with SB had lower sleep apnea severity than those without SB. SB was not related to hypertension, respiratory diseases or the metabolic syndrome. SB was not related to insomnia, nocturnal sweating, RLS or excessive daytime sleepiness.
Subjects with SB had based on SF-12, a lower mental quality of life than those without SB ($p = 0.002$) but no difference was found in physical quality of life. MRI of upper airway in those subjects with SB had significantly smaller volumes of the retropalatal airway ($p = 0.042$) and tongue ($p = 0.0145$) compared to non-SB.
Subjects using CPAP full-time had a decreased prevalence of SB from 15.8% to 10.8% while no change in SB prevalence was observed in those subjects not using CPAP. Noncompliant CPAP subjects were more likely to report SB at baseline (27.2% vs 15.8% for fully treated and 12.6% for partially treated, $p = 0.007$).
Conclusions: SB is most prevalent among young OSA patients with a lower OSA severity. Subjects with SB had smaller volumes of the retropalatal airway and tongue compared to non-SB and lower mental quality of life. CPAP treatment of OSA decreases SB symptoms significantly but subjects with bruxism are also less likely to adhere to treatment.

PO-1-059 / AS-6 Presenter

THE SEVERITY OF OSA IS RELATED TO THE COLLAPSIBILITY OF UPPER AIRWAY IN EXPIRATORY PHASE

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Introduction: Collapsibility of upper airway is related to the severity of obstructive sleep apnea (OSA). Asymmetric dynamic changes of the upper airway throughout the whole respiratory phase was reported by Schwabs et al. The collapsibility of upper airway is different during expiration and inspiration. We hypothesized that the collapsibility of upper airway during expiration but not inspiration correlated with the severity of OSA.
Methods: Overnight Polysomnography (PSG) was done in every subjects. Gender, age, and body mass index (BMI) were recorded. Upper airway image by ultrafast Computed Tomography (CT) simultaneously with flow measurement were performed in these subjects at quiet respiration. Upper airway area changes over the narrowest portion and the simultaneous flow were measured for at least 3 smooth respiration. Upper airway collapsibility is defined as the variation of upper airway area divided by simultaneous flow changes. Resistance, as a reciprocal of collapsibility, was also calculated and correlated with the severity of OSA.
Results: From 2008 July to 2009 June, 36 subjects were invited to join the study. 14 subjects were normal (AHI < 5, mean AHI = 1.04 ± 1.37/hr) as control. 10 patients were mild to moderate group(AHI between 5 and 30, mean AHI = 18.3 ± 8.06/hr) and 12 patients were severe cases (AHI > 30, mean AHI = 65.89 ± 22.44/hr). The airway changes correlated better with the flow changes in severe cases. The collapsibility of the upper airway (area changes/ flow changes) of all cases is correlated well with the severity of OSA (AHI) in expiratory phases ($R2 = 0.372$, $p < 0.01$), where as in inspiratory phases, there show no correlation ($R2 = 0.009$, $p = 0.89$). The resistance also show negative correlation with AHI in expiratory phases ($R2 = 0.634$, $p < 0.001$), in inspiratory phase, there is no correlation ($R2 = 0.020$, $p = 0.47$).
Conclusion: The upper airway changes are correlated with the severity of OSA in expiratory phase only. The measurement of upper airway for the pathogenesis of OSA has to consider the phase changes throughout the respiration.

PO-1-060

ROLE OF CARBON DIOXIDE MONITORING DURING POLYSOMNOGRAPHY IN PAEDIATRIC OBSTRUCTIVE SLEEP APNOEA (OSA)

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Polysomnography (PSG) is the gold standard for diagnosing paediatric OSA. Carbon dioxide (CO_2) monitoring is included in the paediatric PSG. In congenital airway disorders it is known that CO_2 can be elevated with minimal symptoms in infants. In severe OSA, CO_2 is elevated but in less severe disease its value is poorly understood.
Aim: To assess if CO_2 monitoring assists in categorising the severity of OSA.
Methods: An audit of 256 diagnostic sleep studies from a tertiary paediatric sleep service was conducted over a four year period. The primary clinical diagnosis was OSA. Studies were divided into three diagnostic groups: normal, mild and moderate-severe. Studies were included if the minimum transcutaneous CO_2 was >35 mmHg and there was an increase of >10 mmHg during REM epochs. A two-by-two table analysis was performed to ascertain odds ratio, sensitivity and specificity for each of the diagnostic groups.
Results: A total of 256 studies were audited. The number of studies in each diagnostic group are: normal (N = 106, M : F 2:1), mild (96, 1.9:1) and moderate-severe (54, 1.25:1). CO_2 rise in REM was noted in 37 of the mild group and 37 of the moderate-severe group. The odds ratio (CI) of diagnosis of OSA with increase in CO_2 was 0.96 (0.52–1.75) for the mild group and 3.32 (1.57–7.06). Sensitivity and specificity for the mild group were 38% and 60%, respectively, for the moderate-severe group were 69% and 60%.
Conclusion: These results demonstrate that classification of the severity of OSA can be assisted by a rise in REM of >10 mmHg using transcutaneous carbon dioxide in a patient group referred to a sleep disorders clinic. Transcutaneous carbon dioxide is a useful adjunct for diagnosis of OSA. CO_2 within a limited channel acquisition profile may aid in the triage of patients.

PO-1-061

PREDICTIVE FACTORS TO DEPRESSION IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Inctroduction: Depression is a major risk factor to decrease quality of life in patients with obstructive sleep apnea. We tried to figure out the characteristics of patients with depression and investigate the predictive factors for the severity of depressive mood in OSA patients.
Methods: All patients complain of snoring and sleep apnea from September 2009 to august 2010 performed overnight polysomnography. We obtained demographic, socioeconomic and medical data with variable questionnaires include Epworth Sleepiness Scale, Multi-Dementional Fatigue Inventory, Sleep Trait Anxiety Inventory, Medical Outcomes Study sleep scale with sleep problems index, Sleep related Breathing Disorder. To evaluate depressive mood, Beck Depression Inventory were used. We compared variables include PSG parameters between depression group and non-depression group based on BDI and investigated factors to predict the depression score by multivariate linear regression analysis.
Results: Total 604 patients diagnosed as to have obstructive sleep apnea Male were 516 and female were 88. Mean age was 49.2 years, and mean apnea-hypopnea inde was 29.4. Mean BDI score was 10.4. Total 286 patients classified as depression group. Women had more frequent depression than men. Depression is significantly related with diabetes, stroke, low educational status, unemployed status, and negatively influenced all questionnaire score. Scores of MFI, sleep problems index, educational status, sex, and total sleep time were significant predict factors to depression. MFI was the most predictive factor. R^2 was 0.337. Subgroup by gender presented also MFI was the most predictive factor in men and women.
Conclusions: Depression was more frequent in women, patients with low educational status, unemployed status, diabetes, and stroke. MFI is the most powerful predictor to BDI score in both men and women.

PO-1-062

DESATURATION AT HIGH ALTITUDE IN PATIENTS WITH MILD OBSTRUCTIVE SLEEP APNEA SYNDROME

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Obstructive sleep apnea syndrome (OSAS) is a common condition and has been reported to be exacerbated at high altitudes. In this study, we determined the reduction in saturation of arterial blood oxygen (SpO2) values during sleep at a high altitude in patients with asymptomatic OSAS and compared the values with those obtained at a low altitude.
Methods and subjects: Four healthy male adult volunteers were included in the study. All of them had asymptomatic snoring. Standard all-night polysomnography (PSG) was performed in a hotel near sea level (Nagoya) and in a hotel at an altitude of 2612 m (Senjyoujiki Hotel: S-hotel) on subsequent days. All sleep parameters, as recommended by the AASM Manual, were scored visually. The desaturation speed (%/s) was calculated by dividing the difference between the initial SpO2 value and the lowest value recorded during apnea by interval from the beginning to the point of lowest SpO2 of apnea. All values are reported as means} standard deviation.
Result: The SpO2 values in awake supine patients before PSG at Nagoya and S-hotel were 98 ± 0% and 87.5 ± 3.1%, respectively, with a difference of 10.5%, while the lowest SpO2 values during apnea were 81.2 ± 6.1% and 54.5 ± 12.8%, respectively, with a difference of 27.2 ± 8.6%. The desaturation speed was 0.19 ± 0.02%/s at Nagoya and 0.75 ± 0.22%/s at S-hotel. The apnea-hypopnea index (AHI) and arousal index values at S-hotel were greater than those at Nagoya, with the values respectively being 39.7 ± 10 vs. 9.48 ± 4.2 and 57.1 ± 11.7 vs. 43.8 ± 9.8.
Discussion: At S-hotel, which is located at an altitude of 2612 m, the SpO2 in the awake condition was 10.5% lower than that at Nagoya. However, the lowest SpO2 during apnea at the S-hotel was as much as 26.7% lower than that at Nagoya. Because desaturation speed at high altitude was far greater than that at lower altitude, severe hypoxemia during apnea was observed at high altitudes. As a result, the sleep quality at high altitudes seemed to be poor.

PO-1-063

PROBING THE DYNAMICS OF INTERACTIONS BETWEEN AUTONOMIC SYSTEMS DURING OBSTRUCTIVE SLEEP APNEA

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Background: Patients with obstructive sleep apnea (OSA) are suffered from frequent interruptions of normal sleep cycle and will cause abnormal autonomic neural functions in daytime and during sleep. Evaluation of autonomic functions in patients with OSA may provide useful information about the severity of OSA. However, the prominent features of automomic nervous system dysfunction are most likely occurred during OSA. The inconsistent period of each episode or the intermittent occurrences of OSA present a methodological challenge since evidence showed that traditional analytic techniques are not suitable for such nonlinear and nonstationary physiological signals. Therefore, in this study, we applied an adaptive nonlinear method called Hilbert-Huang Transform (HHT) to probe the complex dynamics of interactions between autonomic systems during OSA.
Method: 99 patients with mild to severe OSA were enrolled in this study and underwent overnight polysomnogram examinations. Heart rate fluctuations (HRF) of patients during sleep were extracted and analyzed by HHT to adaptively decompose complex nonstationary HRF to multiple empirical modes corresponding to different physiologic processes. Then, the empirical mode functions correlated to oscillations originated from the periodic breathing of OSA as well as the parasympathetic-mediated respiratory sinus arrhythmia were identified. Furthermore, the interactions between the two empirical mode functions can be quantified by pearson's correlation.
Results: The correlation of two derived empirical mode functions (R_{hht}) were significantly higher in patients with severe OSA than that in patients with mild OSA ($p < 0.05$) and that in patients with moderate OSA ($p < 0.05$). A moderate correlation was found between AHI index and R_{hht} ($r = 0.423$, $p < 10^{-4}$).
Concusion: Although AHI index remains the gold standard in evaluating the severity of OSA, quantifying the interactions between two different control mechanisms may be an alternative indicator to the severity of OSA by assessing the abnormal interactions between autonomic systems.

PO-1-064

CENTRAL SLEEP APNEA INFLUENCED BY POSITION CHANGE

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Background: It has been established that obstructive sleep apnea hypopnea syndrome (OSAHS) severity as measured by the apnea hypopnea index (AHI) usually increase in supine position due to upper airway anatomy leading to increased upper airway collapsibility. However, the influence of body position on central sleep apneas has not been studied systematically. We report a case of central sleep apnea after medullary infarction showing improvement by position change.
Case: A 62 year old male was requested for the evaluation of sleep apnea. He was diagnosed as bilateral medullary infarction about 16 days ago. He complained of snoring, awakening during sleep and witnessed apneas after medullary infarction. On physical examination, mild weakness (MRC grade 4+) and dysmetria in right upper and lower limbs were identified. Soft palate elevation and gag reflex were sluggish bilaterally. His medical history included confirmed coronary artery occlusive disease with failure of stent insertion, and hypertension. Echocardiography revealed akinesis of apical septum and basal inferior wall of left ventricle, but ejection fraction was 49%, which meant mild left ventricular dysfunction. 24 hour Holter monitoring showed frequent premature ventricular contractions. Whole night polysomnography (PSG) was performed. Sleep efficacy was 50%. Total 43 apneas, which were all central type, were observed and maximal length was up to 23.1 seconds with desaturations to 88.9%. The AHI was 43.2/hr and supine index was 60/hr. All central apnea were seen with supine position, therefore lateral index was zero. CPAP (Continuous positive airway pressure) trial was failed due to discomfortness.
Conclusions: Sleeping with supine body position increases AHI in our patient, even though his apneas were all central type. It could be suggested that changes of lung volume and ventilatory instability depending on body position may be responsible for the change of the respiration drive threshold. Further studies are required to identify precise mechanism.

PO-1-065

EVALUATION OF QUALITY OF LIFE AND MOOD STATUS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Background: There are many studies showing obstructive sleep apnea syndrome (OSAS) may deteriorate the quality of life (QOL) and mood status. The object of study was to evaluate the QOL and mood status in patients with untreated OSA and its relationship with the severity of OSA.
Method: We enrolled the patients who were diagnosed with OSA (apnea-hypopnea index 5 per hr) by overnight polysomnography (PSG). All patients were instructed to fill out the questionnaires on the study night of PSG; the Medical Outcomes Study Short-Form 36 (SF-36) for QOL, and the Symptom Checklist-90-Revision (SCL-90-R), the Beck Depression Inventory (BDI), and the Beck Anxiety Inventory (BAI) for mood status. Subjects who had a history of psychiatric disorders or of taking antidepressant or anxiolytics were excluded. QOL and Mood scales were analyzed with various parameters such as clinical demographics (age, gender, ESS, BMI) and PSG data.
Result: Two hundred fifty five OSA patients (269 male, mean age 50.6 yrs) were included (mean AHI, 29.4 per hr). The number of patients with mild OSA (AHI, 5–15) was 118, moderate (AHI, 15–30) was 78, and severe (AHI more than 30) was 123. Mean BDI and BAI were definitely higher in women than men although their mean AHI was not different. Six of eight domains on the SF-36 and 3 scales (hostility, phobic anxiety, and psychoticism) of the SCL-90-R showed lower scores in women than men. BDI and BAI were correlated with all items of the SF-36 and SCL-90-R. ESS was significantly correlated with BDI, BAI, one of SF-36 (physical health), and all domains of the SCL-90-R in all patients. There were significant differences in mood status (SCL-90-R, obsessive-compulsive, anxiety, and phobic anxiety) among groups (mild vs. mod. vs. Severe OSA, One-way ANOVA). The severity of OSA (AHI) was correlated with mood (obsessive-compulsive).

Conclusion: This study showed that daytime sleepiness may influence on the mood and QOL and, depression and anxiety themselves are strongly correlated with QOL. Severer sleep apneas seemed to be related to be less obsessive compulsive trait than mild or moderate severity.

PO-1-066

IS IT IMPORTANT TO IDENTIFY NOCTURNAL WHEEZE IN THE SLEEP LABORATORY?

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AIM: To assess for nocturnal wheeze using acoustic respiratory monitoring (ARM) in patients undergoing overnight polysomnography (PSG) and to determine its effect on PSG parameters of sleep.
METHODS: Retrospective analysis of 85 unselected patients undergoing PSG together with ARM (Pulmotrack device, Karmelsonix inc.) in a tertiary referral centre. Clinical data including patient demographics, co-morbidities, medications, Epworth Sleepiness Score (ESS) and spirometry were reviewed. PSG data was analysed by a sleep scientist and reported by a sleep physician both of whom were blinded to ARM data which was sent to the manufacturer (Karmelsonix inc.) for independent and accurate analysis and to determine the WheezeRATE. Correlations between PSG and ARM data where analysed using standard statistical methods.
RESULTS: The prevalence of wheeze in the study population was 25/85 (29%). There was a significant correlation between the average WheezeRATE and the Apnoea Hypopnoea Index ($r = 0.40$, $p < 0.001$), the average WheezeRATE and the Cortical Arousal Index ($r = 0.61$, $p = 0.001$) and the average WheezeRATE and total time with SpO2 < 90% ($r = 0.44$, $p = 0.03$). Wheezers tended to have less REM than non-wheezers ($r = 0.42$, $p = 0.002$). There was no significant difference in ESS between wheezers and non wheezers.
CONCLUSION: Nocturnal wheeze is prevalent in patients undergoing PSG. There is a relationship between the presence of nocturnal wheeze and Apnoea Hypopnoea Index (AHI). Nocturnal wheeze appears to increase cortical arousals independent of AHI and therefore may be a cause for sleep fragmentation.

PO-1-067

NEW SIGNIFICANCE OF MEASURING PLASMA VASPIN CONCENTRATIONS IN OBSTRUCTIVE SLEEP APNEA SYNDROME

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OSAS is suggested to be associated with factors common to the development and pathophysiology of metabolic syndrome, such as leptin and insulin resistance. Vaspin is a protein identified within a gene cluster increasingly expressed in visceral fat of obese OLETF rats, an animal model of obesity with visceral fat accumulation or type 2 DM. However, factors affecting and mechanisms regulating plasma vaspin concentrations (Pvas) remain unclear. Thus, we investigated, in OSAS patients considered to have leptin and insulin resistance, whether Pvas are as associated with the severity of sleep-disordered breathing as is leptin. The study enrolled 22 OSAS patients and 6 controls. Moreover, the subjects consisted of 7 patients without DM and respiratory disease who had been diagnosed as having OSAS by PSG. All the patients had received the nCPAP treatment for a period of 6 months. The Pvas in the 22 OSAS patients was 0.9 ± 0.2 ng/ml and concentration in the OSAS group was significantly higher than that in the control group (0.3 ± 0.02 ng/ml). The Pvas in the 7 OSAS patients before the nCPAP treatment was 0.6 ± 0.2 ng/ml and after the nCPAP treatment was 0.3 ± 0.1 ng/ml. Pvas were significantly lower after the nCPAP treatment than before the nCPAP treatment.While past reports have suggested a correlation between vaspin and BMI, this investigation limited to OSAS patients found no correlation between vaspin and BMI. However, strong correlations were recognized between vaspin and AHI, a respiratory disorder index, and the arousal index. Thus, vaspin, considered to be a new biomarker of visceral fat, is associated with respiratory and sleep disorders rather than BMI in OSAS patients, suggesting that Pvas is a potential biomarker of the pathophysiology associated with OSAS.

PO-1-068

THE ROLE OF SLEEP POSITION IN OBSTRUCTIVE SLEEP APNEA SYNDROME IN KOREAN PEOPLE

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Objectives: The aim of this study is to analyze the role of sleep position in obstructive sleep apnea syndrome (OSAS) in Korean people.
Methods: The subjects were 75 obstructive sleep apnea syndrome patients suffering excessive daytime sleepiness or snoring. Patients with co-morbidities of other sleep disorders such as narcolepsy or periodic limb movement syndrome were excluded. All subjects underwent polysomnography. Patients were stratified in a group of position dependent patients (PP) and a group of non-position dependent patients (NPP). We associated the apnea hypopnea index (AHI) of the supine position with the AHI of the other positions.
Results: We identified that a non-supine position was related with the decrease in AHI, especially in the PP group. BMI and AHI were higher in the NPP group. In our study, 61.3% were PP (AHI in supine 2 times greater than AHI in other positions). In polysomnography tests, both group showed no significant difference in AHI in supine position, but NPP group had significantly higher AHI in non-supine position. NPP group showed significantly higher total wake time and respiratory arousal index. PP group had higher average oxygen saturation and higher lowest oxygen saturation.
Conclusion: This study confirms the finding that OSAS is position dependent in more than 50% of patients and non-supine position would lower the AHI of OSAS patients. AHI in non-supine position of PP group was significantly lower than AHI in supine position. Even in NPP group, AHI in non-supine position was lower than AHI in supine position. We may need more comprehensive and in-depth studies to find the efficacy and effectiveness of positional therapy for OSAS patients.
Key words: Obstructive sleep apnea syndrom, Body position, Polysomnography, Positional therapy, Apnea-hypopnea Index

PO-1-069

RELATIONSHIP BETWEEN REDUCED LUNG FUNCTION AND METABOLIC SYNDROME IN AN URBAN MALE WORKING POPULATION IN JAPAN

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Background: Increased risk for metabolic syndrome is reported to be associated with reduced lung function and obstructive sleep apnea (OSA). However, simultaneous analysis of the relationship of metabolic syndrome with lung function and OSA has not been performed.
Objective: To investigate the risk for metabolic syndrome according to the level of lung function and the severity of OSA.
Methods: We previously analyzed the relationships between metabolic syndrome and OSA from a cross-sectional epidemiological health survey conducted in middle-aged male employees at a wholesale company (Chin K, et al. Sleep 2010). In this secondary analysis, we reviewed data from a home cardiorespiratory (type 3) sleep study, metabolic syndrome, and, in addition, spirometry in 273 subjects.
Results: Univariate logistic regression analyses revealed that the percentages of predicted forced expiratory volume in one second (%FEV1), predicted vital capacity (%VC) and predicted forced vital capacity (%FVC), and the respiratory disturbance index (RDI) were significantly related to the presence of metabolic syndrome ($p = 0.0067$, 0.015, 0.0072 and $p < 0.001$, respectively). Multivariate logistic regression analyses revealed that, after adjustment for age, body mass index and smoking,%FEV1,%VC and%FVC were significantly related to the presence of metabolic syndrome ($p = 0.021$, 0.050 and 0.045, respectively), but RDI was not.
Conclusions: We showed epidemiologic evidence to indicate a positive relationship between metabolic syndrome and reduced lung function independent of age, obesity, smoking and OSA.

PO-1-070

EFFECTS OF SLEEP DURATION AND OBSTRUCTIVE SLEEP APNEA ON SERUM LIPID PROFILES IN WORKING AGE MALES IN JAPAN

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Sleep duration is associated with hypertension, diabetes and metabolic syndrome, but the relationship between sleep duration and dyslipidemia (DL) is not well known. The prevalence of DL is higher in patients with than without obstructive sleep apnea (OSA), but few population-based studies have investigated this relationship. In addition, no study has evaluated the associations among sleep duration, OSA and DL simultaneously. We investigated the relationships among sleep duration, OSA and lipid profiles in a population-based study. We analyzed data on 275 male employees of a company in Japan. We measured blood pressure, anthropometric parameters, sleep duration with an actigraph for 7 days and the respiratory disturbance index (RDI) with a type 3 portable device for 2 nights. Fasting blood parameters were obtained from periodic inspection data. Average sleep duration was 6.0 h/day. Of the 275 subjects, 143 (52%) had DL. The RDI, prevalence of severe OSA and a sleep duration <5 h were greater and the mean SpO2 was lower in the group with than without DL. When subjects were divided into 4 groups according to sleep duration, the total cholesterol (TC), RDI, mean SpO2,%Time of SpO2 < 90%, prevalence of no and severe OSA, and Epworth sleepiness scale differed significantly among groups. Multiple regression analysis showed that the TC level was correlated negatively with sleep duration and positively with age and the waist/hip ratio, and that the triglyceride (TG) level correlated positively with the RDI, body mass index and alcohol consumption. Short sleep and OSA was a risk factor for elevation of the TC level and TG level, respectively, in a working-age male population. Correction of sleep status might improve lipid profiles and subsequently decrease cardiovascular risks.

PO-1-071

SLEEP-DISORDERED BREATHING IN PATIENTS WITH MOTOR NEURON DISEASE

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Background and objective: Patients with motor neuron disease may have sleep-disordered breathing even in the early stage. The objective of this study is to evaluate the disturbances of breathing during sleep in patients with motor neuron disease.
Methods: Seven patients (M: F = 2:7, mean age 65 (47–79)) who were diagnosed as motor neuron disease were enrolled. We checked the daytime symptoms such as fatigue that may be caused by sleep-disordered breathing in all patients. All patients underwent pulmonary

function test and routine polysomnography (PSG) accompanied by arterial blood gas analysis (ABGA) before and after PSG to evaluate the sleep apnea or nocturnal hypoventilation.
Results: All patients had daytime symptoms of nocturnal sleep-disordered breathing. To look on the PSG results, two patients showed mild obstructive sleep apnea and the other patients did not have significant sleep apnea. But ABGA showed significant retention of carbon dioxide and reduction of oxygen in all patients.
Conclusion: Even the patients without significant sleep apnea, nocturnal hypoventilation can exist and it causes the daytime symptoms. Even in the early stage patients of motor neuron disease, detailed history taking should be obtained and PSG has to be considered if needed.

PO-1-072

THE RELATIONSHIP BETWEEN OBSTRUCTIVE SLEEP APNEA AND CARTOTID ARTERY ATHEROSCLEROSIS

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Background: Obstructive sleep apnea (OSA) is associated with several cardiovascular diseases. However, the mechanisms are not completely understood. The measure of common carotid artery intima-media thickness (IMT) has been extensively used as an early marker of atherosclerosis. The aim of this study was to test the hypothesis that early signs of atherosclerosis are present in patients with OSA and correlate with OSA severity.
Method: Thirty male patients with OSA were studied by using full standard overnight polysomnography and high-definition echo-tracking device to measure intima-media thickness and carotid artery diameter. Twenty Eight healthy volunteers matched for age and sex were studied by portable respiratory monitoring device. All participants were free of hypertension, diabetes, and were not on any medications. Patients with OSA were naive to treatment.
Result: All patients and normal controls were male. There was no significant difference of age between patients and controls (48.4 ± 8.85 and 48.0 ± 9.77). Significant differences existed between control subjects and patients with mild to moderate and severe OSA (apnea hypopnea index, 1.51 ± 1.15 and 38.51 ± 19.13 respectively) in intima media thickness (0.59 ± 0.064 and 0.93 ± 0.16; p = 0.0023), and carotid diameter (5.79 ± 0.44 and 6.47 ± 0.51; p = 0.0227). Multivariate analyses showed that the apnea hypopnea index correlated independently with intima media thickness and carotid diameter (r = 0.79, p = 0.0008, and r = 0.47, p = 0.0482).
Conclusion: Middle aged patients with OSA who are free of overt cardiovascular diseases have early signs of atherosclerosis, which further supports the hypothesis that OSA plays an independent role in atherosclerosis progression.

PO-1-073

DOES INCREASING THE VENTILATORY RESPONSE TO AROUSAL INDUCE GENIOGLOSSUS MUSCLE HYPOTONIA ON THE RESUMPTION OF SLEEP?

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Arousals from sleep are thought to predispose to obstructive sleep apnea (OSA) by causing hyperventilation and hypocapnia, which reduces airway dilator muscle activity on the return to sleep. Despite this suggestion, studies of brief auditory arousals in patients with and without OSA have not induced hypotonia of the genioglossus (GG) airway dilator muscle. This may have occurred because airway resistance was low prior to arousal in these studies, resulting in a small ventilatory response to arousal (VRA) and minimal hypocapnia. Thus we aimed to increase the VRA in healthy subjects by resistive loading prior to auditory arousal in order to determine whether GG hypotonia on return to sleep then occurs.
Methods: Healthy men and women were instrumented with sleep staging and GG muscle electrodes, an epiglottic pressure catheter and a mask/pneumotachograph. Auditory tones (45–100 dB, 0.5 s, 1000 Hz) were played to induce brief (3–15 s) ASDA arousal following either resting breathing or 5 breaths through an inspiratory resistive load (5–15 cmH_2O/l/s, which was removed as the tone was played).
Results: Adequate data have been obtained in 4 of 7 subjects studied to date. Subjects were normal weight (BMI = 20.5 ± 1.2 kg/m2) and were aged 21 ± 0.4 years. Prior to arousal, ventilation (VI) was lower in the loaded condition than resting breathing (4.0 ± 0.5 vs 5.3 ± 0.4 L/min) but GG did not differ between conditions (1.0 ± 0.1 vs 0.9 ± 0.1%max). The peak of VI and GG during arousal tended to be higher in the loaded condition compared to resting breathing (7.4 ± 0.4 vs 6.8 ± 0.7 L/min and 3.7 ± 1.8 vs 2.1 ± 1.1%max respectively). However, the minimum VI and GG on the return to sleep did not differ between loaded and resting breathing conditions (4.7 ± 0.3 vs 4.6 ± 0.3 L/min and 1.1 ± 0.1 vs 1.2 ± 0.1%max).
Discussion: Although the increase in VRA after loading was small, no period of GG hypotonia was observed in either condition in these preliminary data. Data collection is ongoing.

PO-1-074

TRANSCUTANEOUS CO_2 DECREASES DURING REPETITIVE EPISODES OF APNEA AND HYPOPNEA

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Introduction: It has been previously suggested that the transcutaneous CO_2 ($tcCO_2$) increases during repeated episodes of sleep apnea. On the other hand, sympathetic intrusion during sleep (eg. during arousal) decreases the $tcCO_2$. We compared the $tcCO_2$ levels during presleep wakefulness (sympathetic state), episodes of repetitive apnea with intermittent hypoxemia (sympathetic intrusion) and episodes of non-apneic breathing without hypoxemia (parasympathetic state).
Methods: 154 consecutive cardiorespiratory sleep studies including $tcCO_2$ monitoring were retrospectively analyzed in patient who had been referred to Tampere University Hospital because of suspected obstructive sleep apnea syndrome. Patients were included if 1) they presented with episodes of repetitive arterial oxyhemoglobin desaturation for a minimum amplitude of 4%, repeating during a minimum duration of four minutes and 2) they also had episodes of high (>90%) and stable (±1%) SaO_2. The $tcCO_2$ values (kPa) during the above mentioned episodes and presleep wakefulness were compared in 27 patients who fulfilled these criteria.
Results: $TcCO_2$ increased from presleep wakefulness to episodes of non-apneic breathing (5.26 (SEM 0.17) to 5.87 (SEM 0.20) kPa) (p = 1.0 × 10E-11). The $tcCO_2$ during apneic events was 5.63 kPa (SEM 0.21). This was higher than during presleep wakefulness (p = 2.4 × 10E-6) but lower than during non-apneic breathing (p = 1.4 × 10E-6).

Conclusions: The $tcCO_2$ increase from wakefulness to stable sleep is a physiologic shift between sympathetic and parasympathetic states. This increase is disturbed by sympathetic intrusion associated with repetitive episodes of sleep apnea.

PO-1-075

RELATIONSHIP BETWEEN ARTERIAL STIFFNESS AND INSULIN RESISTANCE IN OBSTRUCIVE SLEEP APNEA SYNDROME WITH METABOLIC SYNDROME PATIENTS

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Purpose: The aim of this study was to evaluate the relationship between the effect of continuous positive airway pressure (CPAP) and the change of arterial stiffness in obstrucive sleep apnea hypopnea syndrome (OSAHS) with metabolic syndrome (MS).
Methods: Fifty OSAHS males with MS as experimental groups and Thirty five OSAHS males without MS as controls were enrolled and were evaluated by polysomnography(PSG) during sleep. Alll subjects were 30–70 years old in hospital from April. 2005 to September. 2010. Cardio-ankle vasucular index(CAVI) is superior to estimate the extent of atherosclerosis in large arteries. Therefore, We measured CAVI as arterial stiffness and insulin resistance in all subjects before and after CPAP treatment.
Result: Apnea-hypopnea index(AHI) in OSAHS males with MS group higher than that in control group. CAVI in OSAHS males with MS group were similar to that in control group. After CPAP treatment, AHI decreased in both groups. CAVI in OSAHS males with MS group strongly decresed compare to control group.
Conclusion: To conclude,these findings suggest the improvements of CAVI in OSAHS males with MS group by CPAP that may contribute to improvements of insulin resistance.

PO-1-076

IMPACT OF INSOMNIA AND DEPRESSION IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Obstructive sleep apnea syndrome (OSAS) is characterized by recurrent episodes of sleep apnea that are associated with hypoxia, arousal, and consequent fragmented sleep. The most common neuropsychiatric manifestation of OSAS is excessive daytime sleepiness that is secondary to the sleep fragmentation and loss of slow-wave sleep. We investigated insomnia and depression in OSAS.
Methods: We studied 16 OSAS patients (mean 62.9 ± 9.6 years). Polysomnography for sleep analysis was performed during natural sleep in all patients and moderate to severe OSAS patients were randomly assigned to receive nasal CPAP treatment. Subjective sleep symptoms, disturbances, and patterns were assessed with the Pittsburgh Sleep Quality Index (PSQI). The total global score ranges from 0 to 21, and greater scores indicate higher levels of sleep symptoms. Subjects with PSQI > 6 were defined as insomnia. Depression was evaluated using two-question case-finding instrument. Daytime sleepiness was quantified using the Epworth Sleepiness Scale (ESS). All patients underwent an otolaryngological evaluation. Deviation of the nasal septum and inferior turbinate hypertrophy were evaluated with nasopharyngoscopy, palate position and tonsil size evaluated by Friedman's classification.
Results: The prevalence of insomnia and depression was 75% and 43.8%, and daytime somnolence was 50% in OSAS patients. About the evaluation in the form of nasal cavity and the pharynx, Deflected nasal septum were 12 cases, the hypertrophic rhinitis were 10 cases. Regarding the scores of tonsillar hypertrophy, 1 patient was classed in grade 0, 9 in grade 1, 3 in grade 2, 2 in grade 3, and 1 in grade 4.
Conclusions: The OSAS patients with depression, the insomnia symptom were recognized frequently. For early detection of depression in OSAS, evaluating two-question case-finding instrument in addition to PSQI would be a useful. Grasp of the OSAS pathophysiology by the evaluation of not only the OSAS severity (or AHI) but also the otolaryngology was indicated to provide beneficial information for the improvement of the depression symptom.

PO-1-077

DAYTIME HYPERCAPNIA IN PATIENTS WITH SLEEP APNEA HYPOPNEA SYNDROME

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Objectives: To evaluate the incidence and factors related to daytime hypercapnia in Chinese patients withsleep apnea hypopnea syndrome(SAHS).
Methods: To assess the prevalence of daytime hypercapnia($PaCO_2$ > 45 mmHg) in Chinese patients with OSAHS, 1441 patients with SAHS had daytime arterial blood gas analysis were recruited from 2007 to 2009 in Peking University People's Hospital.145 patients underwent pulmonary function test and had FEV1/FVC ratio over 70% were under further analysis sex, BMI, pulmonary function, poly somnogram and blood gas analysis results were recorded. Linear regression analysis were used to evaluate the relationship between $PaCO_2$ levels and related parameters. Comparison was done between hypercanpnic and eucapnic patients.Finally, we evaluated the treatment effect of noninvasive ventilation(CPAP or BiPAP) on 49 patients with OSAHS(20 with hypercapnia and 29 eucapnia).
Results: Daytime hypercapnia occurs in 25.2% of 1441 patients with OSAHS. 26.9% in the 145 with FEV1/FVC ratio over 70% and OSAHS. $PaCO_2$ was correlated with BMI, PaO_2 and the severity of nocturnal hypoxemia as reflected by the mean SpO_2 and SIT_{90}.This was also confirmed by the comparison between the hypercapnic and eucapnic patients. One week of noninvasive ventilation treatment induced significant improvement of sleep breathing disorder in both hypercapnic and eucapnic patients, however, daytime PaO_2 and $PaCO_2$ only improved in the hypercapnic group($P < 0.05$), but not in the eucapnic patients. $PaCO_2$ level in 13 of the 20 hypercapnic patients returned to normal level (<45 mmHg).
Conclusions: Hypercapnia occurred in a large part of patients with SAHS and normal FEV1/FVC value. BMI, nocturnal hypoxemia and daytime PaO_2 level are all contributed to the development of daytime CO_2 retention in SAHS. Short term treatment using noninvasive ventilation can effectively decrease CO_2 level, and may correct daytime CO_2 retention. [Key words] Obstructive sleep apnea hypopnea syndrome; Daytime hypercapnia; Continuous positive airway pressure.

PO-1-078

DIFFERENTIAL CONTRIBUTION OF REM- AND NREM-RELATED ABNORMAL BREATHING TO DAYTIME SLEEPINESS IN PATIENTS WITH OSA

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The excessive daytime sleepiness is the fundamental symptom in patients with OSA, and is estimated by asking the patients about the self-administered questionnaire of ESS. Although ESS is approved for association with some of PSG parameters such as minimum SO2 and AHI, detailed relations between ESS and specific parameters of sleep-disordered breathing (SDB) during REM and NREM phases have not been systematically analyzed. We, therefore, attempted to examine the influence of SDB-related parameters in REM and NREM on the ESS of OSA patients. Forty patients with morbid OSA were recruited. They were evaluated for overnight PSG monitoring, and their leukocyte counts as well as NT-proBNP concentrations in the blood harvested within 3 hours after awakening were measured, as well. Taking the ESS as dependent variable, its correlation with 18 independent variables including age, BMI, neutrophil number, NT-proBNP concentration, times of nocturnal urination, and 13 PSG parameters were estimated with multivariate analysis by partial correlation coefficient allowing evaluation of true relation between independent and dependent variables. Distribution of sleep stage (N1, N2, N3, and REM), arousal index, heart rate, minimum SO2, AHI (REM and NREM), hypoxic time (REM and NREM), and hypocapnic time (REM and NREM) were used as the PSG parameters. We found that, although the daytime sleepiness estimated by ESS became better with age, it was aggravated by overweight, nocturia, increased heart rate during night, and prolonged N2 time. The daytime sleepiness was evidently worsen along with decrease in minimum SO2, and increase in REM-related hypoxic time and NREM-related hypocapnic time, while it was improved by increase in REM-associated AHI. In conclusion, the daytime sleepiness is underestimated by the elderly. Hypoxia during REM and hypercapnia during NREM function as the factor aggravating the daytime sleepiness. Although we found that REM-related AHI restrains the excessive daytime sleepiness, further study warrants elucidation of the mechanism explaining this peculiar phenomenon.

PO-1-079

ASSOCIATION OF OREXIN GENES MUTATIONS AND OBSTRUCTIVE SLEEP APNEA A MULTI-STAGES SEQUENTIAL STUDY

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Background: Obstructive sleep apnea (OSA) is considered a complex genetic disease. Several candidate genes have been studied for association with OSA. In our current study we investigated the association of orexin genes and obstructive sleep apnea in a cohort of Japanese subjects.MethodsOur study group included 50 patients with laboratory confirmed OSA through full night polysomnography where only moderate and severe cases of OSA were chosen. Another group included 50 control subjects without OSA. Genetic studies included genotyping assay, gene sequencing followed by functional gene expression assay and quantitative phenotyping assessment for orexin concentration in plasma. The study was approved by the Ethics Review Board for Human Genome Studies at Fujita Health University
Results: A novel single nucleotide deletion in the orexin gene was found in one patient in heterozygote form.Two single nucleotide mutations in the orexin gene were identified in the study group with significant difference between patients and controls.By using Spicing Site Prediction Programs, one of these mutations showed change of the Spice Donor site in some of them or change of the score in others.In vitro assessment of the splicing pattern followed by in vitro functional study for the transcriptional activity revealed significant findings as regard one of these mutations.Furthermore, quantitative phenotyping assessment for the plasma orexin level supported our in vitro functional results.
Conclusions: This genetic association, case-control study identified two single nucleotide mutations in the orexin genes showed significant differences between patients and control. Furthermore, functional assessment supported our association study. Orexin genes could be involved in the pathogenesis of OSA.

PO-1-080

QUALITY AND QUANTITY OF SLEEP IN PATIENTS WITH COPD ADMITTED TO AN ACUTE RESPIRATORY WARD

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Aims of the study: To measure length, continuity and quality of sleep in patients with chronic obstructive pulmonary disease admitted to an acute respiratory ward.
Method: A prospective observational study involving 36 quasi-consecutive patients (20 males, mean age 72 yrs, range 51–91), with severe airway obstruction (FEV1/FVC 45% SD±10) during 41 admissions. Usual sleep at home and daily sleep in hospital was assessed by use of questionnaires, Likert scale for quality of sleep, nurse observations and actigraphy.
Results: There were 140 admission days, 40 in single room and 100 in 4 bed cubicles. Average length of stay was 5 days (range 1 to 30). There was no significant difference in age and severity of airway obstruction between men and women. Bed time and wake up time were earlier in hospital by 33 min (95%CI 5–72 min) and 21 min (95% CI 1.5–44 min) respectively. Latency to sleep was significantly longer in hospital (mean difference 43 minutes, 95%CI 29–58 minutes). Total sleep time (TST) assessed subjectively was significantly reduced compared to home by 2 hours and 26 minutes (95%CI 2.4–2 hrs). Subjects overestimated TST by 54 min (95%CI 22–87 min) compared to actigraphy TST. There was no difference in sleep latency and TST between sleep in single room compared to 4 bed cubicles.
There was no correlation between severity of airway obstruction measure (FEV1/ FVC) and total sleep time. Perceived sleep quality did not improve between the first day of admission and up to 10 days stay. The number of awakenings through the night was higher in hospital than at home (mean difference 1.2, 95% CI 0.8–1.5) and in 4 bed

cubicles than in single room (4 and 2 respectively). The most common reasons for sleep fragmentation were voiding, nurse intervention and noise. Lunch and dinner were earlier in hospital by 1.30 and 1 hour respectively.
Conclusion: In patients with severe COPD, admission to hospital is associated with severe disruption of sleep continuity, length and daily routine. Attention and modification of some of the identified factors associated with sleep disruption may be beneficial to patients' care.

PO-1-081

CLINICAL FEATURES OF RESPIRATORY FAILURE AND HEART FAILURE IN PATIENTS WITH SLEEP DISORDERED BREATHING

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Objective: To assess clinical characteristics of heart failure and respiratory failure in patients with sleep disordered breathing (SDB).
Methods: Symptoms, signs, laboratory tests, clinical courses, blood gases responses to voluntary hyperventilation test were analyzed in 29 patients with SDB. All were diagnosed as right or left heart failure and respiratory failure from 1994 to 2009 in Peking University People's Hospital.
Results: 13 were male and 16 female. 14(48.3%) were diagnosed as obstructive sleep apnea syndrome at first visit. Chief complains includes dyspnea, edema, cough, snoring, hypersomnolence, oliguria and altered mental status. Common signs include obesity, narrow upper airway, cyanosis, moist rales at the base of lungs, enlarged border of cardiac dullness, edema. Polycythemia was seen in 13(44.80%), among 26 patients who had underwent pulmonary function tests, 14 had FEV1/FVC =>70%, the others were FEV1/FVC < 70%, with 6 patients had 50% predict value <= FEV1 < 80% predict value and 6 patients had 30% predict value <= FEV1 < 50% predict value. After positive airway pressure treatment, symptoms and arterial blood gases test results improved. Chest *X-ray*, CT scan and UCG show pulmonary vascular congestion and edema with cardiomegaly and possible pleural effusion, pulmonary hypertension, left ventricular diastolic dysfunction. In 11 patients, voluntary hyperventilation induced significant improvement of SpO_2, $PaCO_2$ and PaO_2, and most of the parameters returned from type II respiratory failure to normal level.
Conclusion: The mobidity of SDB remained to be recognized. This cases report indicated that obese patients complaining of severe dyspnea and edema may have respiratory failure and bilateral heart failure secodary to SDB. The respiratory failure can be completely reversed by voluntary hyperventilation, and noninvasive treatments only could achieve good outcomes in most of the patients.
Key words: sleep disordered breathing, heart failure, respiratory failure, voluntary hyperventilation, noninvasive ventilation

PO-1-082

RELATIONSHIP BETWEEN AIRWAY VOLUME AND SLEEP-DISORDERED BREATHING

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Introduction: Early detection and prevention of OSAS is very important, because several reported the relationship of OSAS and cerebrovascular disorder, or cardiac disorder recently. The purpose of this study is to clarify the relation between airway volume and sleep-disordered breathing (SDB).
Materials and Methods: Thirty five Japanese female patients, who were diagnosed as jaw deformity. The average age and BMI were 24.0 years and 20.2 kg/m2, respectively. Based on the angle of ANB, these patients were divided into three groups; skeletal 1, 2 and 3. Using polysomnography, AHI, 3% ODI an arousal index were measured. 3D images of the airway were reconstructed using a CT analyzing computer software. The upper and lower boundary were defineded as be at the level of the hard palate and the base of the epiglottis, respectively. From the 3D reconstructed models, the following parameters on the airway were obtained: the volume of upper airway (total volume), the volume between the level of the hard palate and the top of uvula (volume of HP-TU), the volume between the top of uvula and the base of the epiglottis (the volume of TP-BE).
Results: The average of total volume in the skeletal 1, 2 and 3 group was 15.4 cm^3, 13.7 cm^3 and 11.2 cm^3, respectively. The average of HP-TU volume was 8.6 cm^3, 6.2 cm^3 and 5.6 cm^3 in the skeletal 1, 2 and 3 group, respectively. The average of TP-BE volume was 6.6 cm^3, 7.3 cm^3 and 5.5 cm^3 in the skeletal 1, 2 and 3 group, respectively. The average of AHI was 1.5/hr, 1.7/hr and 2.3/hr in the skeletal 1, 2 and 3 group, respectively. The average of 3% ODI was 0.4/hr, 0.6/hr and 1.0/hr in the skeletal 1, 2 and 3 group, respectively. The average of arousal index was 8.3/hr, 10.2/hr and 13.7/hr in the skeletal 1, 2 and 3 group, respectively. There were no significant differences. The Spearmans correlation coefficient by rank test was found to be a negative correlation between the HP-TU airway volume and 3% ODI ($p < 0.05$).
Discussion: If oral appliance will be treated for OSAS, it is important to the measurement of HP-TU airway volume using CT scan when the mandible was displaced anteriorly at pre-treatment.

PO-1-083

COMPLICATED EFFECTS OF REM- AND NREM-RELATED VENTILATORY IMPEDIMENTS ON MINIMUM SO_2 IN OSA PATIENTS

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The severity of OSA is generally diagnosed by the number of apnea/hypopnea events (AHI), but minimum SO_2 ($minSO_2$) and the period of hypoxic time during sleep are equally important for judging it, as well. About 10 years ago, Bixler et al. demonstrated that $minSO_2$ in patients

with sleep disordered breathing (SDB) was improved with age, indicating that the clinical severity of SDB decreased along with age. However, this important finding has not been reliably reexamined so far. We, therefore, attempted to investigate the impact of age on minSO_2 in OSA patients by considering the interactions of various SDB-related parameters in REM and NREM phases. Forty patients with morbid OSA (overall AHI: more than 5) were enrolled and evaluated for overnight laboratory PSG. In addition, neutrophil counts as well as NT-proBNP concentrations in their blood samples harvested within three hours after getting up were measured. The correlations between minSO_2 (dependent variable) and 18 independent variables including age, BMI, neutrophil count, NT-proBNP concentration, daytime sleepiness (ESS), number of nocturnal urination times, and 12 PSG parameters were estimated with multivariate analysis by partial correlation coefficient allowing evaluation of true relation between dependent and independent variables. Distribution of sleep stage (N_1, N_2, N_3, and REM), arousal index, heart rate, AHI (REM and NREM), hypoxic time (REM and NREM), and hypocapnic time (REM and NREM) were introduced as the PSG parameters. Partial correlation analysis revealed that, opposed to Bixlers finding, minSO_2 decreased with age. Furthermore, MinSO_2 decreased with REM-related AHI, but increased with increased heart rate during sleep and prolonged hypocapnic time in NREM. Interestingly, minSO_2 decreased with enhanced NT-proBNP concentration in the blood, suggesting that a transient pulmonary edema induced by apnea-evoked cardiac failure worsened gas exchange in the lung. These findings indicate that minSO_2 is worsened by aging in a complicated combination with REM- and NREM-associated ventilatory impediments.

PO-1-084

PATHOGENESIS OF OBSTRUCTIVE SLEEP APNOEA IN QUADRIPLEGIA

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Introduction: Obstructive sleep apnoea (OSA) is estimated to be 2 to 5 times higher in patients with quadriplegia than in able-bodied (AB) individuals. In order to better understand the causes of OSA in quadriplegia we aim to investigate upper airway function in quadriplegia. High nasal resistance predisposes to OSA in AB individuals. In patients with quadriplegia, the spinal sympathetic circuits lose tonic control and induce vascular engorgement of the airway causing the nasal mucosa to thicken. We therefore hypothesized that nasal (Rna) and pharyngeal (Rph) resistance will be 1) elevated in patients with quadriplegia and OSA compared to AB individuals with and without OSA, and 2) reduced to AB levels with decongestant.
Methods: AB and patients with quadriplegia both with and without OSA are being recruited. Subjects are instrumented with epiglottic and choanal pressure catheters, a nasal mask and pneumotachograph. All measurements are performed while subjects are supine during wakefulness. Rna and Rph (in cmH_2O/l/s, calculated from mask, choanal and epiglottic pressures at a flow rate of 200 ml/s), were determined for 5 minutes, before and 5–10 minutes after application of decongestant (0.5 ml of phenylephrine 0.5%).
Results: One patient with quadriplegia (20 years old) and one healthy AB individual (45 years old) have been studied to date. The patient with quadriplegia showed elevated resistance at baseline (Rna = 6.26, and Rph = 5.29, compared to Rna = 2.43, Rph = 1.05 in the AB). After decongestion, the Rna was 1.51 in the patient with quadriplegia and 0.80 in the AB. The Rph was similar to baseline after phenylephrine.
Discussion: Although very preliminary, these data suggest that after quadriplegia the Rna is particularly elevated. This is probably due to the partial loss of function of the autonomic nervous system. The high Rna in patients with quadriplegia appears to be significantly reduced by the application of decongestant. The high Rna and Rph observed are potentially one of the risk factors for OSA in quadriplegia but further data are required.

PO-1-085

IMPACT OF MASKED HYPERTENSION/MORNING BP SURGE IN OBSTRUCTIVE SLEEP APNEA SYNDROME

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Background: The frequent hypoxic episodes and arousal during sleep in obstructive sleep apnea syndrome (OSAS) result in an increase in nocturnal blood pressure, and may lead to sustained hypertension. The aim of this study was to investigate the relationship between OSAS and abnormal circadian rhythm in blood pressure.
Methods: We studied 26 patients with OSAS (age 49.3 yrs). Twenty four hour ambulatory BP monitoring (ABPM) was performed in all patients without taking antihypertensive medication. Masked hypertension was defined as clinic BP < or = 140/90 mmHg and 24-hour ambulatory BP > or = 130/80 mmHg. The following ABPM-related prognostic features were studied absence of nocturnal dip (< or = 10% fall in night time systolic BP) and morning surge (> or = 20 mmHg rise in the first four morning readings from wake-up as compared to average night time BP). OSAS severity was evaluated using standard polysomnography.
Results: Three patients (12%) were normotensive, six patients (23%) exhibited masked hypertension, and 17 hypertension (65%). Apnea-hypopnea index was significantly lower in masked hypertension than that in hypertension. Morning BP surge was observed in 12 patients (46%). All moderate OSAS (6 patients) showed morning BP surge. Apnea-hypopnea index in morning BP surge group was significantly lower than that in non-morning BP surge group. Thirteen patients (50%) showed nondipping pattern. Of 10 nondippers were severe OSAS. Apnea-hypopnea index and lowest SpO_2 were worse in nondippers compared with those in dippers, but did not reach significant level.
Conclusion: Masked hypertension/morning BP surge may relate with pre-hypertensive status in patients with OSAS.

PO-1-086

DIFFERENTIAL EXPRESSION OF HEMI-CHOREA IN INTRA-SLEEP AWAKENINGS: EVIDENCE FROM ONE CASE OF DIABETIC STRIATOPATHY WITH SLEEP APNEA SYNDROME

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Background: Unilateral chorea and corresponding neuroimaging abnormalities of the striatum have been recently described as a rare

syndrome associated with uncontrolled diabetes mellitus. Despite specific clinical manifestations and imaging findings, the pathogenic mechanisms underlying this syndrome are still not fully understood. Moreover, sleep data and movement analysis across sleep related awakenings are lacking in these patients.
Methods: We report the case of one patient diagnosed with diabetic striatopathy and subjected to video-polysomnographical recordings.
Results: Sleep recordings revealed a severe obstructive sleep apnea syndrome with fragmented sleep. Video recordings showed that the involuntary movements ceased during sleep and were re-initiated during intra-sleep awakenings. Interestingly, the movements during slow wave sleep (SWS) awakenings seemed to have a more similar pattern with the diurnal movements as compared to the ones expressed during rapid eye movement (REM) sleep awakenings.
Conclusions: Our patient presented sleep disturbances related to severe sleep apnea syndrome. We bring evidence, for the first time to our knowledge, of different characteristics of the involuntary movements expressed during REM awakenings versus NREM awakenings in striatopathy. This confirms the differential motor control across biochemically and physiologically distinct sleep stages. Furthermore, we qualitatively analyzed the involuntary movements expressed during REM awakenings versus SWS awakenings. Our observations are in line with evidence coming from patients with Parkinson disease and REM sleep behavior disorder, who show a differential motor control during REM sleep as compared to diurnal time. We suggest that the diabetic striatopathy entity can be used as a neurological model to study motor control and underlying biochemical changes related to different stages of sleep

PO-1-087

INSOMNIA AMONG SLEEP APNEA PATIENTS AND CONTROLS

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Background: Insomnia and obstructive sleep apnea (OSA) often coexist, but the nature of their relationship is unclear. The aims of this study were to compare the prevalence of initial and middle insomnia between OSA patients and controls as well as to study the influence of insomnia on sleepiness and quality of life in OSA patients.
Material and methods: Two groups were compared, untreated OSA patients (n = 824) and controls 40+ years from the general population in Iceland (n = 762). Controls were sub-divided into OSA high and low risk based on the multivariable apnea index (MAP). All subjects answered the same questionnaires on health and sleep and OSA patients underwent a sleep study. Altogether, 53% of controls were males compared to 81% of OSA patients.
Results: Difficulties maintaining sleep (DMS) were more common among men and women with OSA compared to the general population (52 vs. 31% and 62 vs. 31%, respectively, $p < 0.0001$). Difficulties initiating sleep (DIS) and DIS+DMS were more common among women with OSA compared to women without OSA. OSA patients with DMS were sleepier than patients without DMS (Epworth Sleepiness Scale: 12.2 vs. 10.9, <0.001) while both DMS and DIS were related to lower quality of life in OSA patients as measured by the Short Form 12 (physical score 39 vs. 42 and mental score 36 vs. 41, $p < 0.001$). DIS and DMS were not related to OSA severity. Altogether, 12% of the controls were in high risk for OSA based on the MAP index and they were more likely to be suffering from DIS than low risk controls.
Conclusion: DMS is almost twice as common among OSA patients compared to controls while the prevalence of DIS is similar between the groups. Insomnia has an additional negative influence on quality of life and sleepiness in this patient group. It is relevant to screen for insomnia among OSA patients and treat both conditions when they co-occur.

PO-1-088

DETECTION OF SLEEP APNEA IN PATIENTS WITH ATRIAL FIBRILLATION USING BERLIN QUESTIONNAIRE AND PORTABLE MONITORING

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Introduction: Atrial fibrillation (AF) is one of the most common arrhythmia. Sleep Disordered Breathing (SDB) is supposed to correlate with AF according to recent studies. In field of cardiology, Berlin Questionnaire (BQ) is widely used to estimate risk for co-existing SDB. In our study we used unattended Portable Monitoring (PM) to detect SDB in AF patients to compare both diagnostic approaches.
Methods: We included 81 patients (51 males, 30 females, mean age: 63 ± 9,6 years, BMI: 29,2 ± 5 kg/sqm) with a documented AF in this monocentric prospective study. All patients had an indication for rhythm control therapy as recommended in actual guidelines (antiarrhythmic medication, electrical cardioversion, catheter ablation of pulmonary veins). Before treatment BQ was completed by all patients to estimate risk for SDB. In addition all patients got PM, recording nasal flow, respiratory movements, oxygen saturation and ECG.
Results: PM detected SDB in 49 of 81 subjects (AHI = 12,2 ± 6,9 per hour, cut off 5 per hour).
29 subjects showed mild, 14 moderate and 4 patients severe levels of SDB.
BQ classified 43 of 81 subjects to be at high risk for SDB (53%). PM confirmed SDB in only 31 of these 43 patients (BQ: sensitivity 63%, specificity 62%).
Conclusion: A remarkable prevalence of SDB was detected in patients with AF and an indication for rhythm control therapy by both BQ and PM.
Screening for SDB should be part of routine examination of AF patients, as treatment of SDB is supposed to reduce relapse rate of AF after rhythm control therapy.
Further investigation is needed for outlining the best screening method for SDB in AF patients. Therefore all limited methods should be compared with polysomnography which is the gold standard.

PO-1-089 / AS-10 Presenter

AN INDEX BASED ON THE HILBERT TRANSFORM OF THE AIRFLOW SIGNAL THAT ASSESS REGULARITY AND QUANTIFIES DISTURBED BREATHING DURING SLEEP

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An essential part of polysomnographic reports derives from the visual or automated detection of apneas and hipopneas, summarized as events per hour, a widely used index (AHI) of the severity of sleep breathing disorders. Here we propose a mathematical technique that analyses the airflow as a continuous signal and provides an index that varies from normal, regular patterns, to severely disturbed breathing.The Hilbert transform provides the envelope or instant amplitude of a given signal. The coefficient of variation (CV = standard deviation/mean) of the envelope is a dimensionless constant invariant to signal scale. The envelope of a signal generated by a population of asynchronous oscillators is described by the Rayleigh distribution whose CV equals the square root of (4/pi-1), approximately 0.523. The CV can be used as an index to discriminate signals produced by synchronous or asynchronous neuronal populations (Diaz et al. J Neurosci. 27:9238–45, 2007). The envelope CV is 0.523 for signals produced by asynchronous oscillators and less than 0.523 when produced by synchronous oscillators, with smaller CVs indicating higher synchrony and envelope regularity. Envelopes with a CV higher than 0.523 correspond to a pulsating time course. Thus, the CV index for the respiratory signal would provide a value in a range going from regular respiration to high incidence of apneas.The method was applied to the PTAF signal in 90-second windows sliding over 30-second epochs. Time course of the CVs correlates remarkably with state transitions. Frequency distributions of CVs for eupneic subjects typically concentrate in the 0.1–0.3 range and for severely apneic subjects in the 1.0–1.4 range. State or position dependency of apneas is readily assessed by overlaying the CV time course.

PO-1-090

CLINICAL PERFORMANCE OF THE SD-101 FOR THE DIAGNOSIS OF OBSTRUCTIVE SLEEP APNEA SYNDROME

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Study Objectives: The SD-101 is a non-restrictive, sheet-type portable monitoring device with a built-in pressure sensor used to detect respiratory events based on pressure changes corresponding to respiratory movements. This study evaluated the clinical performance of the SD-101 as a screening device for obstructive sleep apnea syndrome (OSAS).
Design: Cross-sectional and multi-center study.
Setting: Sleep laboratory.
Participants: 192 subjects with suspected OSAS.
Interventions: N/AMeasurement and Results: One hundred ninety-two subjects with suspected OSAS underwent overnight polysomnography (PSG) and SD-101 simultaneously at 5 sleep centers; data from 188 subjects were analyzed. The correlation of respiratory disturbance index (RDI) between polysomnography and the SD-101 was 0.901 ($p < 0.05$). The sensitivity and specificity of the SD-101 were 0.817 and 0.903 respectively for AHI cutoff of >15 events/hour and the SD-101 RDI cutoff value of 16.9. The positive and negative likelihood ratios were 8.447 and 0.202, respectively. The areas under the curve (AUC) were 0.918 for apnea/hypopnea index (AHI) cut offs of >15 events/hour. The optimal cut off value of the SD-101 was 16.9 for the same AHI cutoff value.
Conclusion: The present study revealed that the SD-101 was less discomfort, is easy to use compared with other devices and had a relatively high ability to detect OSAS.

PO-1-091

COMPARISON OF FACIAL PHOTOGRAPHIC DIMENSIONS AND BONY MEASUREMENTS FROM MRI IN OSA PATIENTS

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Facial photography is potentially a very useful anatomical phenotyping tool in obstructive sleep apnoea (OSA). We hypothesize that facial photographs relate to OSA because they capture aspects of general and visceral obesity as well as upper airway soft tissue and craniofacial structure. We have previously shown relationships between facial photographic dimensions and obesity and upper airway soft tissue structures. We aimed to assess the relationship between facial photographic measurements and measurements of skeletal structures in subjects with OSA.
Methods: Patients from the Icelandic Sleep Apnea Cohort (ISAC) had magnetic resonance imaging (MRI) and calibrated facial photographs performed. Facial dimensions derived from photographic analysis were compared to those obtained by three-dimensional MRI cephalometry using Bland-Altman plots and correlation.
Results: Preliminary analysis was conducted in 73 (61 male, 12 female) OSA patients (mean [±SD] age 55.6 ± 10.2 years, AHI 41.7 ± 19.9/hr, BMI 32.7 ± 4.9). There was agreement between craniofacial dimensions (SNA, SNB, facial heights) obtained from photographed surface landmarks and bony landmarks. Surface measurements produced generally larger measures of mandibular length (Go-Gn) however the two measures were correlated ($r = 0.53$, $p < 0.001$). The difference between surface and skeletal mandibular width (Go-Go) measurements correlated with measures of obesity (neck circumference $r = 0.38$, $p = 0.001$; body mass index $r = 0.41$, $p < 0.001$).
Conclusions: These preliminary data suggest there are relationships between surface and skeletal measurements of the face and mandible in subjects with OSA, which incorporate measures of obesity. The data support the use of facial photography as a tool for large scale phenotyping studies. Work is ongoing to verify these findings and to further evaluate the influence of obesity, gender and ethnicity.

PO-1-092

SLEEP PERCEPTION IN CHRONIC PRIMARY INSOMNIACS, OBSTRUCTIVE SLEEP APNEA SYNDROME PATIENTS, AND HEALTHY VOLUNTEERS

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Background: The mechanisms of sleep perception by the patient are largely unknown. Moreover, sleep perception might be divers depending on each sleep disorder. The aim of this study was to investigate the differences in sleep perception over patients with chronic primary insomnia(PI) or obstructive sleep apnea syndrome (OSA) with or without insomnia symptoms.
Methods: We enrolled the consecutive 430 patients(age 20–79) who underwent polysomnography(PSG) and sleep questionnaire including depression scale(BDI) and daytime sleepiness(ESS). We divided into 4 groups: Group I(n, 63) with normal controls, Group II(90) with the patients with PI[apneahypopnea index lower than 5 and DSM-IV criteria], Group III (83) with OSA patients (AHI more than 5 per hr) who have a difficulty of sleep onset and maintenance , and Group IV(194) with OSA patients without subjective insomnia symptoms. We compared the differences of sleep parameters obtained from polysomnography among 4 groups and investigated the discrepancy between objective and subjective total sleep time and sleep latency in each group.
Results: Sleep perception was defined as the percentage of the ratio between the total sleep time perceived by the patient and the total sleep time obtained by PSG. Mean Sleep perception of 4 groups were 87.4%, 76.6%, 80.9%, and 93.6%, respectively. Group IV showed the highest and group II had the lowest sleep perception. Group III showed definitely lower sleep perception than group IV and were more depressive. Patients who complaint insomnia tended to report longer sleep latency (67.1 min in group II and 70.7 min in III) than others (29.4 min in group I and 29.5 min in IV) subjectively, but the discrepancy ratio (subjective/objective sleep latency) did not reach to statistical significance among groups.
Conclusion: Patients with insomnia (with or without OSA) appear to underestimate their sleep time as compared with normal controls or patients with OSA. This sleep misperception may be related to higher N2 sleep, WASO, and lower REM sleep (%).

PO-1-093

APPLICATION OF 3D-CT EVALUATION OF UPPER AIRWAY MORPHOLOGY OF OSAS PATIENTS FOR SELECTION OF SURGICAL TREATMENT CANDIDATES

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Obstructive sleep apnea (OSA) is a common form of sleep-disordered breathing characterized by repetitive episodes of partial or complete upper airway obstruction. It usually causes sleep fragmentation, reduced blood oxygen levels, and excessive daytime somnolence. Cognitive deficits, impaired psychosocial wellbeing, reduced driving competence, cardiovascular morbidity, and mortality have been reported. Because the clinical significance of OSA is increasing, more exact diagnosis for successful treatment is required.
Multiple factors like enlarged tonsils, nasal disease, body weight, age and craniofacial morphology causes OSAS. But it is well known that the breathing route affects the upper airway morphology. It has been suggested that patients with OSA have narrower pharyngeal airways than normal persons, therefore breathing with mouth open affect the upper airway morphology of OSA patients significantly compared to non-OSA patients.
To assess the relationship between pattern of breathing and upper airway morphology in OSA patients, we perform 3D-CT examination and evaluate the changes of upper airway morphology with mouth open and close with DICOM viewer (Osirix) .
Eleven patients were examined 3D-CT with both oral breathing and nasal breathing. The results showed that even in awake, upper airway became narrow with oral breathing.
It has been reported that the imaging results while awake do not necessarily reflect conditions during sleep, when tone of the upper airway dilating muscles is decreased. But on the standpoint of relationship between breathing routes and upper airway morphology, 3D-CT while awake can be a useful tool for selection of surgical treatment candidate, especially predict the effects of nasal surgery because it can improve the nasal breathing.

PO-1-094

DETECTION OF SPECIFIC OBSTRUCTION SITES USING FLUID-STRUCTURE INTERACTION ANALYSIS IN CHILDREN WITH OBSTRUCTIVE SLEEP APNEA SYNDROME.

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INTRODUCTION: Obstructive sleep apnea syndrome (OSAS) in children is not rare and is a major health problem. Unfortunately, surgery's success rate is relatively low because obstruction sites of the upper airway vary considerably. Morphological findings from computed-tomography (CT) do not always coincide precisely with the functional obstruction sites in the upper airway. Consequently, establishing a method to detect the specific obstruction sites of the whole upper airway is indispensable to successful treatment of OSAS.
MATERIALS and METHODS: From CT data the constructed 3-D whole upper airway model of a OSAS child with a stopped breath condition was exported to fluid-dynamic software in STL format. Fluid mechanical simulation (FMS) of the airway model was performed for inspiration and exhalation to obtain each pressure value for structural analysis of these airway models. Airway deformation models were manufactured from the analysis results. Finally, FMS of these deformation models during inspiration and exhalation were performed, and the dynamic ventilation conditions of each model were evaluated.
RESULTS: The ventilation condition was presented in the upper airway models as pressure and velocity. Fluid structural interaction analysis (FSI) detected obstruction sites during inspiration and exhalation that were not detected in the airway model alone.
DISCUSSION: We describe a new method combining an airway model with FSI. This method can locate the obstruction sites and simulate

the magnitude of air pressure and velocity, evaluating the ventilation condition more precisely than with a morphological evaluation alone. And it may be more reliable when applied to the clinical diagnosis of OSAS.

PO-1-095

A PRELIMINARY STUDY OF ESTIMATING SEVERITY FOR SLEEP APNEA SYNDROME USING A NONWEAR DEVICE (NEMURI SCAN)

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OBJECTIVE: Existing portable devices for the diagnosis of sleep apnea syndrome (SAS) are recognized as unreliable methods. Polysomnography (PSG) is the gold standard for the diagnosis of SAS. However, PSG is costly and requires the patients to wear the many sensors. The development of a simplified, low-cost, accurate portable device has been anticipated. A nonwear actigraphy (NWA: NEMURI SCAN, Kogure et al., J Physiol Anthropol 2011) device placed under a mattress that can score sleep/wake and in-bed/out-of-bed from body motion in bed was recently developed. The NWA device is low cost and requires no sensor placed on the body. The objective of this study is to explore the capability of estimating severity for SAS from respiratory movements measured by the NWA device.
METHODS: Simultaneous PSG and NWA recordings were made for 13 participants (2 women, 11 men), aged 40–78 (average 56.6 ± 12.5 years). The participants were admitted to hospitals for PSG in diagnosis of SAS. The apnea hypopnea index (AHI), defined as the number of apneas and hypopneas per hour of sleep, was calculated by PSG and NWA for each participant. Ethical approval was obtained prior to the study.
RESULTS: The AHI was 2.0–73.1 (average 32.9 ± 24.1) in PSG and 5.7–56.8 (average 26.2 ± 17.6) in NWA. Pearson correlation coefficients between PSG and NWA were 0.86 ($P < 0.001$) in AHI.
CONCLUSION: Although further study is required to address the validity of estimating severity for SAS, it is indicated that the estimation from respiratory movements measured by the NWA device is a possible method.

PO-1-096

NEUROCOGNITIVE FUNCTION IN OBSTRUCTIVE SLEEP APNEA: A CASE CONTROL STUDY

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Introduction: Previous studies in obstructive sleep apnea (OSA) showing cognitive dysfunction have often employed small groups, drawing controls from clinical populations, and using tests with sparse normative data. We aim to characterize the neurocognitive dysfunction in OSA using a comprehensive battery of tests including event-related potentials (ERPs) and using non-clinical controls.
Methods: We compared 106 cases with OSA (PSG AHI > 5), with controls matched by age, gender and years of education, on a 1:4 ratio, from the Brain Resource International Database. All subjects underwent a standard cognitive test battery and EEG recording concurrent with working memory, Go-No Go and auditory oddball tasks, from which ERP responses were derived. OSA cases were compared with the controls for all outcomes of interest, using mixed effects models.
Results: Tests for verbal memory, working memory, language skill, and behavior control (verbal interference total score) and attention were impaired in OSA subjects ($p <= 0.001$). Analysis of ERP by area under the curve during the working memory and Go-No Go tasks showed OSA subjects to have a significantly increased activation near 100 ms ($p < 0.05$) and beyond 200 ms ($p < 0.01$), corresponding to the N1 and N2 components of the ERP waveform, while having worse performance ($p < 0.001$). However there were no between-group differences in ERP components found in the oddball task ($p > 0.5$). Within cases there was no relationship found between severity of OSA and cognitive function affected or magnitude of amplitude in ERP.
Conclusion: Using a comprehensive assessment battery, we demonstrate impairments related to memory, language skill, behavioral control and attention in OSA patients. Evidence of greater neural processing as observed in ERP responses, associated with poorer performance, may indicate requirement for greater mental effort or focus in OSA subjects.

PO-1-097

DEVELOPMENT OF A DIAGNOSTIC MODEL FOR SLEEP APNEA IN PRIMARY CARE

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Introduction: As a means to diagnose obstructive sleep apnea, in-laboratory polysomnography is costly and resource-intensive. Questionnaires, physical measurements and home monitors have been studied as potential simpler alternatives to in-laboratory polysomnography (PSG) for diagnosis of obstructive sleep apnea (OSA). This study aims to develop a diagnostic model for OSA for use in primary care.
Methods: Participating general practitioners were trained to recognise symptoms of sleep apnea, and recruited patients based on clinical need to establish or exclude the presence of OSA. Assessment was by symptom questionnaires, anthropomorphic measurements, digital photography of the face and profile, and a single channel nasal flow monitor (Flow Wizard, DiagnoseIT, Sydney, Australia) worn at home for 3 nights. Patients also underwent in-laboratory PSG as the reference test, with OSA defined as AHI >= 10.
Results: In the model development sample 25 general practitioners studied 360 patients: 64% male, with mean(SD) age 50.3(12.5) years, BMI 29.8(6.6) kg/m^2, ESS 9.6(4.8). Mean PSG apnea-hypopnea index (AHI) was 19.6(19.6)/hour, with 58% having PSG AHI >= 10 and 21% having AHI >= 30. The nasal flow monitor alone yields high accuracy for predicting OSA with area under receiver operating curve (AUC) 0.87. Sensitivity was 0.87 (0.80–0.91) and specificity 0.77 (0.69–0.83) at a threshold of 18 events/hr on the flow monitor. A six-element model adding symptoms, BMI, hip circumference, and nasal width from photography to the flow monitor modestly improved OSA prediction (AUC 0.88).
Discussion: The results suggest that testing with a portable monitor may be appropriately applied at the primary care setting in concert with clinical assessment and knowledge of test characteristics.

PO-1-098

PREDICTORS OF WEIGHT GAIN IN PATIENTS WITH SUSPECTED SLEEP APNEA

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Background: Obesity is the main risk factor for obstructive sleep apnea. According to clinical experience, patients frequently continue to gain weight also after the sleep apnea diagnosis and successful treatment. We hypothesised that higher level of sleepiness, shorter habitual sleep duration, higher depression scores, graving for high-fat, high-carbohydrate type of food, low plasma insulin-like growth factor-1 and leptin levels would correlate with weight gain.
Materials and methods: Consecutive patients (n = 223; M 123, F 100) referred for a sleep study because of suspected sleep apnea were recruited. Of this cohort, 59.6% (n = 133; M 75, F 58) participated in the 3-year follow-up. In the evening prior the overnight in-hospital sleep study, patients were weighed and the height was measured. After a standard hospital dinner, patients completed a questionnaire battery including the Epworth Sleepiness Scale (ESS), habitual sleep duration, depression scale (DEPS), and VAS of graving for various food categories. Blood for plasma IGF-1 and leptin concentration assessments was drawn after an overnight fast in the morning after the sleep study.
Results: Median BMI at baseline was 31.1 (range from 19.9 to 56.5) kg/m2. After a 3-year follow-up, median change in BMI was +0.33 (range from −13.4 to +7.5) kg/m^2 and did not differ between CPAP-users and non-users. Change in BMI correlated positively with the scores in the baseline depression score (Spearman r = 0.19, p = 0.346) but not with the plasma IGF-1 or leptin levels, ESS score, habitual self-reported sleep duration or graving for various food categories.
Conclusions: Depressive symptoms at baseline were associated with weight gain during a 3-year follow-up in patients with suspected sleep apnea. Prospective studies are warranted whether weight gain is related to depression per se or the antidepressive medication and whether a dietician consultation should be focused particularly in depressive sleep apnea patients.

PO-1-100

CORRELATION ANALYSIS BETWEEN SLEEP VIDEOFLUOROSCOPY AND POLYSOMNOGRAPHY

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Background: The treatment of obstructive sleep apnea syndrome (OSAS) is focused on the way how to improve the upper airway obstruction. Sleep videofluoroscopy (SVF) is a kind of localization technique combining fluoroscopy and video recording and enabling direct visualization of dynamic airway change. The purpose of this study is to find correlations between SVF and PSG.
Methods: Retrospective review was made of 112 OSAS patients who underwent PSG and SVF from August 2009 through June 2010. PSG variables include respiratory disturbance index (RDI), supine apnea-hypopnea index (AHI), non-supine AHI, longest apnea time & lowest O_2 saturation and positional dependency (PD), Mouth-opening angle (MOA) at normosaturation and desaturation, MOA difference (MOA desaturation – MOA normosaturation) and obstruction site, were evaluated as SVF variables.
Results: The severer OSAS patients showed the smaller MOA difference. Soft palate (SP) obstruction group was more likely to have PD than tongue base (TB) obstruction group and PD was inversely related to OSAS severity. When adjusted for OSAS severity, patients with SP obstruction alone tended to have PD more than those with TB obstruction only in the severe group (P = .025 by Chi square test).
Conclusion: It is suggested that knowledge of these SVF variables can improve our understanding of PSG results. The data also reinforce the necessity of not only monitoring PSG evaluation of every suspected OSAS patient, but also SVF reporting the localizing obstruction site.

PO-1-101

THE STUDY OF GEOMETRIC PARAMETRIC FOR THE UPPER AIRWAY OF OSA

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Purpose: In this study, we hypothesized that the Obstructive sleep apnea syndrome (OSA) patients with a narrow upper airway. Therefore, used 3D CT scanning provides a stable and thorough presentation of upper airway morphology, and tried to understand the relation between the geometry of upper airway and OSA.
Methods: Participants were grouped to be normal control and OSA by results of overnight polysomnography (PSG). 3D geometry model of upper airway was generated by segmentation from CT images on NCHC OSAMed platform. The statistical relation of geometry parameters, i.e. the area of the hard palate, minimum cross-section of upper airway and stenosis ratio, with AHI are established via parametric studies and the analysis of receiver operating characteristic (ROC) and the optimal diagnostic cut-off point has been determined.ResultThere are 10 normal subjects (AHI < 5, mean AHI = 0.96?1.56 /hr) as control, and 14 (AHI > 5, mean AHI = 51.55?22.31 /hr) patients with OSA in this study. The minimum cross-section area of upper airway correlated better with the flow changes in severe cases. The stenosis ratio of the upper airway of OSA group is correlated well with the AHI even in all cases (R = 0.767, p < 0.01), but no correlation between area of choana and AHI (R = 0.362, p = 0.08). From the analysis of receiver operating characteristic, the optimal stenosis ratio is 84% (Sensitivity = 0.931, Specificity = 1.0, Accuracy = 0.954, AROC (area under the ROC curve) = 0.947).
Conclusion: The geometry parameter correlations with AHI of upper airway are investigated in this study. Using CT or MRI image scanning with stenosis ratio can be rapidly sieving the patient with or without OSA.

PO-1-102

EVALUATION OF NEUROMUSCULAR ACTIVITY IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA USING CHIN SURFACE ELECTROMYOGRAPHY OF POLYSOMNOGRAPHY

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Objectives: This study was designed to assess the validity of chin surface electromyography of routine polysomnograph in evaluating the neuromuscular activity of obstructive sleep apnea subjects and probe the neuromuscular contribution in the pathogenesis of obstructive sleep apnea.
Methods: This was a randomized cases study in sleep laboratory. The chin surface electromyography of routine Polysomnograph during normal breath and obstructive apnea were quantified in 36 male adult obstructive sleep apnea subjects who have similar cross section area of pharynx at the level of uvular root and upper edge of epiglottis evaluated by computer-assistant fibrolaryngoscope. The chin surface electromyography change from normal breath to obstructive apnea was expressed as percent compensated electromyography value, percent compensated electromyography value = (normal breath surface electromyography-apnea surface electromyography)/ normal breath surface electromyography, and the percent compensated electromyography value between subjects was compared and analysed.
Results: Percent compensated electromyography value of the subjects varied from 1% to 90% and had significant positive correlation with apnea hypopnea index (R2 = 0.382, P = 0.000). Nevertheless, the body mass index and lowest oxygen saturation did not show statistic correlation with percent compensated electromyography value.
Conclusions: Recording and analyzing of chin surface electromyography of routine Polysomnograph is a good way for survey study of neuromuscular activity in obstructive sleep apnea patient population. The neuromuscular contribution is different between subjects in the pathogenesis of obstructive sleep apnea and percent compensated electromyography value can reflect this difference.

PO-1-103

SLEEP-APNEA ANALYSIS WITH A NEW NONINVASIVE PIEZOELECTRIC SENSOR

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Introduction: Fastening belt sensors to their chest/abdomen and setting a flow sensor to nose and many other sensors/electrodes to patients are cumbersome to both the patients and physicians at the preparation for polysomnography (PSG) for monitoring sleep and sleep apnea. Furthermore, the uncomfortable sensor attachment may cause a stress that might affect the quality of sleep and the result of PSG. A new piezoelectric sensor is noninvasive because it neither contacts to their skin nor binds their body but has a comparable performance for cardiorespiratory monitoring to that of PSG, and therefore, it is suitable for sleep-apnea monitoring.
Methods: Ten healthy volunteers and forty-three cardiology inpatients underwent PSG simultaneously with respiratory monitoring by a thin piezoelectric sensor, which was placed under a towel spread on patients' bed. They were diagnosed as having sleep disordered breathing (SDB) when they exhibited apneas more than 10 times in total during cheyne-stokes-like breathings appeared in the respiratory signal. In addition, at most 5 representative episodes of OSA/CSA were collected from each patient to evaluate the accuracy rate in determining OSA and CSA by the observatory analysis of the respiratory signal obtained by the piezoelectric sensor.
Results: By the analysis of apneic events during cheyne-stokes-like breathings, we found SDB in 97% (31/32) of the patients with apnea hypopnea index (AHI, judged by PSG) of >15 and no one in 21 patients (including 10 healthy volunteers) with AHI < 15 (sensitivity 97%, specificity 100%). Selected 107 obstructive and 88 central apnea events in the piezoelectric-sensor signal of 43 patients were verified by PSG analysis; 86 and 89% of them were correct, respectively; 10 and 5% of them were inversely scored; remaining 4 and 7% of them were not accompanied by a decrease in SpO2 (>= 4%).
Conclusion: In the present study, we propose a simple but effective method for the screening of SDB, in which we do observatory analysis of the cheyne-stokes-like breathing signal obtained by a new noninvasive piezoelectric sensor.

PO-1-104 / AS-7 Presenter

EPILEPSY AND DEMENTIA COEXIST FREQUENTLY IN OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: Obstructive sleep apnea syndrome (OSAS) is a disorder associated with frequent awakening and repeated hypoxia during sleep. Therefore, it is reasonable to assume that OSAS potentially causes brain damage so that it might be a risk of brain diseases. However, there is an inevitable difficulty in dealing with the issue because OSAS is one of the common diseases in adults. It means that even if OSAS and a

brain disease coexist, the two diseases do not necessarily have etiological relationship. In this study, we present our patients with adult-onset epilepsy or with dementia who also have OSAS and then try to find a clue to the issue.
Cases: The subjects who met all of the followings were selected in this study: 1) ones who came to our department because of the first-time episode of epilepsy or dementia; 2) the age was over thirty; 3) no apparent causes of epilepsy such as cerebral apoplexy, encephalitis, brain tumor and brain contusion were revealed; 4) presence of sleep related breathing disorders was suggested by interview and PSG was performed.
Results: From Feb 2004 through Feb 2011, 16 patients (14 men and 2 women) met the above conditions. The average age at the onset of epilepsy or dementia was 54.8 ± 15.7 years (30–74). The average apnea-hypopnea index (AHI) was 35.72 ± 15.16/h (10.7–62.2). The median AHI was 32.2/h. The average lowest SpO2 was 81.1 ± 9.5%. 9 patients showed only epilepsy and 2 had only dementia. 5 patients presented both epilepsy and dementia. The average age at the onset of epilepsy and dementia was 53.6 ± 16.5 and 68.4 ± 5.3 years, respectively. 5 of 8 patients aged over 60 have both the diseases.
Conclusions: Epilepsy and dementia coexist frequently in OSAS, especially in aged patients with OSAS. It suggests that OSAS might be a risk factor of brain diseases.

PO-1-105

ACOUSTIC RHINOMETRY IN OSA PATIENTS

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Background: Obstructive sleep apnea syndrome (OSAS) is caused by various factors, and it is still unclear how nasal breathing disorder affects OSAS severity. The aim of this study was to evaluate the relationship between apnea hypopnea index (AHI) and upper airway variables (nasal resistance, minimal cross-sectional area and cavity volume).
Subjects: A retrospective clinical survey was conducted on 334 consecutive adult subjects suspected to have OSAS. All of them underwent polysomnographic diagnosis, acoustic rhinometry (AR), rhinomanometer (RM) and cephalometry (298 males and 36 females; age 44 y, body mass index (BMI) 26.2 kg/m2, AHI 24.1/hr, respectively median).
Methods: Polysomnography (PSG) was performed using Alice4 system (Respironics Murrysville, PA, USA) and AR was performed using SRE2100 (RhinoMetrics; Lynge, Denmark). The following measures were recorded: minimal cross-sectional area (MCA) in centimeters squared between 0 and 1.5 cm (MCA1), between 1.6 cm to 5.4 cm (MCA2) behind the nostril; nasal cavity volume (VOL) in centimeters cubed between 0 and 2 cm (VOL2), between 0 and 4 cm (VOL4), between 0 and 6 cm (VOL6) behind the nostril; nasal resistance. Subjects were divided into 2 groups from the PSG results, i.e., controls and OSAS group. We analyzed the relationships between the two groups in terms of the parameters of PSG, AR, RM and cephalometry by using logistic regression analysis. As for comparison of the above indicated variables, OSAS group was divided into 4 groups by obesity and age (cut off 25 kg/ m2, 50 y respectively).
Results: 1) When comparing the controls (n = 37) and OSAS group (n = 297), there were significant differences in BMI, age and MPH. 2) When comparing the controls (n = 37) and non-obese and younger (n = 71), there was a significant difference in MCA1 (p = 0.032).
Discussion: The difference in MCA1 between the two groups may suggest that nasal breathing disorder influence on OSAS. Therefore nasal therapy should be considered as one of the OSAS therapies.

PO-1-106 / AS-10 Presenter

ORAL FLOW MEASUREMENT FOR ACCURATE RECOGNITION OF RESPIRATORY EVENTS

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Objective: The purpose of this study is to elucidate the usefulness of oral flow (OF) measurement during sleep.
Methods: We conducted a prospective study on Japanese adults. The nasal flow and oral flow were measured separately under polysomnography. The nasal flow was measured with a nasal mask using a pneumothacometer or pressure sensor, and the OF was measured in 2 cm in front of lips using a pressure sensor. Nasal resistance was measured with the anterior method of rhinomanometry in the supine position.
Results: The OFs were basically divided into three patterns, postapneic OF, OF during snoring, spontaneous arousal-induced OF (SpAr-induced OF), and others. The postapneic OF began apnea, hypopnea, and snoring, accompanied by respiratory arousals and postapneic hyperventilation. The OF during snoring refers to OFs occurring during snoring. Many of repeated flow limitations were associated with OF during snoring. SpAr-induced OF began during stable breathing preceded by spontaneous arousals, accompanied by an EMG activation and a reduction of nasal flow, but was not accompanied by apnea/hypopnea. Multivariate regression analyses showed that the determinant that most significantly predicted SpAr-induced OF was nasal obstruction.
Conclusions: Respiratory events such as flow limitation, snoring, hypopnea, or apnea could be scored accurately by introducing oral flow measurement. Clinicians and technologists should be aware of "OFs hidden in respiratory events".

PO-1-107

DETECTION FOR JUDGING METHOD TO MOVE MANDIBLE FORWARD IN THE MIDDLE

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Objective: To detect a judging method moving mandible forward in the middle.
Method: 110 Obstructive Sleep Apnea cases were treated with mandibular advancement aplliances. Moving mandible in the middle was judged by general method that upper and lower midline of incisor area keep the same line before and after advancing and advancing distance of bilateral posterior teeth was equal. The digital film imaging of temporomandibular joint by transcranial projection was taken. Bilateral condyle position at the closing occlusion, maximum open bite position and occlusion with reconstructing occlusal wax wafer in place were compared.
Results: 100 cases had the same medline of incisor area before and after mandibular advancement,the same advancing distance of bilateral posterior teeth in the same cast and of condyle in the digital film imaging of the temporomandibular joint by transcranial projection. Only 10 cases had different advancing distance of condyle in the digital film imaging of temporomandibular joint by transcranial projection.
Conclusion: The same advancing distance of bilateral posterior teeth and permanent midline of incisor area before and after mandibular

advancement could not conclude the advancing distance of bilateral condyle in the digital film imaging of the temporomandibular joint by transcranial projection after mandibular advancement was equal,but it was an important judging proof.

PO-1-108

EFFECTS OF BREATHING ADJUSTMENT ON SLEEPINESS AND SLEEP LATENCY

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Objective: The breathing pattern during sleep stages 1 and 2 is different from that observed in other stages. Ono et al. (2010) reported that the (expiratory):(pause + inspiratory) time ratio was approximately 1:3 during S1 and S2. This study examined whether it would be easier to fall asleep when performing this breathing pattern intentionally.
Methods: Twenty-six university students with a tendency for insomnia participated in the study. They were divided into two groups: experimental (n = 14) and control (n = 12). Sleepiness was measured using the Stanford Sleepiness Scale (Hoddes et al., 1973). Sleep latency was measured using the TMIN-LHI (Miyashita, 1994). Participants in both groups were asked to perform calculation tasks in order to regulate their arousal levels. Participants in the experimental group were then asked to adjust their breathing pattern keeping (expiratory):(pause + inspiratory) at 1:3 for 10 min, while those in the control group continued breathing normally. The second session was conducted using the same procedure in the following week.
Results: SLEEPINESS: A three-way ANOVA of Groups (experimental, control) × Time (before and after intervention) × Sessions (1, 2) was conducted. SSS scores obtained after intervention were higher than those obtained before intervention in both groups (p < .01). In particular, the after intervention scores of the experimental group were higher than that of the control group (p < .01). SLEEP LATENCY: The mean sleep latencies were as follows: before the experiment (M = 42.14), during the experiment (M = 23.86), and during follow-up (M = 26.07). The results of one-way ANOVA and multiple comparison tests indicated that sleep latencies during the experiment and follow-up were shorter than that before the experiment (p < .01).
Discussion: Breathing adjustment elicited a higher level of sleepiness than normal breathing. Sleep latencies during the experiment and follow-up were shorter than that before the experiment. These results suggest that breathing adjustment is an effective procedure for people who have a tendency toward insomnia.

PO-1-109

UTILITY OF PORTABLE DEVICE WITH AIRFLOW,OXYGEN SATURATION AND RESPIRATORY EFFORT IN THE DIAGNOSIS OF SLEEP APNEA HYPOPNEA SYNDROME

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Objective: To validate the usage of monitoring airflow, oxygen saturation and respiratory effort in the diagnosis of sleep apnea hypopnea syndrome(SAHS).
Methods: Seventy subjects suspected with SAHS diagnosis underwent PSG and portable monitoring testing sepatately in the sleep lab. The portable monitoring device records nasal airflow, oxygen saturation and respiratory effort. Apnea hypopnea index(AHI), lowest oxygen saturation($LSaO_2$), oxygen desaturation index(ODI_4) and percentage of different type of sleep breathing events(central, obstructive, mixed and hypopnea) accounting for the total numbers of sleep disordered breathing were also analyzed. Pair t test was used for the comparisons of different parameters, and linear regression was used to describe the corelationship by the two methods. The agreement between the two measures was analyzed using *Bland-Altman* plot.
Results: 58 of the 70 subjects were diagnosed as SAHS with an AHI over 5 by PSG testing. Mean AHI[27.4(24.9) vs 28. 6(26.6), p = 0.205], ODI[22.5(24.9) vs 20.6(24.3), p = 0.199] and $LSaO_2$[78.8(12.6) vs 79.4(11.5), p = 0.550] values derived from PMD and PSG did not show significant differences respectively. *Bland-Altman* plot also showed high agreement between PMD and PSG in regard to AHI, but not to ODI_4 and $LSaO_2$. The PMD device can also identify major part of the different events which may be helpful to clinical decision making.
Conclusion: Portable monitoring device recording airflow, oxygen saturation and respiratory effort shows great agreement with PSG in regard to AHI, and the identification of different types of respiratory events.
Key words: Obstructive sleep apnea hypopnea syndrome; diagnosis; AHI; portable monitoring device

PO-1-110

PSG SPECTRAL ANALYSIS IN OSA PARTICIPANTS FROM A BRAZILIAN POPULATION BASED STUDY: CLINICAL IMPLICATIONS AND NEURAL CONECTIVITY USING PARTIAL DIRECTED COHERENCE

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Obstructive Sleep Apnea Syndrome is a common sleep disorder with neurocognitive impairments. The pathophysiological mechanisms underlying the side effects of OSA are not completely understood and their effects in brain activity are not completely clear. In order to access the dynamic of electroencephalographic (EEG) power bands (delta, theta, alfa1, alfa2, beta1 and beta2) in participants with OSA, we compare them in relation with participants without OSA (control group) inside a population-based study from Sao Paulo(Brazil) called EPISONO. Fast Fourier Transformation was spectral analysis technique choosed and Partial Directed Coherence (PDC) was also calculated to evaluate the brain information connectivity based on Granger Causality.
938 valid full night polissonography (PSG) EEG were analyzed from a total base of 1101 participants of EPISONO study. Patients with OSA (evaluated using PSG criteria) showed higher levels of alpha frequencies during the REM stage (p = 0.003) in C3 and C4 electrodes. Delta frequencies were found during the slow wave (S3-S4) sleep in O1 (p = 0.02)and C4 electrodes (p = 0.03). These findings can be explained by the presence of arousals during these sleep stages. Related to PDC, a smaller correlation between C3-C4 electrodes and O1-O2 electrodes were found only in severe OSA participants in comparison with control group only during the REM stage. This finding presents the lack of

information shared between brain hemispheres during REM probably caused by hypoxia for long periods related with severity of OSA.
EPISONO study is a population based study designed to access the prevalence of several disorders related with sleep and other population aspects. Because of this design we cannot estimate the participants length of time with OSA syndrome. This is the main limitation of our study. Our research should be especially useful to sleep health professionals or professionals interested in analysis of biomedical signals.

PO-1-111

A CASE OF CENTRAL SLEEP APNEA IN CHIARI MALFORMATION TYPE I SYNDROME

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Chiari Malformation (CM) Type I is characterized by cerebellar tonsil herniation through the foramen magnum. Among the CM patients, Central sleep apnea (CSA) is often present but it is rare without other neurologic symptoms. We report on a child with only clinical signs of central sleep apnea who, on imaging, was found to exhibit Chiari type I malformation.
Case presentation: A 10-year-old girl was admitted to our affiliated sleep clinic because of nocturnal sleep apnea and excessive daytime sleepiness. No neurologic abnormality was apparent by physical examination. A polysomnography revealed a severe CSA. The AHI was 41.7 events /hr and the minimal oxygen saturation reached was 84%. Administration of acetazolamide resulted temporary improvement of sleep respiratory disturbance, but the symptom became worsen again by discontinuation of the medication. Magnetic resonance imaging (MRI) revealed a cerebellar tonsillar herniation below the foramen magnum. Neither syringomyelia nor bulbar were noted. These findings were consistent with Chiari type I malformation. She underwent a posterior fossa and superior cervical spine decompression. Initially, her symptoms diminished dramatically after decompression. Physiologic improvement was confirmed by further polysomnographic studies. She remained asymptomatic 12 months after surgery.
Discussion: Recently some researchers described that decompressive surgery in patients with craniovertebral junction malformations resulted in decreased respiratory events during sleep and the effect was more pronounced in patients with central apnea. Craniocervical sagittal section MRI is recommended when central sleep apnea without an obvious cause is discovered in a young patient.

PO-1-112

POLYSOMNOGRAPHIC FINDINGS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA WITH AND WITHOUT EXCESSIVE DAYTIME SLEEPINESS

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Obstructive sleep apnea syndrome (OSAS) is a common disorder in the general population. Excessive daytime sleepiness (EDS) is a frequent symptom of patients with OSA. Obstructive sleep apnea and EDS lead to an increased risk of motor vehicle accidents through multiple pathways. We investigate correlation between EDS with polysomnography(PSG) variables. This is a retrospective study of 126 consecutive patients with OSA who underwent sleep PSG. Subjective sleepiness was assessed using the Epworth Sleepiness Scale. Absence of EDS was defined as having an ESS score of <10. Polysomnographic recordings were compared in patients with and without excessive daytime sleepiness. 71 patients with EDS and 55 patients without EDS were studied. Patients with EDS had lower saturation of oxygen longer total sleep time shorter sleep latency more total Respiratory Disturbance Index and more total limb movement than patients without EDS. EDS and non-EDS patients did not differ in the sleep efficiency sleep stage distribution and number of awakening. Our results suggest that there is correlation between excessive daytime sleepiness and respiratory sleep variables in PSG and desaturation of oxygen at night. Patients with more severe daytime sleepiness are characterized by more severe nocturnal hypoxemia.

PO-1-113

PRESUMPTIVE DIAGNOSIS OF SLEEP APNEA VIA SKYPE, COST-EFFECTIVE ACCESS TO SLEEP MEDICINE PHYSICIAN

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Background: Obstructive sleep apnea (OSA) affects 24% of American adult population and a much higher percentage of Asians. Genetically-determined craniofacial features of Asians make them at risk for OSA. Sleep medicine specialists are predominantly in America and Europe and much less in Asia. It has been postulated that metabolic syndrome and cardio-cerebral-renal diseases so prevalent among Asians are largely due to long standing OSA that remain undiagnosed. The advent of broadband Skype allows patient in Asia to consult with sleep specialist in the U.S.
Method: Three patients from Asia (Singapore 2, Taiwan 1), one patient from Florida initiated remote online consultations with sleep specialist at Chanwell Clinic in Silicon Valley, California. These involved three-part process; first by telephone where history, Epworth Sleepiness Scale (ESS) were taken, then a date and time was set for Skype video examination of the upper airway Mallampati Score (MS), craniofacial features for micrognathia (M), retrognathia (R), mid-facial hypoplasia (FH) and finally onsite physical examinations, cardiac non-invasive studies and polysomnogram (PSG) were done at the Cardiac Sleep Lab.
Result: Singapore 1 (BMI 26, ESS 9, MS 4, M+), Taiwan (BMI 25, ESS 12, MS 4), Florida (BMI 27, ESS 14, M 4, M+, R+, FH+), Singapore 2 (BMI 22, ESS 10, MS 2). Index of OSA suspicion for Singapore 1, Taiwan and Florida were high, PSG confirms unusually severe OSA (Singapore 1 AHI 83, Florida AHI 69) and moderate OSA (Taiwan AHI 17). Singapore 2 was tested with overnight pulse oximeter, PSG was deemed unnecessary since OSA suspicion was low.
Conclusion: The presence of MS 3 or 4, M, R or FH seen in Skype predict the presence and severity of OSA. Sleep Medicine physicians could extend their reach to potential patients all over the world in the presumptive diagnosis of OSA via Skype video examinations and conferencing. Patient could have access to world class sleep medicine specialist through cost-effective adaptation of Skype which is widely present in mobile phones, tablet and desktop computers in homes, schools and the workplace.

PO-1-114

CAN A SMALL CHANGE IN OXIMETER AVERAGING TIME AFFECT THE RESPIRATORY DISTURBANCE INDEX?

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Introduction: AASM 2007 guidelines recommend that polysomnography (PSG) procedures use oximeters with averaging time (aT) of 3 seconds or less. This is to ensure rapid changes in SpO2 associated with respiratory events are detected. Recent studies have shown conflicting results, some proving no significant difference in Respiratory Disturbance Index (RDI) when investigating averaging times between 2 to 6 seconds. We hypothesize that the same oximeter, set on 2 different aT values (3 and 4 seconds) will generate RDIs that are significantly different.
Method: 39 patients undergoing full PSG were simultaneously monitored with 2 Masimo oximeters, Alice 5 in-built Masimo SET and Masimo Radical 7. The same oximeter algorithm is used (Masimo SET) and finger probes were placed on the same hand. One oximeter was set to an aT of 3 seconds (Alice 5 in-built Masimo). The Radical 7 was set to 4 seconds aT. RDI was calculated twice using one oximeter signal at a time. Same scorer analyzed both set of oximetry data. Analysis of data using the 2nd oximeter signal was conducted a month later after data was blindly renamed and assigned to the same scorer. The AASM criteria for PSG data analysis were used and the AASM alternative hypopnea definition was adopted. Paired t-test was used to calculate how significantly different the two methods means of RDIs.
Results: There is a significant difference in RDI generated from oximeters set with 2 different averaging times ($p < .001$). In the 39 simultaneously recordings of SpO2, the mean RDI was lower using the 4sec aT oximeter (RDI_aT3secs = 31.29 ± 29.32 versus RDI_aT4secs = 28.63 ± 28.95, $p =< .001$). The Mean difference was 2.67 (95% IC 1.45 to 3.88). There is a high correlation of 0.992 between the two methods.
Conclusion: There is a significant difference in RDI values calculated from same oximeter set to 2 different averaging times of 3 and 4 seconds. Thus, when interpreting RDI values, one should note the averaging time used in the acquiring of the SpO2 signal. A difference of 1 second in averaging time can significantly alter an RDI value of the same patient.

PO-1-115

POSITIVE EFFECT OF NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE ON CEREBRAL PERFUSION IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Objectives: To investigate the cerebral perfusion changes after nasal continuous positive airway pressure (CPAP) in patients with obstructive sleep apnea (OSA),
Methods: we enrolled 30 patients with severe OSA (apnea-hypopnea index 30/hr). 99 mTc-ethyl cysteinate dimer (99 mTc-ECD) brain single-photon emission computed tomography (SPECT) scans were performed before and after usage of nasal CPAP for more than 6 months. in.
Results: After long-term -CPAP usage, cerebral blood flow increased in the left fusiform gyrus, right inferior parietal lobule, bilateral inferior frontal gyrus, and middle frontal gyrus. Regional CBF of left superior temporal gyrus and right insula was negatively correlated with Epworth sleepiness scale. Positive correlation was found between rCBF in the right superior frontal gyrus, bilateral cingulate gyri, right parahippocampal gyrus, and left precentral gyrus and mean duration of the CPAP usage a day and between rCBF in the right parahippocampal gyrus and right superior frontal gyrus and the mean frequency of CPAP usage per week.
Conclusions: These findings suggested that increased rCBF and positive correlation of rCBF changes in prefrontal cortices and temporal area after long-term CPAP treatment may explain positive effect of CPAP on OSA and cognitive improvement by CPAP.
Key words: OSA, SPECT, cerebral blood flow, continuous positive airway pressure.

PO-1-116

WHAT SHORT-TERM ADHERENCE OF CPAP THERAPY SHOULD BE USED TO DETERMINE ITS EFFECTIVENESS ON MORTALITY IN PATIENTS WITH OBSTRUCTIVE/CENTRAL SLEEP APNEA (OSA/CSA)?

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Background: The long term adherence of CPAP in patients with OSA/CSA has significantly lowered the mortality rate.The minimal length of adherence to CPAP in determining mortality among OSA patients is unclear.
Methods and Results: We retrospectively examined the causes of deaths in 4,056 patients with OSA or CSA in a long-term study of 13 years follow-up from December 1990 to December 2003 based on ONSLEEP registry database that features 4,056 patients(OSA 4,000 and CSA 56), male 3,259(80.3%), age 51.2 ± 13.3 years, BMI 27.9 ± 4.7 kg/m^2, AHI 39.7 ± 32.7 events/h. And we compared the CPAP users, non-users in relation to the duration of CPAP use and mortality within one year. The number of deaths 144 (121 male and 23 female). The major causes of deaths were cardiovascular events including cardiac disorders, sudden death and stroke,34.7%. The number of CPAP users were 2,298, 73 died (mortality rate 3.2%, 6.9 /1000 persons/year) in 13 years; and 39 (39/73 = 53%) within one year; 31 within half a year (31/39 = 79.5%). The CPAP non-users were 1,758, 71 died (mortality rate 4.0%, 10.4/1000 persons/year) in 13 years, and 15 patients (15/71 = 21%) within one year. Patients' characteristics on gender, age, BMI, AHI between the two cohorts, only AHI is statistically significant for users and non-users, with 60 and 66.4 events/h, respectively. Major causes of deaths within one year among the CPAP users were 15 cardiovascular events, 5 COPD, 4 infections, 10 unknown; and in the non-users,7 cardiovascular events, 2 infections, 3 unknown. In the Kaplan-Meier survival analysis, significant difference was not found between the CPAP users and non-users at one year. The CPAP users compared with non-users, early deaths due to pulmonary disorders were more prevalent and might result in compromising the effectiveness of CPAP.
Conclusion: CPAP should be used at least longer than one year to evaluate the effectiveness on mortality. The preexisting co-morbidities would be the confounding factors to early mortality among OSA/CSA patients.

PO-1-117

IMPROVEMENT IN NEUROCOGNITIVE FUNCTION IN COMPLIANT CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) USERS

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Introduction: Daytime sleepiness and neurocognitive dysfunction are common symptoms of obstructive sleep apnea (OSA). It is unclear whether CPAP fully reverses the neurocognitive dysfunction associated with untreated OSA. We explored the effects of 6 months CPAP therapy on neurocognitive function in compliant users.
Methods: In this prospective trial, OSA patients performed a computerised, neurocognitive test battery at baseline and after 6 months of compliant CPAP therapy (>6 hrs use per night). The test battery assessed sensori-motor function, attention, working memory, executive function and motivation. Performance at baseline and after CPAP therapy were assessed, and compared to a normative dataset of performance variables previously collected from healthy controls.
Results: Performance data from 202 OSA patients (age 49.2 ± 12.6, range 20–70 yrs; body mass index (BMI) 33.5 ± 8.0; Epworth sleepiness scale (ESS) 12 ± 5) and 60 controls (age 32.3 ± 12.6, range 19–76 yrs; BMI 25.5 ± 4.3, ESS 4 ± 2) were analysed. At baseline, the OSA group demonstrated impaired performance compared to controls in Stroop Colour ($p =< 0.001$), Stroop Text ($p =< 0.02$), Letter Cancellation Task (LCT) hits ($p =< 0.001$) and commissions ($p =< 0.05$), n-back ($p =< 0.001$) and Psychomotor Vigilance Task reaction time ($p =< 0.001$). In the OSA group, compliant CPAP users at 6 months (n = 49) showed improved performance in Stroop Colour ($p =< 0.001$), LCT hits ($p =< 0.02$) and n-back ($p =< 0.017$) compared to baseline. Despite these improvements over time, performance in this group of compliant CPAP users remained impaired when compared to controls in Stroop Text ($p =< 0.01$), n-back ($p =< 0.01$) and LCT hits ($p =< 0.001$) and commissions ($p =< 0.03$).
Discussion: Improvements in executive function at 6 months in compliant CPAP users implies that some degree of specific neurocognitive function may be regained with continued usage. The test battery effectively identified the neurocognitive dysfunction associated with OSA and subsequent improvement of some cognitive domains with adherent CPAP therapy.

PO-1-118

ONE NIGHT CPAP WITHDRAWAL IMPAIRS PERFORMANCE AT A DRIVING SIMULATOR TASK FASTER THAN SLEEP RESTRICTION TO 5 HOURS WITH TREATMENT IN OSA PATIENTS

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Introduction: Sleep restriction and missing 1 night's continuous positive air pressure (CPAP) treatment are scenarios faced by obstructive sleep apnoea (OSA) patients, who must then assess their own fitness to drive. This study aims to assess the impact of this on driving performance.
Method: 11 CPAP treated participants (50–75 yrs), drove an interactive car simulator under monotonous motorway conditions for 2 hours on 3 afternoons, following;(i)normal night's sleep (average 8.2 h) with CPAP (ii) sleep restriction (5 h), with CPAP (iii)normal length of sleep, without CPAP. Driving incidents were noted if the car came out of the designated driving lane. EEG was recorded continually and KSS reported every 200 seconds.
Results: Driving incidents: Incidents were more prevalent following CPAP withdrawal during hour 1, demonstrating a significant condition time interaction [$F(6,60) = 3.40$, $p = 0.006$]. KSS: At the start of driving participants felt sleepiest following CPAP withdrawal, by the end of the task KSS levels were similar following CPAP withdrawal and sleep restriction, demonstrating a significant condition, time interaction [$F(3.94,39.41) = 3.39$, $p = 0.018$]. EEG: There was a non significant trend for combined alpha and theta activity to be highest throughout the drive following CPAP withdrawal.
Discussion: CPAP withdrawal impairs driving simulator performance sooner than restricting sleep to 5 h with CPAP. Participants had insight into this increased sleepiness reflected by the higher KSS reported following CPAP withdrawal. In the practical terms of driving any one incident could be fatal. The earlier impairment reported here demonstrates the potential danger of missing CPAP treatment and highlights the benefit of CPAP treatment even when sleep time is short.

PO-1-119 / AS-9 Presenter

CARDIOMETABOLIC AND NEUROBEHAVIOURAL CHANGES AFTER CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) TREATMENT FOR OSA: A 12-WEEK RANDOMISED SHAM-CONTROLLED STUDY.

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Introduction: Visceral abdominal adiposity (VAA), insulin resistance (IR) and OSA often co-exist. However the role of OSA in impaired metabolic health is poorly understood because there are no randomised trials of the effect of CPAP on VAA and the data on CPAP and IR are inconsistent. The aim of this study was to assess the effect of CPAP on important intermediate markers of cardio-metabolic health and neurobehavioural function in men with OSA without type II diabetes (DM).
Methods: Sixty-five men with moderate to severe OSA (mean ± SD, age = 49 ± 12 y, apnea hypopnea index (AHI) = 39.9 ± 17.7 events/h, body mass index = 31.3 ± 5.2 kg/m^2, ESS = 10 ± 4.4), who were CPAP naive, without DM, were randomised in a 12-week double blind sham-controlled parallel group study, to receive either active (n = 34) or sham (n = 31) CPAP. The primary outcome was VAA change (CT scan) from baseline to week 12. Secondary outcomes were IR and disposition index (minimal model), liver fat, total fat and lean muscle (DEXA), arterial stiffness, objective and subjective sleepiness (modified MWT and ESS), and driving ability (AusEd).
Results: CPAP, compared to placebo, significantly decreased AHI by 33 events/h (mean difference −33.0 events/h; 95%CI, −43.9 to −22.2, $p < 0.0001$) There were no between group differences in the change in VAA (−13.0 cm^3 −42.4 to 16.2, $p = 0.37$) or IR (−0.13 [min^{-1}][ƒÊU/mL])$^{-1}$;

–0.40 to 0.14, p = 0.33) after 12 weeks. Objective and subjective sleepiness improved in both groups (both $p < 0.05$). The changes in all other secondary outcomes were not significantly different between groups. There were no correlations between the change in VAA or IR with CPAP use, OSA severity, BMI or sleepiness.
Conclusion: Twelve weeks of therapeutic CPAP did not significantly improve VAA or IR in men with moderate to severe OSA without DM.

PO-1-120 / AS-19 Presenter

THE EFFECT OF CONTINUOUS POSITIVE AIRWAY PRESSURE USAGE ON SYMPTOMS OF OBSTRUCTIVE SLEEP APNEA: REAL EFFECTS OR EXPECTATION OF BENEFIT?

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Background: Poor compliance with medical treatments is a major limitation to healthcare effectiveness. Continuous Positive Airway Pressure (CPAP) is the standard treatment for Obstructive Sleep Apnea (OSA) with the level of pressure individually titrated for each patient. As such, the effective dose of treatment is a function of the amount of time patients use the device. We explored whether symptom improvement associated with high device usage may be related to a placebo-like expectation of benefit using data from two placebo-controlled crossover trials.
Methods: Patient-level meta-analysis of two trials using two sleepiness-related symptom questionnaires (ESS, Epworth Sleepinss Score and FOSQ, Functional Outcomes of Sleepiness Questionaire). Mixed model analysis of variance was used to quantify the effects of real vs. placebo-device treatment, compliance, interaction of treatment and compliance and regression to the mean.
Results: Compliance between real and placebo-device treatment was closely related ($r = 0.74$, $p < 0.001$). High compliance with either real or placebo CPAP was associated with greater improvement in sleepiness (mean = 2.2 points; 95%CI = 1.0–3.3, $p < 0.001$) and functioning (mean = 1.1 points, 0.5–1.7, $p < 0.01$). High use of real CPAP (4+ hrs/night) reduced ESS to a greater degree than high use of placebo. In the FOSQ the same trend was evident but not statistically significant. The association between symptomatic benefit and hours of use of CPAP may not be linear as improvements beyond 6 hours of use were not discernable.
Conclusions: As expected, higher hours of real CPAP use resulted in greater improvements in symptoms. However, some of this effect was also seen in higher users of placebo CPAP. Compliance with real and placebo therapy was highly correlated, so this effect may arise from expectations of benefit or from other unidentified patient-specific factors.

PO-1-121 / AS-26 Presenter

A COMPARATIVE EFFECTIVENESS TRIAL OF CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) VERSUS ORAL APPLIANCE (OA) THERAPY IN OBSTRUCTIVE SLEEP APNEA (OSA)

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Objectives: To compare the effects of OSA treatment with CPAP and OA therapies on cardiovascular and neurobehavioural health outcomes.
Methods: In this randomised crossover trial, we compared the effect of 1-month treatment with CPAP versus mandibular advancement splint (MAS) therapy on blood pressure (24-hr and central), sleepiness (ESS), simulated driving performance (AusEd) and quality of life (FOSQ and SF36) in 108 patients with OSA (AHI >= 10). Patients were first titrated and acclimatised to both devices (~6 weeks each) before commencing treatment on each device for 1 month. 2-week washouts occurred after acclimatisation and between treatments and the order of each was randomised.
Results: Patients were middle aged (49 ± 11 yrs) and overweight (BMI 29.5 kg/m^2) and most were male (n = 102/126). Mean AHI was 25.4 ± 12.5/hr and 82% had moderate or severe OSA (AHI > 15/hr). Clinic BP was 123 ± 14/80.6 ± 9 mmHg with 38% on BP medication. Patients did not report excessive sleepiness (ESS 9.1 ± 4.2) however quality of life scores (FOSQ and SF36) were below normal. The AHI fell to 4.5 ± 0.7/hr on CPAP and 11.1 ± 1.2/hr on MAS (both $p < 0.05$ vs baseline and $p < 0.05$ CPAP vs MAS). In contrast, self reported compliance on MAS was higher (CPAP 5.2 ± 2 hrs, MAS 6.5 ± 1.3 hrs, $p < 0.0001$) and more than twice as many patients preferred MAS to CPAP (44 vs 20%). Overall, 24 hr BP variables were not reduced by CPAP or MAS however in hypertensive patients BP did fall, albeit by a similar amount (~2–4 mmHg) on both treatments. ESS improved by 1.6 ± 0.3 on CPAP and 1.9 ± 0.3 on MAS and FOSQ by 1 ± 0.2 on both CPAP and MAS, (all $p < 0.001$ versus baseline). Similarly, most SF36 domains improved on both treatments however in 4 domains they were greater on MAS than CPAP. There were also improvements in aspects of driving performance with both treatments.
Conclusions: This randomised trial showed that treatment of moderate-severe OSA with either CPAP or MAS has similar effects on health outcomes. The results are most likely explained by a greater efficacy with CPAP being offset by a greater compliance with MAS. Patient preference favoured MAS.

PO-1-122

LONG-TERM COMPLIANCE OF CPAP IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Background: Although nasal positive airway pressure therapy (CPAP) is the most widely accepted and effective therapy available for the treatment of obstructive sleep apnea syndrome (OSA), short-term and long-term compliance was not so longer than expected.
Methods: We enrolled consecutively 1260 OSA patients who were recommended to use the nasal CPAP in the outpatient clinic of Samsung Medical Center from Jan. 2005 to Dec. 2010. After the instruction of CPAP, 935 patients (74.2%) had agreed to use CPAP, but 325 patients (25.8%) declined it. We investigated the overall compliance of nasal CPAP use and discomfort from CPAP and compared the clinical characteristics between patients with CPAP maintenance and those with CPAP discontinuance.
Results: Among 935 patients, 53.4% (n = 500) had continued CPAP use (<2 yrs, n = 240; 2–3 yrs, n = 133; 4–5 yrs, n = 3) and 46.5% (n = 435) discontinued it. Seventy-three% (n = 319) had stopped the CPAP within 1 month and 25.2% (n = 110) were within 6 months. In patients with CPAP maintenance, 48.5% of patients had used CPAP > 90% of nights and 62% slept with CPAP > 6 hrs of nocturnal sleep time. Patients with CPAP maintenance showed significantly higher AHI (47.3/hr vs. 25.5/hr) and larger BMI (27.3 vs. 24.1 kg/m^2) than patients with CPAP discontinuance ($p < 0.05$). Most common discomfort from CPAP use was the mask-fitting problem (45.1%).
Conclusions: Over 70% of patients stopped the CPAP use within 1 month and the main problem was mask-fitting. When patients continued to CPAP use more than 6 months, they appeared to maintain the CPAP for a long-time than expected. Severe OSA and overweight seems to be the important factors to maintain the CPAP in the OSA patients.

PO-1-123 / AS-19 Presenter

THE ROLE OF SOCIAL COGNITIVE THEORY (SCT) IN CPAP ADHERENCE: DATA FROM TWO RANDOMISED CONTROLLED STUDIES

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Background: Social cognitive theory (SCT) relates to how humans make choices. Previous data has shown how it may underpin CPAP adherence.
Methods: The first study (S1) was an RCT of 206 males and females (age range: 22–80) with OSA (mean AHI = 35 ± 26.5) who were randomised to receive either cognitive behaviour therapy (n = 109) or social reciprocity (afternoon tea) (n = 97) to improve CPAP adherence over a 26 week period. The second study (S2) included 65 men with OSA (age = 49 ± 12 y, AHI = 39.9 ± 17.7) who were randomly assigned to receive either therapeutic (n = 34) or sham (n = 31) CPAP therapy for 12 weeks. SCT (self-efficacy, outcome expectation, social support) was measured in both studies before and after treatment. CPAP adherence was recorded as average nightly use.
Results: SI found CPAP use increased by 1.5 hours (95%CI 1.03–1.96, $r = 0.41$, $p < 0.00001$) for every 1 unit increase in the self-efficacy scale at baseline. No component of SCT changed with either intervention. S2 found that for every 1 unit increase in baseline self-efficacy, CPAP adherence improved by 0.78 hours, however this was not significant ($p = 0.12$). Change in self-efficacy was positively correlated with adherence ($r^2 = 0.55$, $p < 0.0001$). In S2, outcome expectation significantly worsened with sham compared to therapeutic CPAP after 12 weeks (mean diff 1.0; 95%CI 0.38–1.62, $p = 0.0023$). No other group differences were found.
Conclusions: Self-efficacy predicted CPAP use in both studies. In S2, those individuals who reported the greatest fall in self-efficacy scores were more likely to be non-users. The experience of sham CPAP resulted in reduced outcome expectation. Previous successful underlying experiences are likely to be driving adherence regardless of educational intervention or treatment modality.

PO-1-124

TRANSVENOUS PHRENIC NERVE STIMULATION IMPROVES CHEYNE-STOKES RESPIRATION IN PATIENTS WITH CHRONIC HEART FAILURE

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Background: Cheyne-Stokes respiration (CSR) may accelerate progression of congestive heart failure (CHF) and is associated with poor survival. Phrenic nerve stimulation (PNS) may interrupt CSR and improve CHF outcomes. We report the first clinical use of transvenous PNS in CHF patients with central sleep apnea and CSR.
Methods: Twenty-three CHF patients with central sleep apnea and CSR were enrolled. A single stimulation lead was placed at the junction between the superior vena cava and brachiocephalic vein or in the left pericardiophrenic vein. PNS stimulation was performed using the Eupnea System software (Cardiac Concepts Inc., Minnetonka, MN). Respiratory properties were assessed prior to and post-PNS. PNS was assessed at a maximum of 10 mA.
Results: No adverse events were seen under maximum normal stimulation parameters for a maximum single 12 hour sleep cycle. Phrenic nerve stimulation was able to reproducibly slow the rate of breathing in a predictable manner and raise end-tidal expiratory CO_2. When PNS was applied following a series of central sleep apneic events, a trend towards stabilization of breathing and heart rate, as well as improvement in oxygen saturation, was seen. There was a significant improvement in indices of apnea/hypopnea, central apnea, oxygen saturation and sleep efficiency after PNS versus pre-PNS (all $P < 0.01$).
Conclusion: Unilateral transvenous PNS proved to be a safe and feasible treatment and by effectively improving CSR, it will be a promising treatment for CHF patient with CSR.

PO-1-125

EFFECT OF CPAP THERAPY ON NEUROPSYCHOLOGICAL FUNCTIONS FOR PATIENTS WITH SLEEP APNEA SYNDROME

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Over 20 years, numerous studies have assessed a wide range of cognitive deficits associated with obstructive sleep apnea syndrome (OSAS). With functional magnetic resonance imaging (fMRI), a few report said that the deficits persist after CPAP therapy. We should run back over Neuropsychological functions, referring the outcome of fMRI of OSAS. Neuropsychological functions in 26 patients with OSAS were evaluated before and at least 6 month after continuous CPAP therapy. Neuropsychological examinations using 3 batteries Kana pick out test (KPT), Trail making test (TMT), and, Miyake's retention Test (MRT) were performed. The patients included 24 men and 2 women with a mean AHI 45.7 SD21.4 (range 20 to 114), mean age 54.3 SD14 (range, 30 to 74 years). After 6 month CPAP therapy, CPAP titlation was performed (mean AHI 4.5 SD 2.98).
KPT and MRT for irrelevance for words of meaning represented significant difference between before CPAP therapy and after one were found. No significantly differences on TMT and KPT for relevance for words of meaning among them.
The KPT is a popular test of attention in Japan. This task requires parallel processing of reading and picking Kana (Japanese syllabogram), and demands an appropriate allocation of attentional resources to the two activities. The KPT is a suitable test of working memory and executive function. TMT is thought to be two part neuropsychological test, in which visuospatial ability and executive function are evaluated, and to reflect frontal area function. MRT is neuropsychological test of short term memory test regarding to relevance or irrelevance for words of meaning.
These results suggested that the neuropsychological outcomes after CPAP therapy were effective not only for attention ability but also for short time memory.

PO-1-126

HOURS OF NIGHTLY NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE USE IS ASSOCIATED WITH WEIGHT CHANGE IN PATIENTS WITH OSAHS

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Obesity is one of the strongest risk factors for obstructive sleep apnea-hypopnea syndrome (OSAHS). People of Asian origin, such as the Japanese, are likely to develop OSAHS even with mild degrees of obesity, suggesting that, in addition to obesity, cranio-facial morphology is also an important contributor for the development of OSAHS. Nasal continuous positive airway pressure (nCPAP) is known to alleviate sleep-related disturbances and may reduce the risk of hypertension and cardiovascular disease. A number of previous studies have shown that habitual sleep duration may be an important determinant of body weight with short sleep duration being an independent risk factor for obesity. Using an electronic database of number of hours of nightly CPAP use, we estimated the habitual sleep time of patients during nCPAP and examined its relationship to association with changes in body weight. In obese patients with OSAHS, percent weight gain over 9 years displayed a U-shaped relationship with the minimal weight gain in patients with 5 to 6 hours of habitual sleep. In contrast, weight gain was the largest in patients with sleep time of less than 4 hours per night or more than 8 hours per night. These results suggest that changes in body weight in patients with OSAHS are associated more with habitual sleep time.

PO-1-127 / AS-19 PRESENTER

MASK DESENSITIZATION IMPROVES NASAL PAP COMPLIANCE IN NON-ADHERENT PATIENTS WITH SLEEP APNEA

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Background: 31 patients, M : F 12:19, ages 46 to 99, with obstructive sleep apnea (OSA), who were either positive airway pressure (PAP) non-adherent (PAPNA) or PAP intolerant (PAPI), underwent a nasal mask desensitization program (NMD) to increase patient compliance with PAP therapy. Untreated OSA drives the progression of cardio cerebral-renal diseases (CCR) and leads to a 300% increased risk of stroke, myocardial infarction, and sudden cardiac death, as well as a 700% increased risk of auto accidents. The implications on morbidity, mortality and healthcare costs are considerable.
Method: NMD includes 2–5 weekly/biweekly visits to the PAP Clinic; sleep technicians (RPSGTs) encourage patients to achieve consistent PAP usage. PAP usage, mask leak, & apnea hypopnea index (AHI) data were analyzed. Interviews were conducted to address treatment compliance concerns. After RPSGTs optimize mask fit, air pressure, humidity, and device cleanliness, patients undergo 30-minutes of NMD, a nap in the lab with the new treatment adjustments.
Results: PAP adherence (PAPA) is defined as = or >4 hours usage per night, at least 70% of the time. 65% of patients (20/31) achieved PAPA. 52% of patients (16/31) already achieved PAPA by their second NMD visit. 67% maintained PAPA even 3 months after NMD, and patients who relapsed were recalled for a second round of NMD.
Conclusion: Achieving PAPA is one of the major challenges of effective treatment of OSA. Our NMD program improved PAPA in a majority of PAPNA/PAPI patients. Treating OSA prevents cardio-cerebral-renal deterioration, improves quality of life, and reduces health care costs. We recommend sleep medicine physicians continue PAP Clinic every three months to monitor compliance and implement NMD if patients fall below PAPA.

PO-1-128 / AS-26 Presenter

WITHDRAWN

PO-1-129

INSOMNIA AMONG SLEEP APNEA PATIENTS BEFORE AND AFTER TREATMENT WITH CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP)

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Background: Insomnia and obstructive sleep apnea (OSA) are both common problems with high co-morbidity. However, the nature of their relationship is unclear. The aim of this study was to assess insomnia prevalence among OSA patients before starting treatment with continuous positive airway pressure (CPAP) and at a two year follow up.
Material and methods: Altogether 824 untreated OSA patients underwent a medical examination and answered questionnaires on health and sleep at baseline and follow up. This is an ongoing study and to date 650 patients have finished the follow up.
Results: When untreated, the majority of OSA patients (57.6%) reported difficulties maintaining sleep (DMS). OSA patients with DMS were older, sleepier during the day, more obese and reported poorer mental and physical health compared to other OSA patients. Furthermore, 15% of untreated OSA patients reported difficulties initiating sleep (DIS) and 28% reported early morning awakening (EMA). At the two year follow up, complaints of DMS were reported among 43.9% of non CPAP users, 40.6% of partial users and 25.1% of full CPAP users ($p < 0.0001$). Complaints of DIS were reported among 15.2% of non CPAP users, 11.9% of partial users and 7% of full CPAP users ($p < 0.0001$). Complaints of EMA were reported among 27.8% of non CPAP users, 26.3% of partial users and 16.3% of full CPAP users ($p = 0.01$). Complaints of DIS and EMA were negatively associated with CPAP compliance.
Conclusion: The prevalence of insomnia, especially DMS, is high among untreated OSA patients but these symptoms improve with successful CPAP treatment. OSA patients with symptoms of DIS and EMA might benefit from additional treatment for insomnia in order to improve CPAP compliance.

PO-1-130

TRANSIENT INCREASE IN INTERICTAL SPIKES AFTER INTRODUCTION OF NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE FOR OBSTRUCTIVE SLEEP APNEA AND EPILEPSY

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Introduction: In patients with epilepsy and obstructive sleep apnea (OSA), seizure frequency and interictal epileptiform discharges usually decrease after introduction of nasal continuous positive airway pressure (nCPAP). However, we reported 1 patient showing transient increase in interictal spikes immediately following nCPAP treatment.
Case report: An Eighteen-year-old obese woman started to have complex partial seizures at the age of 13. Her seizures sometimes evolved into generalized. Her seizures were well controlled by Carbamazepine (CBZ) and she was seizure free for the last 2 years. She felt excessive daytime sleepiness and had witnessed loud snoring and was referred to our clinic. She underwent polysomnography (PSG), which showed severe OSA with apnea and hypopnea index (AHI) of 59.5 and generalized spike and wave complex (GSWC) (33 times per night). She was introduced nCPAP 2 weeks later, and PSG on nCPAP showed normalized AHI of less than 5. However, GSWC increased to almost 4 times as many as those of previous study (142 times per night). Follow-up PSG was taken again following 4 months of nCPAP treatment and GSWC frequency went back to her baseline level (36 times per night). She was seizure free for 1 year after nCPAP introduction. The dosage of CBZ was almost same and its serum concentration was also quite consistent.
Discussion: We reported one case showing transient increase in interictal spikes after nCPAP introduction. New onset seizure after nCPAP introduction was also reported in previous study. These findings suggested that acute drastic defragmentation in sleep architecture in OSA by nCPAP could sometimes increase epileptiform discharges, even if the change itself improved the sleep quality. Acute change in arterial blood gas by acute release of airway collapse may also contribute the increase in epileptiform discharges. We should be cautious about the increase in epileptiform discharge or new appearance of seizure immediately after nCPAP introduction.

PO-1-131

EARLY EFFECTS OF CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) IN A RODENT MODEL OF ALLERGIC RHINITIS

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Background: Continuous positive airway pressure (CPAP) is the most used treatment in obstructive sleep apnea. In a previous study, we demonstrated that nasal CPAP induces an early local inflammation which results in neutrophil extravasation in the nasal mucosa of a rat model. The impact of nasal CPAP on a previously inflamade nasal mucosa may be even greater.
Objectives: To evaluate the early nasal CPAP effects in a rat model of allergic rhinitis (AR).

Study design: Twenty Sprague-Dawley rats were sensitized with intraperiotoneal ovoalbumina (OVA). Nasal inflammation was induced by the administration of OVA intranasal drops during consecutive days. The same procedure was performed in 20 control rats treated with saline solution. Then, the allergic and non allergic rats were randomized to nasal CPAP at 10 cm H_2O pressure for 5 hours or to sham CPAP. Degree of nasal inflammation was assessed by directly evaluating the percentage of neutrophils, eosinophils, basophils and lymphocytes in the nasal mucosa. Un-paired Mann Withney test was used to analyse differences between groups.
Results: The highest inflammation (percentage of neutrophils) was observed in the group of AR without CPAP (1.24 ± 0.94%), followed by non allergic (NA) with CPAP (0.64 ± 0.30), AR with CPAP (0.64 ± 0.40), and NA without CPAP (0.21 ± 0.29).
Conclusions: Acute administration of nasal CPAP or allergy sensitization can produce, individually, neutrophil extravasation on the nasal mucosa of a rat model. The application of a second source stimulus (nasal CPAP on a previously allergic mucosa) is not responsible of an increased inflammation.

PO-1-132

WEB-BASED FOLLOW-UP OF CPAP COMPLIANCE IN OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: Despite its fast penetration in many fields, the application of information and communication technologies in the clinical practice is still very limited, especially in respiratory medicine. The availability of tools such as the Internet has grown rapidly and, although the web-based information is easily accessible on various aspects of health, it is rarely considered as an option for management of the Obstructive Sleep Apnea Syndrome (OSAS).
Objective: To develop and to assess the feasibility of a web-based follow-up of continuous positive pressure airway pressure (CPAP) therapy in patients with OSAS.
Methods: A personal easy-structured web site was created for this study and each patient was given access to his/her own data exclusively. By visiting the web site, patients could answer to a weekly questionnaire about symptoms, sleep quality, potential CPAP side effects, physical activity and body weight, having the patient access to continuously updated temporal trends in graphical format. Moreover, informative documents about OSAS and CPAP therapy were available to free download.
Results: On a total of 163 consecutive patients of the Sleep Clinic, 66 reported minimum knowledge of the Internet and agreed to participate. After 12 weeks of monitoring, the participation rate was high (82%). In addition, patients responded to a satisfaction survey through the website itself, showing a level of agreement to the statement "Overall I am satisfied with the web service" of 4.3 ± 0.58 points (1 = I strongly disagree, 5 = I strongly agree) and their potential interest in participating in a long-term web-based monitoring.
Conclusions: The results of this pilot study show the potential usefulness of the Internet as a tool to support home monitoring of CPAP treatment in OSAS. Other options, such as videoconference calls, should be necessary to be integrated in this web tool in the near future.

PO-1-133

TREATMENT EFFECT OF CONTINUOUS POSITIVE AIRWAY PRESSURE ON ATTENTION IN UNTREATED PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Background & Objectives: To evaluate the changes of attention before and after therapeutic continuous positive airway pressure (CPAP), we measured the P300 and Continuous Performance Tests (CPT) in OSA patients before and after CPAP treatment.
Method: Auditory & visual P300 studies and CPT were performed in 47 patients with (45 males, mean age 42.3 years) with OSA (mean apnea-hypopea index, 53.7 per hr) and 35 healthy control (22 males, mean age 40.6 years). The diagnosis of OSA was based on standard criteria using nocturnal polysomnography. OSA patients had repeated auditory and visual P300 studies after 6 months of therapeutic CPAP.
Result: The auditory P300 was significantly prolonged mean latency and decreased mean amplitude at fronto-centro-parietal areas in OSA patients compared to those of normal controls (p less than 0.05). The visual P300 was significantly prolonged mean latency and non-significantly decreased mean amplitude at fronto-centro-parietal areas in OSA patients. In all three steps of CPT, mean correction rate was non-significantly lower in OSA patients than that in control group. After CPAP treatment, the auditory P300 latency was shortened at all electrodes although it did not reach statistical significance. The visual P300 latency, amplitudes of auditory and visual P300 was not changed by therapeutic CPAP for 6 months.
Conclusion: Our findings in ERP and CPT may support that untreated OSA patients had significantly impaired attention deficits. Successful CPAP treatment induced a shorter latency of auditory P300 but not in visual P300 latency, amplitudes of auditory and visual P300.

PO-1-134

AN AUDIT OF CPAP TITRATION STUDIES PERFORMED IN A SINGAPORE TEACHING HOSPITAL SLEEP LABORATORY

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Introduction: With the advent of autotitrating PAP (APAP) machines. There has been a general reduction in the number of CPAP titration studies worldwide. An audit was done to determine the numbers and various characteristics of patients undergoing titration studies in our laboratory.
Methods: A retrospective case review was done on patients who underwent CPAP titration studies between January and December 2010.
Results: There were 36 patients in total of which there were 24 males and 12 females. Of these 20(55.6%) were Chinese, 12(33.3%) Malay, and 3(8.33%) of Indian ethnicity and 1 other. The mean age of the cohort was 52.6 ± 15.1 years. Their mean BMI was 36.9 ± 9.3 kg/m^2. The mean ESS score was 10.7. Their mean RDI pre-treatment was 52.1 ± 30.0 compared to the mean post-titration RDI which was 12.2 ± 17.9 ($p < 0.05$). The mean titrated CPAP pressure was 11.1 ± 3.3 cmH_2O. Twenty two patients (61.1%) were adherent to CPAP at the last clinic visit. TYhe majority (72.2%) had either hypertension, hyperlipidaemia or diabetes mellitus.
Conclusions: The number of CPAP titration studies that were performed is small. There may be more than one reason for this. The

patients who underwent these studies were predominantly male, middle aged, obese, had severe OSA and were borderline hypersomnolent. The mean CPAP pressure that was determined for the group was not high. The mean post-titration RDI's while significantly improved were however not within normal limits.

PO-1-135

THE DEGREE OF SLEEP DISTURBED BREATHING AFFECTS THE CARDIAC SUPPORTING EFFECTS OF BI-LEVEL POSITIVE AIRWAY PRESSURE VENTILATION IN PATIENTS WITH HEART FAILURE

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Introduction: Noninvasive positive airway pressure ventilation including adaptive servo ventilation has been widely used in the treatment of patients with congestive heart failure (CHF) in both acute and chronic phase. Major concern in this treatment is possible deterioration of cardiac function by PAP itself. We, therefore, conducted a study about the effects of bi-level PAP to cardiac function and its relation to degree of sleep disturbed breathing (SDB).
Methods: In 10 stable CHF patients, apnea-hypoxia index (AHI) is obtained by portable polysomnography (ASA2100, Nihon Kohden, Japan). We performed fixed level of positive airway pressure (CPAP) (PEEP 4 cmH_2O) followed by bi-level PAP (EPAP/IPAP 4/9 cmH_2O) for five minutes each while continuously monitoring intra-cardiac pressures and cardiac index (CI) using Swan-Ganz catheter.
Results: AHI was 26.5 ± 19.9/hr. CPAP tended to decrease CI, but Bi-level PAP has no significant change compared with control (control 1.93 ± 0.53 L/min/m^2, CPAP 1.76 ± 0.39 L/min/m^2, Bi-level PAP 1.93 ± 0.46 L/min/m^2). The difference of CI after application of CPAP or Bi-level PAP ($f.\geqslant CI = CI_{Bi\text{-}levelPAP}\text{-}CI_{CPAP}$) showed significant inverse linear relationship against AHI ($f.\geqslant CI = -0.007+0.348\ R^2 = 0.64$). When the patients are divided into two groups (milder SDB with AHI < 30/hr and more severe SDB with AHI >= 30/hr), the $f.\geqslant CI$ in the former patients is significantly larger than the latter patients 0.29 ± 0.13 vs 0.03 ± 0.08 L/min/m^2, p = 0.008).
Conclusion: Our result showed that bi-level ventilation was more effective than CPAP in the patients with milder SDB and this implies that there may be several different mechanisms in the favorable effect of positive airway ventilation in the treatment of heart failure patients.

PO-1-136

CONTINUOUS POSITIVE AIRWAY PRESSURE EFFECT ON ADIPOSE TISSUE IN OBSTRUCTIVE SLEEP APNEA

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Objectives: To investigate the effect of Continuous Positive Airway Pressure (CPAP) treatment on regional adipose tissue distribution in patients with moderate or severe range OSA.
Methods: We compared the 2 months of therapeutic and sham CPAP (in random order) on abdominal subcutaneous, visceral and liver fat, liver enzymes and plasma glucose. Magnetic resonance imaging (MRI) and spectroscopy (MRS) were used to quantify abdominal and liver fat respectively using validated techniques. Measurements were obtained at baseline and at the end of both treatment arms. Statistical analysis was performed using paired t-tests or Wilcoxon signed rank tests.
Results: 38 eligible patients were randomly assigned to a treatment order with 27 patients having complete MRI/MRS data. No significant difference was observed in subcutaneous (SCAT) and visceral adipose tissue (VAT), liver fat and serial glucose measurements between treatment modalities. Alkaline phosphatase (ALP) decreased while on therapeutic CPAP but other liver enzymes (AST, ALT, Gamma GT) remained unchanged.
Conclusions: In this randomized placebo controlled trial, there was no change in adipose tissue distribution after 8 weeks of therapeutic CPAP compared with 8 weeks of sham CPAP. Longer treatment duration may be necessary for VAT, SCAT and liver fat reduction in patients with OSA.

PO-1-137

THE RESULTS OF TWO-PIECE PALATOPHARYNGOPLASTY (TWO-P4: MODIFIED UVULOPALATOPHARYNGOPLASTY) FOR SEVERE OSAS

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Two-piece palatopharyngoplasty (Two-P4) for OSAS is a new surgery modified uvulopalatopharyngoplasty (UPPP). Two-P4 makes two separated scars on both sides of soft palate and reserving middle soft tissue intact. These scars pull the reserved middle soft palate to each side and pharyngeal space becomes wide and deep after several weeks. We guess that middle soft palate including uvula becomes buffer zone against separated scars.
Fifty-two patients of OSAS received Two-P4 during 2002 and 2010. Forty-four patients out of 52 patients underwent polysomnography before and after surgery. We recruited 35 patients with severe OSAS (AHI > 30) who received polysomnography before and after surgery. The age ranged from 17 to 74, average 40.5 ± 12.1 years old, including 34 men and 1 woman. Their average BMI is 28.0 ± 4.3 kg/m^2 and 27.6 ± 4.1 kg/m^2 three months after surgery.
The average AHI of the 35 patients decreased from 62.3 ± 22.0 to 18, 2 ± 20.1 after surgery. The total success rate is 77.1% (27/35) by 50% AHI decrement and AHI under 20 after surgery. Epworth Sleepiness Scale (ESS) score improved 12.2 ± 5.0 to 7.2 ± 3.8. According to the Friedman's anatomical stage, the success rate of the 16 patients with stage 1 was 93.8%, 16 patients with stage 2 was 75%, 7 patients with stage 3 was 57.1%. None of 35 cases complaint permanent soft palate insufficiency, or stenosis of the nasopharynx.
Classical UPPP makes single line scar, which makes pharyngeal space narrow. Two-P4 makes two separated scars, and two scars makes pharynx wide. Another important point is the indication of the surgery. Friedman's anatomical stage 1 is most suitable for the soft palate surgery. But even with the stage 3, the success rate of Two-P4 is 57.1%. Two-P4 is a successful surgical procedure for severe OSAS (AHI > 30), which could establish high success rate (77.1%).

PO-1-138

EFFECTS OF ORTHOGNATHIC SURGERY ON AIRWAY AND SLEEP DISORDERED BREATHING

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Background: In 1985, Guilleminault reported a case of Sleep Disordered Breathing (SDB) that developed after orthognathic surgery. However, orthognathic surgery has been widely accepted as one of the options for treating SDB. Thus, respiratory status after orthognathic surgery is controversial. This study investigated the effects of orthognathic surgery on SDB.
Method: Seventeen patients with jaw deformity, who underwent two-jaw surgery (Le Fort I osteotomy and sagittal split ramus osteotomy; SSRO) in our hospital, were enrolled. Seven patients underwent mandibular setback surgeries and five of these patients underwent two-jaw surgery; the other ten patients underwent mandibular setforward surgeries and eight of these patients underwent two-jaw surgery. Using polysomnography (Alice 5; Respironics; Murrysville, PA), Apnea Hypopnea index (AHI), 3% oxygen drop index (ODI), and arousal index were measured. Then 3D images of the airway were reconstructed from CT data using Mimics Version 13.1. The upper and lower boundaries were defined as the level of the hard plate and the base of the epiglottis, respectively. From the 3D reconstruction models, the following volumes of the airway were measured: the volume of the upper airway (total volume), the volume between the level of the hard palate and the tip of the uvula (volume of HP-TU), and the volume between the tip of uvula and the base of the epiglottis (the volume of TP-BE).
Result: Mean AHIs were 2.94/hr and 1.07/hr before and after surgery, respectively ($P < 0.01$). Total volumes were 10.4 cm^3 and 15.6 cm^3 before and after surgery, respectively ($P < 0.01$). Especially, the volume of HP-TU was significantly increased after surgery ($P < 0.035$).
Discussion: It was suggested that mandibular setforward surgeries increase the airway space and improve SDB. However, mandibular setback surgeries did not significantly change respiratory status.

PO-1-139

EFFECT OF NASAL SURGERY ON JAPANESE OSA PATIENTS

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Back ground: Japanese OSA have multifactor and we have to evaluate and select treatment methods case by case. We considered that nasal respiratory function is as one of the factors related to sleep quality.
Objective: To compare a severity of OSA and sleep structure pre and post nasal surgery.
Subjects and methods: Retrospectively, we enrolled 30 OSA patients who received nasal surgery. And compare PSG parameter pre and post operatively. In 7 case out of 30, we rescored including CAP (cyclic alternating pattern) parameters as sleep stabilization.
Results:
1. Success rate of nasal surgery is 11.1% (50% reduction & AHI < 20).
2. There were no statistical difference with AHI between preope and postope state. (43.2 vs 36.5 $p = 0.057$).
3. Some parameter such as sleep efficiency, oxygen saturation improved, but almost parameter did not change.
4. In 7 case, no parameter improve but CAP rate after surgery.

Conclusion: It is difficult to improve OSA severity with nasal surgery alone. But nasal surgery is useful for OSA patients because of improvement of sleep stabilization.

PO-1-140

THE EFFECT OF TONSILLECTOMY OR ADENOTONSILLECTOMY ON QUALITY OF LIFE IN PEDIATRIC SLEEP-DISORDERED BREATHING PATIENTS

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It is well known that the general population of children with Sleep-disordered breathing (SDB) shows dramatic improvements in the physiological parameters of sleep after those surgeries. However, there are few report related to the evaluation of the changes of the quality of life for children with SDB after tonsillectomy or adenotonsillectomy in Japan.
We evaluated the effect of tonsillectomy or adenotonsillectomy on quality of life (QOL) in 24 pediatric SDB patients (age range, 3 to 12 years; median age, 4.6 years) with the translated version of OSA-18, an 18-item QOL survey. Twenty three children who underwent tonsillectomy or adenotonsillectomy showed improvement in physiological parameters of sleep and quality of life after those surgeries. One child with worsened physiological parameters of sleep after surgery due to re-enlargement of adenoid did not show enough improvement in quality of life after surgery. Even in Japan, the OSA-18 can be useful for the evaluation of the effect of surgical treatment on QOL in SDB children.

PO-1-141

ROLE OF THE DENTISTRY AND ORAL-MAXILLOFACIAL SURGERY IN MANAGEMENT OF PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME BY A PANEL OF DOCTORS

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Patients with obstructive sleep apnea syndrome (OSAS) are generally referred to dentistry or oral-maxillofacial (OMF) surgeons by their physicians. Treatment options include the use of corrective oral appliances (OA) or maxillomandibular advancement (MMA) in some cases; however the treatment decision is made by physicians and not by dentists. Given this fact, Tokyo Medical University Hospital has set up a panel of doctors with expertise in relevant fields (circulatory internal medicine, otorhinolaryngology, OMF surgery), who function as a team

to collectively examine OSAS patients. This panel, which has been evaluating 1148 OSAS patients since November 2004, then reaches a consensus on an optimal treatment plan. In the present study, we evaluated the efficacy of such team-mediated management by retrospective examination of the patients clinical records. The following treatment regiments were employed by the different specialists : continuous positive airway pressure (CPAP) by internists, uvulopalatopharyngoplasty (UPPP) by ENT doctors, and OA and MMA by DOMF surgeons. Some patients received combined treatments (CPAP/OA, OA/CPAP, CPAP or OA/MMA) and others were followed up without any of the above therapies. The average apnea-hypopnea indices (AHI; times/h) of patients (total number) before treatment were 50.1 for CPAP (n = 760), 40.2 for UPPP (19), 19.7 for OA (245), 32.6 for MMA (5), 35.1 for CPAP/OA (5), 24.7 for OA/CPAP (1), 51.9 for CPAP or OA/MMA (2), and 15.8 for follow-up only (111). Post-operative, mean AHI scores were 7.9 for OA and 9.8 for MMA, a remarkable improvement. These findings suggest that the treatment of OSAS by OMF surgeons as a team with internists and ENT doctors provides much better efficacy and more efficient management for the affected patients.

PO-1-142

PERIOPERATIVE MANAGEMENT IN THE SURGICAL TREATMENT OF OSAS IN OUR HOSPITAL

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It is known that nasal respiration disorders at night affect sleep disordered breathing. In our hospital, the patients of obstructive sleep apnea syndrome (OSAS) are treated at both cardiovascular internal medicine and otorhinolaryngology. When the patients in OSAS complained night-time nasal obstruct, night-time mouth-breathing or night-time dry mouse, more treated with operation. Operation has a lot of risks, which are OSAS, obesity, general anesthesia, airway edema, bleeding and oral breathing makes high risk in the perioperative management of OSAS. Otorhinolaryngologists have difficulty with these management. So, this is the case of the nasal surgical treatment of OSA by otorhinolaryngologist in our hospital, so that nCPAP failures with night-time nasal obstruct could restart nCPAP because of nasal cavity reform by operation. They have had deviation and allergic rhinitis and hypertrophic rhinitis. At the last of operation, we would insert the hand-made nasal airway (18Fr Nelaton catheter) through the bilateral common nasal meatus, and hand-made nasal packs at nasal cavity by and pressing on the several surgical point. After operation, the patient would enter the ICU by Anesthesiologist and use the biPAP by airway control one day. The patient of of the nasal surgical treatment of OSA could spent a perioperative period on lower lisks.

PO-1-143

GLYCATED HEMOGLOBIN IMPROVEMENT BY ORAL APPLIANCE THERAPY IN OBSTRUCTIVE SLEEP APNEA SYNDROME PATIENTS WITH DIABETES MELLITUS

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Aim: It has been indicated that obstructive sleep apnea syndrome (OSAS) is independently associated with glucose intolerance and insulin resistance. The effects of treatment with CPAP on glycemic control has remained controversial. The aim of this study was to evaluate the influence of oral appliance (OA) therapy on glycated hemoglobin (HbA1c) of OSAS patients with diabetes mellitus.
Methods: Ninety-eight diabetes mellitus patients (mean age: 54.3 years) diagnosed with OSAS (mean AHI: 18.5) were studied before and after the insertion of an OA with an average interval of 90 days. The patients were randomly assigned to periodontal treatment and control groups. Patients in the periodontal treatment group were divided into three groups (normal, mild and moderate, and severe) according to the severity of periodontal disease.
Results: AHI showed a significant ($p < 0.01$) fall to 5.3 in all patients. HbA1c reduced significantly ($p < 0.01$) from 6.9 to 6.5%. Both the periodontal treatment (n = 50) and control (n = 48) groups showed a significant reduction of HbA1c. The severe periodontal (n = 22) showed a significant reduction in HbA1c. Otherwise, normal (n = 10) and mild and moderate (n = 18) groups showed no significant reduction. Insulin sensitivity is influenced by chronic inflammation in periodontal disease. Most OSAS patients breathe through their mouth during sleep. An OA can prevent the drying of patients' oral cavities due to nocturnal mouth breathing. This could result in the amelioration of periodontal disease and inflammation, and, consequently, a significant reduction of HbA1c.
Conclusion: This data suggest that dental treatment such as OA therapy and periodontal treatment for OSAS patients with diabetes mellitus can lead to a substantial reduction in HbA1c.

PO-1-144

DENTAL AND SKELETAL CHANGES AFTER LONG-TIME ORAL THERAPY OF OBSTRUCTIVE SLEEP APNEA

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Objective: Oral appliances (OA) have been established as an alternative treatment option for obstructive sleep apnea and hypopnea syndrome (OSAHS). Although the short-term therapeutic effect of OA has been proven through various studies, there are very few follow-up examinations concerning long-term dental or skeletal side effects caused by the appliances.
Methods: 25 OSAHS patients had been treated with OA for a mean duration of 5 years. Their cephalometric films before and after 5 years wearing were used to investigate the dental, skeletal and airway changes. 13 OSAHS patients also kept the dental study models, which were used to investigate the dental side effects.
Results: After 5 years wearing, retroclination of the maxillary incisors (3.3 degree) and proclination of the mandibular incisors (1.8 degree)

could be found, accompanied by reductions in overbite (1.4 mm) and overjet (1.1 mm). The MP-FH, MP-SN angles increased 1.3 degree, and the face height increased 2.5 mm. The distance between the hyoid and FH plane increased 2.3 mm. In the three-dimensional (3D) dental study, the arch width between each pair of upper molars increased by 1.24+1.83 mm and 0.33+0.53 mm, respectively, while for lower first molars it increased by 0.78+0.823 mm. The upper incisors were over-erupted about 0.3 mm while the upper molars were depressed about 0.3 mm.

Conclusions: Long-term OA use can cause dental and skeletal changes. But most of the changes were too minor to imperil the security of OA therapy.

PO-1-145

TREATMENT OF OBSTRUCTIVE SLEEP APNEA AND HYPOPNEA SYNDROME WITH ORAL APPLIANCE : LONG-TERM FOLLOW-UP

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Objective: To investigate the long-term efficacy of oral appliance treating of obstructive sleep apnea and hypopnea syndrome in long-term treatment.

Methods: A total of 55 patients were included in the study. They were divided into four groups by the period of treatment, including control group, 1–2 years group, 2–6 years group and 6–9 years group. The polysomnographic study was used to investigate the efficacy of four groups.

Results: The apnea-hypopnea index (AHI) decreased significantly in all groups. The control group decreased from 24.50(14.65, 54.05) to 7.40(2.12, 10.00) events per hour ($p < 0.001$), The 1~2 years group decreased from 19.50(12.15, 39.23) to 1.80(0.70, 6.58) events per hour ($p = 0.001$), The 2–6 years group decreased from 25.00(11.41, 42.60) to 4.50(1.35, 7.90) events per hour ($p = 0.001$), The 6–9 years group decreased from 26.2(16.95, 47.45) to 4.00(1.90, 26.70) events per hour ($p = 0.043$). There was no significant difference between the four groups. The longest apnea decreased significantly in control group, 1–2 years group and 2–6 years group. The lowest SaO2 increased significantly in control group and 2–6 years group.

Conclusions: The oral appliance is an effective therapy for patients with OSAHS in long-term treatment. However, it's recommend to make appointments with patients as a follow-up supervision if there is any efficacy decrease.

PO-1-146

COMPARISON BETWEEN MONOBLOCK AND DUALBLOCK TYPE OA (SOMNODENT MAS) FOR THE SAME OSA PATIENTS

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Introduction: There are 2 main non-invasive treatments for OSA patients, CPAP and OAT (Oral Appliance Therapy). To this point in time OAT has been indicated for mild to moderate cases. However OAT usage expands to those severe patients who cannot tolerate, are not appropriate for, or do not continue to use CPAP, or use OA whilst travelling. Combined CPAP and OAT is another emerging option.

Efficient and simple structured Monoblock type OA are widely used in Japan given the Governmental insurance coverage which began in April, 2004. However, Monoblock type OA take more time and are complicated to re-titrate, adjust and also prevent jaw movement, limiting patient adherence.

The principle and preferred treatment choice for OAT is Dualblock type OA both in Europe and North America due to comfort, ease of titration and optimized patient adherence.

We made an investigation as a comparison between the Monoblock type OA and the Dualblock type OA (SomnoDent MAS) which is now used by over 70,000 patients (2010. December).

Aim: Efficacy Comparison between Monoblock type OA and the Dualblock type OA (SomnoDent MAS).

Object: Patient selection was based on OSA patients who are treated with OAT and agreed to participate in the research.

Method: The patients first used Monoblock type OA and subsequently used the Dualblock type OA (SomnoDent MAS). An Alice5 PSG and LS-100 were used to compare results. We conducted a survey by questionnaire to compare comfort.

Result: Objective results were almost equivalent, however Dualblock type OA (SomnoDent MAS) compliance was significantly superior. Mouth opening in Dualblock type OA (SomnoDent MAS) was shown to have no effect.

PO-1-147

OPTIMAL CPAP PRESSURE AS A PREDICTOR OF ORAL APPLIANCE TREATMENT OUTCOME IN OSA

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CPAP is the standard treatment for OSA however oral appliances (OA) are an alternative treatment often preferred by patients. This simpler and more portable treatment may be a viable replacement or temporary treatment solution for some patients. However not all patients will experience equal efficacy with OA compared to CPAP. It has been proposed that CPAP pressure may predict OA treatment response, with patients with higher CPAP pressure requirements likely to fail OA treatment.

Methods: Optimal CPAP pressure, based on 95th percentile pressure on autoset CPAP, was compared between OA treatment responders (>50% AHI reduction) and non-responders (<50% AHI reduction) in participants in a randomised cross-over trial comparing both treatments. Logistic regression analyses were used to assess if CPAP pressure was useful as a predictor of OA treatment outcome.

Results: OA treatment responders (N = 79) compared to non-responders (N = 24) were younger (47.6 ± 11.3 vs. 55.4 ± 10.3 years, $p = 0.003$), with smaller neck circumference (40.4 ± 7.3 vs. 42.1 ± 2.8 cm, $p = 0.003$) and lower BMI (28.9 ± 5.6 vs. 31.1 ± 5.3 kg/m^2, $p = 0.059$). However baseline AHI did not differ between groups. There was a trend for OA responders to have a lower CPAP pressure requirement than

non-responders (10.3 ± 1.9, range 4–18 cmH_2O vs. 11.2 ± 2.3, range 7–17, p = 0.057). Logistic regression showed that the addition of CPAP pressure as a predictor variable slightly enhanced prediction of OA treatment outcome (OR 0.79, 0.63–1.00 95%CI, p = 0.05). Area under the ROC curve was 0.63. A CPAP pressure threshold of 11.5 cmH_2O yielded 89.9% sensitivity and 41.7% specificity in classifying patients.
Conclusions: Although there was a trend for OA treatment non-responders to require higher CPAP pressures, this alone was not adequate to reliably predict OA treatment outcome in this patient population.

PO-1-148

DIFFERENCES BETWEEN A RIGID ORAL APPLIANCE AND A SEMI-RIGID APPLIANCE FOR THE TREATMENT OF OBSTRUCTIVE SLEEP APNEA SYNDROME

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Background: Over seventy types of oral appliances for the treatment of obstructive sleep apnea syndrome have been reported. Among these appliances, a rigid oral appliance (rigid OA) or a semi-rigid appliance (Silensor) are mainly used in clinical settings. However, the mechanisms underlying the effectiveness of these oral appliances remain unclear. This study investigated the efficacy and mechanism of a rigid OA and a silensor for the treatment for OSAS.
Materials and Methods: Fourteen patients, 12 males and 2 females, with OSAS, were enrolled. Six patients were treated with a rigid OA, and eight patients were treated with a silensor. The average age and body mass index were 58.2 years (49~68 years) and 25.6 kg/m^2 (23.0~30.7 kg/m^2) in the rigid OA group, 54.5 years (36~62 years) and 23.5 kg/m^2 (20.6~27.2 kg/m^2) in the silensor group, respectively. Polysomnography and CT examination were performed twice in each patient: at the initial consultation and after improvement of subjective symptoms. Using CT analyzing computer software (Mimics Version 13.1), 3D images of the airway were reconstructed. The upper and lower boundaries were defined at the level of the hard palate and the base of the epiglottis, respectively. Using these reconstructed 3D models, the airway parameters were measured. These data were analyzed statistically using Wilcoxon singed-rank test.
Results: The apnea-hypopnea index (AHI) significantly improved from 23.4/hr to 8.1/hr in the rigid OA group ($p < 0.05$) and from 20.3/hr to 9.7/hr in the silensor group ($p < 0.01$). CT images, demonstrated that the area of the tongue base and the area posterior to the PNS were increased in the rigid OA group and in the silencer group, respectively.
Conclusions: It was suggested that both the rigid OA appliance and the silensor appliance improved respiratory status, but that there were differences in the positions of the airway affected by these two appliances.

PO-1-149

MULTIPLE ASSESSMENTS IMPROVE PREDICTION OF ORAL APPLIANCE TREATMENT OUTCOME IN OSA: POTENTIAL IMPORTANCE OF PATIENT PHENOTYPING

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Oral appliances (OA) can effectively treat OSA however not all patients respond to treatment. The ability to pre-identify such patients using simple clinical assessments is highly desirable. Spirometry, nasal resistance and cephalometry have individually shown some initial predictive utility but not on prospective validation. We hypothesise that single assessments are inadequate due to the complex upper airway response to OA and inter-individual differences in mechanisms of response. Combining results from structural and functional tests into a single prediction model may provide more accuracy.
Methods: 29 OSA patients underwent 3 assessments before using an OA. Prediction models to classify patients as responders (AHI reduction > 50%) or non-responders (AHI reduction < 50%) were developed using logistic regression and classification and regression tree (CART) analyses. Key measures from each test, SNA angle (cephalometry), nasal resistance and MEF50/MIF50 ratio (spirometry), were used singly or combined as independent predictors.
Results: Logistic regression showed each test variable individually had some predictive value (area under ROC curve [AUC] 0.7). Combing variables further enhanced prediction (AUC 0.81–0.88). However the best model incorporated variables from each of the 3 assessments (AUC 0.94). A CART analysis model allowing patients to be classified based on all 3 results performed substantially better than those with only single variables.
Conclusion: Prediction of OA treatment outcome improved when predictor variables from different assessments were incorporated into the prediction model. Multiple assessments that phenotype different aspects of patient upper airway function and craniofacial structure may be needed to accurately predict OA treatment outcome.

PO-1-150

A MANDIBULAR ADVANCEMENT APPLIANCE THERAPY FOR A CASE WITH COMORBIDITY OF SLEEP BRUXISM AND MILD OBSTRUCTIVE SLEEP APNEA

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Introduction: Previous studies reported that respiratory sleep disorders were observed concomitantly with sleep bruxism (SB). However, there is little reliable evidence in efficiency of a mandibular advancement appliance (MAA) for patients with comorbidity of SB and obstructive

sleep apnea (OSA). We experienced a case with these two disorders who wore a MAA and showed improvement in quality of sleep.
Methods: A 52-year-old office worker was referred by his family dentist to our department due to frequent stomatitis. He wore a dental soft splint for the maxilla because sleep bruxism was suspected as a cause of the frequent stomatitis, and many deficits were detected in the splint in only a few days. He also complained daytime sleepiness and his Epworth Sleepiness Scale (ESS) was 11 out of a maximum of 24. His past medical history was unremarkable during the past 3 years. His body mass index (BMI) is 21.3. A MAA was fixedly set to advance the mandible 3 mm.
Results: Before the MAA therapy, the diagnostic polysomnography (PSG) recording showed that the patient suffered from mild OSA and SB (AHI, 10.5/hr; bruxism episodes per hour: bruxism index, 5.1/hr; lowest SpO_2, 88.6%; arousal index, 16.5/hr; snoring index, 144/hr; periodic leg movement index, 3/hr; sleep efficiency, 62.8%; stage 1 NREM sleep, 41.4%; stage 2 NREM sleep, 29.0%; slow wave sleep, 0%; REM sleep, 29.6%). Most of the bruxism events were accompanied by arousing events and leg movements. Six months after the start of MAA therapy, his daytime sleepiness and frequency of snores were subjectively reduced and ESS decreased to 6. The frequent stomatitis also disappeared.
Discussion: These results suggest the possibility that a MAA therapy improve quality of sleep for patients with comorbidity of SB and OSA.

PO-1-151

EFFECTS OF THE SILENSOR TREATMENT FOR THE OBSTRUCTIVE SLEEP APNEA SYNDROME CASES

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Background: Although a mandibular repositioning device (MRD) in treating obstructive sleep apnea (OSAS) is very effective, this device may generate side effects such as temporomandibular joint disorder and deviation of occlusion. A semi-rigid silensor (Erkodent Gmbh, Tuttlingen, Germany) has been reported with a low frequency of side effects in the previous report. The purpose of this study is to determine whether the silensor is effective or not in treatment of OSAS.
Materials and Methods: Thirty-five patients (27 males and 8 females) with OSAS, who were treated with the silensor, were enrolled. The average age and body mass index (BMI) were 52.2 years (23~72 years) and 24.5 kg/m^2 (19.3~31.6 kg/m^2), respectively. These patients were classified into two groups based on the length of the connector of the apparatus; 0–2 mm and 3–4 mm. A polysomnography test was performed in two times; at first visit and often improvement of subjective symptoms. These datas were analyzed statistically using a Wilcoxon singed-rank test.
Results: The apnea-hypopnea index (AHI) improvement significantly in all OSAS patients, mild to moderate OSAS patients, severe OSAS patients, 0 to 2 mm group patients, 3 to 4 mm group patients (91.4 %: $p < 0.01$, 88.9%: $p < 0.01$, 100%: $p < 0.05$, 86.4%: $p < 0.01$, 100%: $p < 0.01$, respectively). The side effects of silensor consisted only of broken the apparatus and damaged to buccal mucosa.
Conclusions: The silensor was useful in treatment of the patients with OSAS. Especially, silencer was suitable for first phase of treatment with oral appliances for OSAS, because the effect of silensor was equal to that of another oral appliance, and had few side effects.

PO-1-152

INCREASED SEXUAL DESIRE WITH TESTOSTERONE ADMINISTRATION IN MEN WITH OBSTRUCTIVE SLEEP APNEA: AN 18-WEEK RANDOMIZED DOUBLE-BLIND PLACEBO CONTROLLED STUDY

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Background: Sexual dysfunction, biochemical testosterone (T) deficiency, obesity and OSA coexist. Large studies show that half of all men with OSA have erectile dysfunction, and that sexual dysfunction is common. Nevertheless, sexual dysfunction often remains undiagnosed due to patient or doctor embarrassment despite the existence of therapies which are effective in other contexts. Here we comprehensively assess the impact of T administration on sexual desire, erectile function and general and disease specific quality of life and cognitive function in obese men with OSA.
Methods: 67 middle aged (age 49 ± 1.1, mean ± SEM), obese (BMI 35.8 ± 0.57) men with moderate-severe OSA (AHI 31.8 ± 2.4) received 3 intramuscular injections of 1000 mg T undecanoate or placebo at 6 weekly intervals. SF36, FOSQ, sexual function by visual analogue scales and computerised cognitive testing were assessed at 0, 6, 12 and 18 weeks. Polysomnography (PSG) occurred at 0, 7 and 18 weeks.
Results: T administration, compared with placebo, significantly increased blood T and suppressed gonadotrophins ($P < 0.001$). T increased sexual desire by 16% (mean difference between groups, 5.4–26.8% 95%CI, $p = 0.004$), but did not alter erectile or orgasmic function, quality of life (FOSQ, SF-36), reaction time (PVT), spatial cognition (Tower of London) or executive memory (Stroop), irrespective of baseline T. T therapy increased vitality ($p = 0.004$), 'feeling down' ($p = 0.002$), and orgasmic ability ($p = 0.016$) and reduced nervousness ($p = 0.032$), but only in those with low baseline T. These effects did not correlate with any changes in AHI or ODI.
Conclusions: 18 weeks of T therapy improves sexual desire in obese men with OSA, and improves orgasmic function only in those with low baseline T. T therapy variably controls different facets of sexual function. However, the decision to use T therapy to improve sexual function in obese men with OSA requires consideration of both risks and benefits.

PO-1-153

SLEEP DISORDERED BREATHING AND LONG-ACTING HYPNOTIC USE AFFECT DAYTIME PHYSICAL ACTIVITY AMONG INPATIENTS WITH SCHIZOPHRENIA

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Objective: This study evaluated factors influencing daytime activity among inpatients with schizophrenia.
Method: This study enrolled 546 inpatients with schizophrenia (300 men and 246 women, mean age 57.6 years old). Activity among

participants was assessed by 3-axis accelerometer with pulse oximeter for 24-hours. Mean activity per hour on lighting-up time at each hospital ward was analyzed as daytime activity index. After simple regression analyses, multiple linear regression was performed to explore determinants of daytime activity index.
Results: 3% oxygen desaturation index, dose of long-acting hypnotics (half-life period above 24 hours) and age had significant statistical negative correlation with daytime activity index in simple regression model. 3%ODI, dose of long-acting hypnotics, age and biologically plausible predictors (sex, body mass index) were included in the original multiple linear regression model. The final linear regression model included 3%ODI ($p < 0.001$), long-acting hypnotics ($p < 0.001$), sex ($p = 0.045$), age ($p = 0.006$) ($R^2 = 0.08$, $F = 11.6$, ANOVA $p < 0.001$).
Conclusion: In this study, sleep disordered breathing and long-acting hypnotics use were risk factors for reduction of daytime activity among inpatients with schizophrenia. Screening for sleep disordered breathing is necessary to identify with negative symptom. Furthermore, attention to activity change among patients using long-acting hypnotics might be needed.

PO-1-154 / AS-26 PRESENTER

EFFECTIVENESS OF A NASAL AIRWAY STENT ON OBSTRUCTIVE SLEEP APNEA

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We report promising preliminary findings regarding the clinical effectiveness of a novel nasal airway stent (NAS) that was developed for the treatment of obstructive sleep apnea (OSA). The device is constructed using resilient semi-rigid silicone rubber and was designed to be safely and comfortably inserted into the upper airway. The NAS contains an expandable distal end, located within the nasopharynx and retropalatal oropharinx, that is encapsulated by a nontoxic water-soluble material. Following device placement, the distal end of the device is released and expands to maintain an air flow passageway of 5–10 mm in diameter. Effectiveness of the NAS on sleep disordered breathing was assessed by polysomnographic studies before and during placement of the device in five patients with OSA. The NAS did not normalize the disordered breathing, but significantly improved the apnea hypopnea index (from 31.9 ± 22.6 to 16.2 ± 15.7), 3% oxygen desaturation index (from 30.3 ± 27.4 to 13.5 ± 14.6) and arousal index (from 28.4 ± 18.3 to 17.5 ± 10.8). None of the patients experienced traumatic side effects such as nasal bleeding, pain, or discomfort following placement of the device. The NAS appears to be a useful alternative or additive treatment for patients with OSA. The device may be used as an immediate therapeutic tool while a patient undertakes a weight loss program or as an alternative for patients who cannot tolerate a nasal continuous positive airway pressure treatment. The NAS affects obstruction of nasopharynx and partly oropharynx but not of hypopharynx, therefore the combination of the NAS and an oral appliance may provide additional benefits. Further studies are necessary to confirm our preliminary results.

PO-1-155

THE EFFECTS OF TESTOSTERONE ON VENTILATORY RESPONSES IN MEN WITH OBSTRUCTIVE SLEEP APNOEA – A RANDOMISED, PLACEBO CONTROLLED TRIAL

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Introduction: We recently presented in abstract form that testosterone (T) worsens sleep disordered breathing at 7 but not after 18 weeks in men with OSA. Whether these effects are mediated by changes in ventilatory responses (VR) is not known. To our knowledge the effect of T on VR in men with significant OSA has not been studied before.
Methods: 21 obese men with OSA were randomised in a 18 week double-blind placebo controlled parallel group study to 3 intramuscular injections (0, 6, 12 weeks) of either 1000 mg T undecanoate or placebo (mean body mass index (BMI) = 37.7 ± 0.9 kg/m^2, apnea hypopnea index (AHI) = 32.6 ± 2.2 events/hr). VR testing was performed using Duffin's modified rebreathing method before (week 0), during (week 6), and at the end of treatment (week 18) in hyperoxic (pO_2 150 mmHg) and hypoxic (pO_2 50 mmHg) conditions to determine the ventilatory recruitment threshold (VRT) and chemosensitivity (CS), alongside overnight polysomnography. Data were analysed by mixed models and are described as overall mean differences between groups (95%CI).
Results: A significant increase in blood T levels (5.65 nmol/L, 0.51 to 10.8, $p = 0.03$), and lean muscle mass (2.36 kg, 0.8 to 3.9, $p = 0.007$) between the two groups was observed. There were no significant differences following T treatment overall at 6 weeks or at 18 weeks in: hyperoxic VRT (1.39 mmHg, −3.16 to 5.93), hyperoxic CS (−0.22 L/min/mmHg, −1.11 to 0.67), hypoxic VRT (0.9 mmHg, −5.16 to 6.96) or hypoxic CS (−0.73 L/min/mmHg, −3.2 to 1.74); all $p > 0.05$. Positive correlations were found at week 6, but not week 18, between changes in: blood T levels and hyperoxic VRT ($r = +0.55$, $p = 0.03$) and hyperoxic VRT and time spent below 90% ($r = +0.57$, $p = 0.03$).
Conclusion: T treatment did not significantly change VR in these men with moderate-severe OSA. However T levels correlated with hyperoxic VRT, and then with overnight hypoxia. Whether testosterone mediates acute, but not chronic, worsening of OSA through alterations in hyperoxic VRT requires further evaluation.

PO-1-156

SLEEP DISTURBANCE IN PRE-SCHOOL CHILDREN WITH OBSTRUCTIVE SLEEP APNOEA SYNDROME

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Backgrond: Sleep disordered breathing in children is most prevalent in the pre-school years and has been associated with sleep fragmentation and hypoxia. We aimed to compare the sleep and spontaneous arousal

characteristics of 3–5 y old children with obstructive sleep apnea to that of non-snoring control children, and to further characterize the arousal responses to obstructive respiratory events.
Methods: 73 children (48 male) underwent overnight polysomnography; 51 for assessment of snoring who were subsequently diagnosed with OSA (obstructive apnea hypopnea index (OAHI) > 1 events/h), and 22 control children recruited from the community (OAHI < = 1 and no history of snoring).
Results: The OSA group had poorer sleep efficiency ($p < 0.05$), spent a smaller proportion of their sleep period time in REM ($p < 0.05$) and had significantly fewer spontaneous arousals ($p < 0.001$) compared with controls. 25% of the children with OSA had a Sleep Pressure Score above the cut-off point for increased sleep pressure. In children with OSA, 62% of obstructive respiratory events terminated in a cortical arousal, and 21% in a sub-cortical arousal. A significantly higher proportion of obstructive respiratory events terminated in a cortical arousal during NREM compared to REM ($p < 0.001$).
Conclusions: These findings suggest that in pre-school children, OSA has an effect on sleep and arousal patterns. Given that these children are in a critical period for brain development, the impact of OSA may have more severe consequences than in older children.

PO-1-158

POLYSOMNOGRAPHIC ASSESSMENT OF SLEEP BRUXISM IN CHILDREN WITH SLEEP RELATED BREATHING DISORDER

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Background: To investigate incidence of bruxism in children with sleep related breathing disorder and the relevance between sleep stage, position and bruxism.
Methods: Total 66 children and adolescents who visited sleep clinic at CHA Bundang Medical Center were subjects of our study and pediatric sleep questionnaire and PSG were done. Aspects of bruxism with regard to sleep stage and position using additional masseter electrodes according to 2007 AASM bruxism criteria were studied.
Results: Of total 66 patients, PSQ respondents were 62 and mean value was 0.38, 34 patients (52%) scored over 0.33 at PSQ and was corresponded to risk group of obstructive sleep apnea. Their mean AHI was 5.5 and mean RDI was 11.3 and children with AHI score over 1.0 who correspond to SRBD was 41 which was 62.1% of total patients. Patients and parents who answered having bruxism was 24 and occupied 36.4% of the patients. On the PSG assessment of bruxism, surprisingly, all subjects had bruxism that frequently occurred after brief arousal with respiratory events or movements. Bruxism index for each corresponding sleep stage N1, N2, N3 and REM sleep were 13.1, 1.9, 0.7 and 3.1. Bruxism occurred more frequently on N1 sleep and decreased at slow wave sleep. Bruxism index increased with arousal index and show statistical significance ($P = 0.033$). Also comparing frequency of bruxism on supine and non-supine sleep position, frequency increased on supine position with statistical significance.
Conclusion: On the PSG assessment of bruxism according to 2007 AASM criteria in children with sleep related breathing disorder, sleep bruxism occurred in every patient related with arousal. Frequency of bruxism significantly increased at stage N1 sleep and supine position as respiratory events or arousals were usually aggravated in same supine position during N1 or N2 sleep stage in patients with sleep related breathing disorders. It is assumed that PSG based bruxism is common movement phenomenon related with arousal in children with sleep related breathing disorder.

PO-1-159 / AS-06 Presenter

UNUSUALLY SEVERE REM SLEEP APNEA HYPOPNEA IN A CHILD, STRENGTHENS GENETIC LINKAGE WITH PARENTS

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Background: Obstructive sleep apnea hypopnea (OSAH) in children has health implications such as behavior disorders, attention deficit, learning difficulty and growth retardation. Most common cause of OSAH in age group 3 to 6 years is often attributed to adenoid tonsillar hypertrophy. REM OSAH in children may have specific, unique genetic linkage with parents.
History: Child 3.5 years, 39 inches, BMI 17 seen with snoring, attention deficit disorder, growth retardation, Mallampati 4, micrognathia, normal looking tonsils. Father age 35, 67 inches, BMI 41 has loud snoring, short neck, hypertension, diabetes, cardiomegaly, and diastolic dysfunction. Mother has Mallampati 4, micrognathia, and short neck.
Method: Both father and child underwent polysomnography (PSG).
Result: Child: RDI non-REM 19, RDI REM 98, Lowest Sa02 83%. Father: RDI non-REM 10, RDI REM 73, Lowest Sa02 87%.
Discussion: Asian's craniofacial features predispose to the development of OSAH. Both father and child have almost similar PSG pattern of unusually severe REM OSAH in contrast to moderate OSAH during non-REM sleep. There are reports that in children the correction of respiratory disorders was more complete in non-REM sleep, so that adenotonsillectomy can be considered a more effective treatment than for REM obstructive disorders. Children with OSAH do not keep adequate airflow when upper-airway inspiratory-pressure drops during REM sleep, hence a more collapsible upper airway, compared with that of control subjects during REM sleep.
Conclusion: REM OSAH in children may have specific, and unique genetic linkage within the larger universe of genetically link craniofacial features among Asians with OSAH. Further clinical study is needed to validate this conclusion.

PO-1-160

ARE CHILDREN EASILY PREDISPOSED TO OBSTRUCTIVE SLEEP APNEA?

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An excessive volume of soft tissue relative to the size of the craniofacial hard tissue, which is an indicator for disharmony of the anatomical balance in the upper airway, is a risk factor for obstructive sleep apnea (OSA) in adult patients since it increases the collapsibility of the upper airway. In contrast, the contribution of maxillofacial morphology to the pathogenesis of OSA in a pediatric population has not been examined. We hypothesized that the disharmony of the anatomical balance seen in adult OSA patients can also be observed in pediatric OSA patients. The study protocol was approved by the ethics committee of the Neuropsychiatric Research Institute. A total of 7 pediatric OSA patients (5.3 ± 2.0 yrs.) with an apnea-hypopnea index (AHI) above 1/hour after adenotonsillectomy and 31 adult OSA patients (43.8 ± 10.2 yrs.) with a matching skeletal pattern according to the cephalometric parameters

SNA, SNB and ANB were recruited to this study. All subjects were male Japanese. Using upright lateral cephalograms, we compared the Lower Face Cage size (LFC), tongue size (TG), and the anatomical balance determined as the ratio of TG/LFC between pediatric and adult OSA patients. LFC ($p < 0.05$) and TG ($p < 0.05$) in the pediatric patients were significantly smaller than those in the adult patients. Moreover, TG/LFC in the pediatric patients was smaller than that in adult patients ($p < 0.05$). These findings suggest that pediatric patients are structurally predisposed to OSA due to a smaller amount of soft tissue compared to adult patients. The increased vulnerability to collapsibility of the upper airway may be offset by some neurophysiological mechanism in pediatric OSA patients.

PO-1-161

A REVIEW OF INDICATIONS FOR POLYSOMNOGRAPHY IN CHILDREN IN AN AUSTRALIAN SLEEP LABORATORY – COMPARISON TO AASM RECOMMENDATIONS

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Background: Polysomnography (PSG) testing is an essential part of investigation for a child with sleep problems. Recently American Academy of Sleep Medicine (AASM) has published practice parameters for respiratory indications for polysomnography in children. This is based on literature review and classifies the indications into three groups standard, guideline and option.
Aim: To describe the indication for PSGs in the last 5 years in a tertiary paediatric sleep medicine service and to stratify them to the diagnostic groups as per AASM. Further review of the guideline and option groups to ascertain the role of PSG in clinical management.
Methods: Retrospective review of our database and studies stratified according to three categories, standard, guideline and options. Qualitative assessment of the guideline and option groups to derive themes regarding clinical management decisions. A department specific practice parameter was derived.
Results and discussion: Total number of studies during 5 years Jan 2006 to Dec 2010; 3871 studies. Study indications were Standard 1935 (49.9.%); Guideline 560 (14.4%); Option 1340 (34.6%); Non classifiable 36 (.9%). Diagnostic studies for suspected OSA formed the largest group with 49.9% of the studies. 50% of studies were assigned to the guideline and option group; these were review studies for home ventilatory support on either CPAP of Bi level support. PSGs for titration of supplemental oxygen and assessing central breathing control in infancy are widely used in this facility. Further evaluation is needed whether less intensive monitoring techniques may be appropriate for some patient groups.
Conclusion: The AASM practice parameters are a useful guide against which local practices could be audited and unit specific guidelines written.

PO-1-162 / AS-2 Presenter

A COMPARISON BETWEEN PRE AND POST-OPERATIVE SLEEP STRUCTURES IN PEDIATRIC OBSTRUCTIVE SLEEP APNEA PATIENTS

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Objective: Adenotonsillectomy is a common procedure in children with OSA. After adenotonsillectomy children grow and become stable in their psychological condition. The objective of this study is to compare the results of pre and post operative Polysomnographic data in terms of sleep structure for each sleep stage in pediatric OSA patients.
Method: Standard overnight multi channel polysomnographically evaluation was performed preoperatively and 1 to 3 months after operation based on the diagnostic criteria of International Classification of Sleep Disorders second edition. This is a retrospective study of sleep structures of pediatric OSA patients. Aged 3 to 6 years, mean 4.5 years, n equal 25.
Results: Children who underwent adenotonsillectomy had significant improvement in the mean AHI from 17.1 to 3.5 1.8. P less than 0.001. Sleep stage 1 and arousals decreased significantly. Stage 1 from 6.8 to 3.9. P less than 0.01 and arousal index from 23.0 to 11.9. P less than 0.001. Changes in slow wave stages were not statistically significant.
Conclusion: We compared sleep structures between pre and post operatively children who underwent adenotonsillectomy. We predicted increase of slow wave stages but identified changes in the sleep structures in the form of reduction of sleep stage 1 and arousal index. We concluded that the changes of these PSG parameters after adenotonsillectomy might gradually improve their physical and psychological conditions.

PO-1-163

THE CIRCADIAN RHYTHM OF PLASMA MELATONIN CONCENTRATIONS IS ALTERED IN HYPOCRETIN DEFICIENT MEN

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Objective: Hypocretin deficiency causes narcolepsy, a condition characterized by excessive daytime sleepiness, cataplexy, and fragmented nocturnal sleep. Recently, it was shown that in various vertebrates hypocretin fibers project to the pineal gland. Moreover in zebrafish hypocretin was suggested to affect diurnal melatonin synthesis. Therefore, this study was performed to assess whether melatonin secretion differs between narcolepsy patients and matched controls.
Methods: Seven male hypocretin deficient narcolepsy patients with cataplexy and seven controls matched for sex, age and body mass index were enrolled. Blood was sampled at hourly intervals for 24-h to measure melatonin concentrations. Sleep was continuously assessed by polysomnography.
Results: Mean 24-h melatonin concentrations did not differ between narcolepsy patients and controls (39.2 ± 16.4 vs. 28.6 ± 4.6 pg/ml, P

= 0.56). However, the percentage of 24-h melatonin that was secreted during daytime was significantly higher in narcolepsy patients (46.6 ± 4.1 vs. 32.5 ± 5.8%) (P = 0.007 for group effect). Moreover, the cross-correlations between melatonin levels with the percentage of time spent in either slow wave sleep, phase I/II non-REM sleep, or time awake were significantly weaker in narcolepsy patients (all P < 0.023).
Conclusion: Hypocretin is not only involved in the regulation of sleep but also in the regulation of the daily rhythm of melatonin secretion. As sleep and melatonin release are normally entrained, the weaker cross-correlation between sleep and plasma melatonin levels in narcoleptic patients indicates that hypocretin deficiency differently affects the circadian distribution of sleep and melatonin release.

PO-1-164 / AS-11 Presenter

AMBULANT SKIN TEMPERATURE REGULATION AND SLEEP ATTACKS IN NARCOLEPTIC PATIENTS

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Introduction: In healthy subjects, sleep propensity increases when the distal skin temperature increases relative to the proximal skin temperature. This increase results from increased blood flow in the skin of the extremities and is controlled by the hypothalamic circadian clock, as is sleep. Narcolepsy is characterized by hypothalamic alterations. Previously, we studied skin temperature in narcoleptic patients in relation to their characteristically increased sleep propensity during the day. Awake narcoleptic patients showed higher distal and lower proximal skin temperatures then controls. This increased distal skin temperature was related to shorter subsequent sleep-onset latency during a multiple sleep latency test protocol.
Methods: In this 24-hour ambulatory polysomnography study, we continuously measured core body, distal and proximal skin temperature in relation to daytime sleep attacks and nighttime sleep, while subjects were outside the hospital and underwent their normal activities. Subjects were 14 medication-free narcolepsy with cataplexy patients, fulfilling the ICSD-2 criteria.
Results: The mean (±SD) number of daytime sleep attacks for each patient was 2.6 ± 1.0. When each individual sleep attack was analyzed separately, a higher mean distal and proximal skin temperature and a higher distal-to-proximal skin temperature gradient (DPG) was seen in the 5-minute window before a sleep attack, compared to the 5-minute window 30 minutes before a sleep attack in 70% of sleep attacks. Mean increases were 0.5 ± 0.3 in distal and 0.3 ± 0.2 degrees Celcius in proximal skin temperature.
Conclusion: In narcolepsy with cataplexy, an increase in distal skin temperature heralds 70% of sleep attacks in daily life outside of the controlled hospital conditions. This is in line with previous findings under controlled MSLT conditions in narcolepsy with cataplexy; and with the increase in distal skin temperature before normal nocturnal sleep in healthy subjects.

PO-1-165

ASSESSMENT OF HIPPOCAMPAL VOLUME IN PATIENTS WITH NARCOLEPSY WITH CATAPLEXY

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Background: To investigate the differences in hippocampal volume (HV) between narcoleptics and normal controls and determine if HV is associated with memory function in narcoleptics, left and right HV and intracranial volumes (ICV) were manually measured and compared between two groups.
Methods: The study consisted of 36 drug-naive narcoleptics with cataplexy and 36 age- and sex-matched controls (mean age, 29.0 years). All subjects underwent 1.6-mm-thick spoiled gradient recalled magnetic resonance imaging and took the Korean California Verbal Learning Test and the Rey Complex Figure Test to assess verbal and visual memory.
Results: The mean ICV was not different between groups (1,599.2 cm^3 in narcoleptics vs. 1,623.5 cm^3 in controls). Bilateral HV was significantly smaller in narcoleptics (left, 2,907.2 mm^3 in narcoleptics vs. 3,092.3 mm^3 in controls, P = 0.005; right, 2,990.8 mm^3 in narcoleptics vs. 3,184.3 mm^3 in controls). Significance of HV differences between groups remained after corrections were made for gender, age, and ICV. In narcoleptics, bilateral HV was positively correlated with mean sleep and REM sleep latencies in multiple sleep latency test. Absolute memory scores were not different between groups and were not correlated with HV in narcoleptics.
Conclusions: Narcoleptics had smaller bilateral HVs compared to controls. HV had a significant relationship with sleep and REM sleep latencies. This study provides supportive evidence of the functional and anatomical deficits in medial temporal areas that are related to the severity of narcolepsy.

PO-1-166

24-HOUR AMBULATORY MONITORING OF SLEEP-WAKEFULNESS PATTERNS IN NARCOLEPSY

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Introduction: Narcolepsy is characterized by excessive daytime sleepiness (EDS), cataplexy and other dissociated manifestations of rapid eye movement sleep (hypnagogic hallucinations and sleep paralysis). EDS is common and associated with a broad range of medical, sleep and psychiatric disorders. The diagnosis of narcolepsy should be confirmed by a whole night polysomnographyic recording followed by a Multiple Sleep Latency Test (ICSD-2). However, MSLT is designed to provide information about the sleep tendency when the patients lie down. We try to detect SOREMPs by 24-hour ambulatory monitoring and diagnose more precisely.
Methods: Twenty-four narcolepsy patients (age range: 15–78 years) and 25 non-narcoleptic patients (age range: 15–68 years). Out of 24 narcoleptics, 22 patients presented typical clinical picture of cataplexy. The primary complaint in non-narcoleptic patients is daytime sleepiness. 24-hour polygraphic recordings were performed with ambulatory monitoring system. Patients were instructed to maintain wakefulness in their rooms, reading books, listening to the radio. Sleep stages were

visually scored for 20-second epochs according to Rechtschahffen and Kales criteria.
Results: 1) Daytime sleep: Two or more sleep-onset REM periods (SOREMPs) during the diurnal monitoring were observed in 92% of narcoleptic patients and 4% of non-narcoleptic patients. 2) Nighttime sleep: The nocturnal SOREMP was observed 77% of narcolepsy patients and 12% of non-narcoleptics. Short sleep latency of less than 8 minutes was also observed in 64% of narcoleptics, vs. 24% of non-narcoleptics.
Conclusion: 24-hour ambulatory monitoring appears to be a useful procedure for diagnosis of narcolepsy. It provides information about the number, duration and types of daytime sleep episodes, as well as documenting nocturnal sleep disturbance.

PO-1-167

STATE SPACE ANALYSIS OF SLEEP STAGE TRANSITIONS IN NARCOLEPTIC PATIENTS AND HEALTHY VOLUNTEERS

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Background: Behavioral states in human sleep are conventionally described by subsequent analysis of characteristic EEG-patterns, representing the static sleep architecture. In this approach, the dynamic properties of sleep, e.g. transitions between different behavioral states, are not represented. Behavioral state instability is believed to be a key feature in narcolepsy with cataplexy, but the dynamic aspect of changes between behavioral states and the underlying pathology in sleep-wake dynamics are poorly understood.
Methods: We analyzed polysomnography recordings of 7 narcoleptic patients and 7 age-, gender- and BMI-matched healthy volunteers in a 2 dimensional state space, which was optimized by statistical modelling for best differentiation of sleep behavioral states. Further data-evaluation was performed for cluster analysis, density estimates and velocity calculations between behavioral states using various bio-statistical approaches.
Results: We observed a uniform characteristic distribution of stable clusters in a reproducible 2-dimensional sleep state space for all patients and volunteers. The presented data is focused on cluster appearance and velocity calculations in 2 dimensions. We find qualitative changes in cluster arrangement, e.g. a reduction in distance between clusters representing WAKE and REM-sleep for narcoleptic patients as compared to the control group. Analysis of velocity distribution (as a measure of EEG-frequency instability) shows higher overall velocities in state space for narcoleptic patients in all EEG derivations, most pronounced in frontal electrodes.
Conclusions: The highly conserved topography of the 2-dimensional state space shows the potential general usefulness of this analysis technique not only in normal, but also in disordered sleep. In narcolepsy, the higher proximity of clusters indicates behavioral state instability. Furthermore, velocity analysis reveals differences between the two groups, as a novel potentially diagnostic criterion not accessible by conventional polysomnography.

PO-1-168

THE BRAIN MICROSTRUCTURAL ABNORMALITIES IN NARCOLEPSY THOSE CAUSE DAYTIME SLEEPINESS AND CATAPLEXY

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Introduction: Fractional anisotropy (FA) and apparent diffusion coefficient (ADC) are two major indices of diffusion tensor imaging (DTI) which can detect microscopic axonal change by the diffusivity of water molecules. In this study, we applied the voxel-based statistic approach for FA/ADC map and conventional voxel-based morphometory (VBM) technique to estimate the brain microstructural change in narcolepsy and to ascertain its relationship to the mechanism of excessive daytime sleepiness and cataplexy.
Method: The study included 12 narcolepsy with cataplexy (NA/CA), 12 narcolepsy without cataplexy (NA w/o CA) and 12 age-matched healthy normal controls (NC). FA/ADC images and gray/white matter images obtained on a 1.5T MRI were statistically compared using voxel-based statistic technique. Furthermore, we investigated the correlation between morphometric changes and sleep indices.
Results: NA group (NA/CA and NA w/o CA) showed higher ADC in bilateral amygdala and left anterior cingulate, lower FA in left medial frontal area, reduced gray matter of left temporal area and left caudate and reduced white matter of midbrain and right precentral area than NC. In comparison with NA w/o CA, NA/CA showed higher ADC in right frontal area, higher FA in right parietal area, higher white matter volume in left cerebellum. In narcolepsy, sleep efficiency (SE) showed negative correlation with ADC and FA in mainly right limbic area, gray matter volume in left precentral area and white matter volume in left cingulate, and positive correlation with white matter volume in left precentral area and bilateral posterior cingulate.
Discussion: The volume reduction in midbrain may reflect the essential abnormality of wake-sleep promoting system in narcolepsy. Higher ADC in right inferior frontal area and higher white matter volume in left cerebellum in NA/CA might be associated with the occurrence of cataplexy. The correlation between SE and many brain area may suggest that the degree of axonal change is related with the disturbance in sleep-wake promoting system originating from brain stem.

PO-1-169

SLEEP, SLEEPINESS AND VIGILANCE IN DOPAMINE- AND HYPOCRETIN DEFICIENT DISORDERS

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Background: Parkinson disease (PD) and narcolepsy with cataplexy (NC) are caused by disturbed neurotransmitter signaling, particularly dopamine and hypocretin (orexin). To better understand sleep-wake disturbances against the background of these differential neurotransmitter deficiencies, we aimed at examining nocturnal sleep, excessive daytime sleepiness, and vigilance in consecutive PD and NC patients, and in matched healthy controls.

Methods: We prospectively included 10 patients with early PD, 10 patients with advanced PD, 10 NC patients, and 10 controls. All participants were examined with nocturnal polysomnography (PSG), multiple sleep latency tests (MSLT), and vigilance tests. Cerebrospinal fluid hypocretin levels were assessed in all patients.
Results: Hypocretin levels were lower in patients with advanced compared to those with early PD, and undetectable in most NC patients. Linear regression revealed that sleep efficiency on PSG was lower in patients with deficient dopaminergic signaling ($p = 0.008$). The amount of deep sleep stage NREM3 and latency to REM sleep was also related to dopaminergic signaling ($p = 0.01$ and $p < 0.001$). Otherwise we could not identify influences of dopaminergic and hypocretinergic signaling on PSG parameters. On the other hand, decreased hypocretin signaling was associated both with decreased mean sleep latencies and increased number of sleep onset REM periods on MSLT (both: $p < 0.001$). Vigilance tests were not influenced by neurotransmitter signaling.
Conclusion: Nocturnal sleep is most altered in patients with advanced PD, i.e. in patients with marked loss of dopamine neurons and partial loss of hypocretin cells. On the other hand, excessive daytime sleepiness was most pronounced in NC patients, i.e. in patients with subtotal loss of hypocretin neurons.

PO-1-170

DIFFERENCES IN FINDINGS OF NOCTURNAL POLYSOMNOGRAPHY AND MULTIPLE SLEEP LATENCY TEST BETWEEN NARCOLEPSY AND IDIOPATHIC HYPERSOMNIA

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Objectives: In order to clarify the difference in the characteristics of daytime sleepiness among narcolepsy with cataplexy (NA with CA), narcolepsy without cataplexy (NA without CA), and idiopathic hypersomnia without long sleep time (IHS without LST), we compared the findings of nocturnal polysomnography (N-PSG) and diurnal variations in multiple sleep latency test (MSLT) parameters among patients with these disorders.
Methods: The patients with NA with CA (n = 52, M : F = 24:28, 27.2 ± 8.9 years), NA without CA (n = 62, M : F = 30:32, 26.7 ± 7.4 years), and IHS without LST (n = 50, M : F = 27:23, 29.5 ± 9.7 years) were enrolled to this study. The polysomnographic findings were compared by using One-way analysis of variance (ANOVA). Diurnal variations in MSLT parameters were also compared with among three groups by Two-way repeated measurements ANOVA (disease group × time period).
Results: The NA with CA group had significantly more disrupted and shallower nocturnal sleep than the other groups. On MSLT, the IHS without LST group had significantly longer sleep latency (SL) compared with the two NA groups. The latter two groups did not show statistical differences in diurnal variation of SL.
Conclusions: The IHS without LST group had milder objective daytime sleepiness compared with the NA groups. In patients with NA, nocturnal sleep disturbances appeared only in cases with CA, despite a similar trend in diurnal changes in sleep propensity between the two NA groups. Our result suggested that objective nocturnal sleep disturbances are specific to NA patients with CA, whereas diurnal variations of sleep propensity are observed irrespective of the presence of CA among NA patients. These findings could be helpful for making treatment plans for patients with these disorder categories.

PO-1-171

THE EFFECT OF STEROID THERAPY FOR 2 PATIENTS WITH NARCOLEPSY

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Introduction: The relation of autoimmune system with narcolepsy was suggested. We used streroid for 2 patients with narcolepsy who had suffered about 1 month before. It was effective for thier symptoms with narcolepsy.
Case 1: An 11 years-old girl could not walk with cataplexy suddenly. At the same time, she became to wake in early morning and not to be able to maintain the night sleep. Somniloquence and myoclonus in falling asleep appeared remarkably. She could not walk without help because of cataplexy. Daytime sleepiness was very strong and she could not keep awake more than 15 minutes. In electroencephalography, time for falling asleep was 0 minute, sleep onset rapid eye movements was demonstrated, and she had seven sleep cycles. The orexin level in cerebrospinal fluid (CSF) was decreased remarkably. She was diagnosed as narcolepsy. About one month after the onset, she was treated with oral prednisolone 1 mg/kg/day. She was medicated with full dose of predonisolone for 2 weeks and decreased gradually. She became to be suffered from cataplexy only in laughing, to be able to walk alone and maintain awakening time in daytime 1 week after the start of treatment.
Case 2: A 13 years-old boy could not walk with cataplexy, suddenly. At the same time, he became to sleep in daytime and not to be able to maintain the night sleep. The orexin level in CSF was decreased remarkably. He was diagnosed as narcolepsy. One month after the onset, he was treated with oral prednisolone 1 mg/kg/day. He was medicated with full dose of predonisolone for 2 weeks and decreased gradually. His cataplexy and daytime sleepiness improved remarkably 2 days after oral prednisolone. Mild sleepiness reappeared with decrease of prednisolone.
Discussion: Steroid therapy revealed thier cataplexy and daytime sleepiness slightly, though cytokines and orexin levels in CSF were not changed from before to after treatment. It seemed that the steroid therapy was effective partly for the symptoms of narcolepsy.
Conclusion: Steroid therapy could be one of the therapies for narcolepsy in early period of suffering.

PO-1-172

INVESTIGATION OF BINGE EATING BEHAVIOURS IN NARCOLEPSY

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Previous work has suggested that eating behaviours in narcolepsy may be abnormal. Binge eating behaviours of individuals with and without narcolepsy were investigated as part of a larger study. Of particular interest was the hypothesised difference in self reported binge eating across the two groups and possible relationships within the narcolepsy group between eating patterns and sleepiness and mood. Our sample consisted of 73 individuals with unambiguous narcolepsy (M = 58.4 yrs, SD = 18.5) and 74 controls (M = 57.2 yrs, SD = 15.4). Groups were matched on age and gender. Controls with a sleep disorder or a disorder that restricted food intake were excluded. Measures used were the

Bulimia Test, Depression Anxiety Stress Scale and Epworth Sleepiness Scale (ESS) and analyses used the Mann Whitney U Test. It was found that individuals with narcolepsy were significantly more likely to report *binge eating* than controls ($p = .001$). A derived *'binge eating factor'* from the Bulimia Test was used (Cronbach's alpha = 0.88). Using this binge factor as the dependent variable it was found that individuals with narcolepsy who had 'moderate to high' *anxiety* and/or *stress* (compared to 'no to mild') scored significantly higher on the binge factor ($p = .001$ and $p = .000$ respectively). No significant differences on the binge factor were found between individuals with narcolepsy who had severe and less *severe daytime sleepiness* (ESS rated both on and off medication) or *depression*. In sum, individuals with narcolepsy were found to be more likely to report binge eating than controls, and those with moderate to high anxiety and stress were more at risk. Understanding such risk factors will aide health professionals in preventing and treating eating disordered behaviours in narcolepsy.

PO-1-173

NEW INSIGHTS IN UNDERSTANDING AUTOMATIC BEHAVIOUR

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Automatic behaviours are stereotyped, repetitive behaviours performed without awareness. Descriptors include "highway hypnosis" and "automatic pilot", portrayed in both non-clinical (sleep deprived) and clinical (hypersomnia) populations. At present little is known about this complex phenomenon, and research in the area is minimal. The high prevalence of automatic behaviour in some individuals with narcolepsy provided the opportunity for new insights on such behaviours. The study was based on an in-depth, phenomenological analysis of the experiences of ten individuals with narcolepsy (with self-reported moderate to severe automatic behaviour). Procedures included two interviews, a family member interview, a one week journal and a one day minimal medication journal. Prominent issues discussed by participants and presented include behaviours associated with automatic behaviour (including errors), internal states of sleepiness and cognitive load, as well as ways of controlling automatic behaviour. Different types of automatic behaviour were identified; Type 1 (sleepiness with low cognitive load), Type 2 (sleepiness with high cognitive load) and Type 3 (high cognitive load without sleepiness). New contributions include; the notion of cognitive load, the Type 3 phenomena, the possible progression of Type 1 to sleep, a new classification of errors (sequencing errors, item/environment intrusions, perseverative action leading to nonsense, context inappropriate behaviours), the importance of adequate medication, as well as a discussion of the key roles of vigilance and feedback in the cognitive mechanism of automatic behaviour. Further research is needed to determine whether these findings in narcolepsy have implications for understanding automatic behaviour in sleep deprived individuals (e.g. shift workers).

PO-1-174

QUALITY OF LIFE IN PATIENTS WITH NARCOLEPSY WITH CATAPLEXY, NARCOLEPSY WITHOUT CATAPLEXY, AND IDIOPATHIC HYPERSOMNIA WITHOUT LONG SLEEP TIME

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Objective: To assess quality of life (OQL) in patients with narcolepsy with cataplexy (NA-CA), narcolepsy without cataplexy (NA w/o CA) and idiopathic hypersomnia without long sleep time (IHS w/o LST) who were taking psychostimulant medication, and to ascertain which factors (including psychosocial and environmental variables) influence QOL in this population.
Methods: A total of 185 patients who had received regular treatment were enrolled (NA-CA, n = 83; NA w/o CA, n = 48; IHS w/o LST, n = 54). Patients were asked to complete questionnaires including the Short Form-36 Health Survey (SF-36), the Epworth Sleepiness Scale (ESS), and items concerning psychosocial and environmental variables.
Results: All 3 diagnostic groups had significantly lower scores in most SF-36 domains compared with Japanese normative data, although the ESS score was significantly reduced with the treatment. Multiple logistic regression analyses revealed that several SF-36 domains were associated with the ESS score, having automony in controlling one's job schedule, having the experience of a divorce or breakup with a partner due to symptoms, having the experience of being forced to relocate or dismiss, and perception of support from others.
Conclusions: Not only severity of subjective sleepiness but also psychological and environmental variables influenced QOL in patients with these hypersomnias of central origin.

PO-1-175

INJURIES AND PROPERTY DAMAGE DUE TO SMOKING IN NARCOLEPTIC PATIENTS

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Objectives: Most fires related to lighted smoking materials occur when a smoker falls asleep, representing a leading cause of death, injury and property damage in the U.S. Smokers with sleep disorders associated with excessive daytime sleepiness (EDS) are expected to be at increased risk. A previous study of attendees of a Narcolepsy Network meeting reported adverse consequences including burns and injuries associated with smoked tobacco. This project seeks to re-examine these findings in a larger sample of narcolepsy patients seen at an academic medical center.
Methods: After being approved by the I.R.B., a questionnaire concerning nicotine use was mailed to a registry of narcolepsy patients

maintained by a U.S. medical center. 110 questionnaires were returned in the postage paid envelope.
Results: The respondents were 60% female and ranged in age from 18 to 87. A lifetime point prevalence of smoking tobacco was described by 54% of respondents. Current cigarettes and cigar use was reported by 16%. Median usage was 1 pack of cigarettes per day. Burns and damage related to smoking was reported by 19 respondents (17%). Reported consequences included clothing burns (15), furniture (12), skin burns (10), and other property (4). These incidents were frequently associated with being asleep. Perceived effect of nicotine on sleepiness was a reduction for 44%, neutral for 40% and increase for 4%.
Conclusions: Persons with narcolepsy who smoke experience injury and property damage due to lighted smoking materials. Even though a significant percentage of respondents perceive nicotine to reduce EDS, smoking cessation should be strongly advised. Effective nicotine cessation strategies need to be identified and specifically studied in patients with narcolepsy.

PO-1-176

DELAY OF GRATIFICATION IN NARCOLEPSY

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Orexins are involved in the regulation of food intake and sleep. Narcolepsy is characterized by a central orexin deficiency. Studies report an increased body weight in narcolepsy. The inability to delay gratification is related to obesity. This study investigates the delay of gratification in patients with narcolepsy. Nine patients organized in the German Narcolepsy Self-help Group (DNG) with polysomnographically verified narcolepsy (F/M 7/2: mean age 37.9 ± 18 years; mean BMI 25.0 ± 4.9 kg/m^2) were included in the study. We designed a board game to assess the delay of gratification. On designated fields patients had to decide whether they choose an immediate small gratification consisting of a small piece of sweetie or whether they continue playing and get double of the amount in the end of the game. The outcome measure is the percentage of decisions in favor of delay. The percentage was calculated for the total game and for the three thirds of the fields. The sleepiness was assed with the Karolinska Sleepiness Scale (KSS) before and after the game. Nine control subjects were individually matched for gender, age and BMI (mean age: 38 ± 18 years; mean BMI 25.3 ± 4.8 kg/m^2). The percentage of decisions in favor of delaying did not differ between patients with narcolepsy (89 ± 10%) and individually matched controls (83 ± 19%, $p = 0.40$). The percentage of decisions in favor of delayed gratification across the time hardly increased little in the narcoleptic group (80%, 91%, 93%) across the 3 thirds. It showed a steep increase in the control group (65%, 86%, 92%). KSS dropped or remained stable in all but one narcoleptic individuals. These preliminary results suggest no obvious peculiarities concerning the delay of gratification in narcoleptic patients. Subtle differences in favor of stronger inhibition may be possible. Remarkably the decisions made induced preferentially the intake of a higher amount of sweeties. The board game paradigm emerged as valuable tool that takes into account the sleepiness of narcoleptic patients. Investigating a larger sample will help control for the large standard deviation.

PO-1-177

TOLERANCE AND EFFICACY OF SODIUM OXYBATE IN CHILDHOOD NARCOLEPSY WITH CATAPLEXY

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Narcolepsy with cataplexy is a disabling lifelong disorder frequently arising during childhood.
Pediatric narcolepsy often results in severe learning and social impairment. Improving awareness about this condition increases early diagnosis and may allow patients to rapidly access adequate treatments including pharmacotherapy and/or non-medication-based approaches. Even though children currently undergo pharmacotherapy, data about safety and efficacy in the paediatric population are scarce.
The present study brings preliminary data on the efficacy of Sodium Oxybate in a childhood and adolescent population of 27 patients suffering from narcolepsy with cataplexy, also confirming a previous report on 8 children. Sodium Oxybate has been shown to be efficacious and well tolerated by the majority of subjects, during a long-term follow-up.
Sodium Oxybate may therefore constitute a very valuable treatment in childhood narcolepsy with cataplexy.

PO-1-178

INTRAVENOUS HIGH DOSE IMMUNOGLOBULIN TREATMENT IN LATE-ONSET NARCOLEPSY WITH CATAPLEXY

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Background: Narcolepsy with cataplexy (NC) is associated with the degeneration of the posterolateral hypothalamic neurons containing hypocretin. Because of the close HLA association, the disorder has been suggested to be autoimmune in nature. We report an outcome of intravenous high-dose immunoglobulin (IVIg) treatment in late-onset narcolepsy and cataplexy patient.
Case: A 55-year-old man presented a 5 months history of sudden sleep attack during wakefulness and intermittent muscle weakness induced by emotions. His Epworth Sleepiness Scale score was 23, which meant severe excessive daytime sleepiness (EDS). Nocturnal polysomnography and multiple sleep latency test findings revealed short sleep latency and 2 SOREM, which were competent with narcolepsy. His HLA DQB1*0602 was positive, and CSF hypocretin level was below 40 pg/ml. Therefore, his initial diagnosis was narcolepsy with cataplexy. A diagnosis of idiopathic narcolepsy-cataplexy was finally made. He has been treated with modafinil and methylphenidate for his excessive sleepiness, and clomipramine for cataplexy. After 5 months, IVIg were administered at the widely used dosage in autoimmune diseases, also suggested in NC: 0.4 g/kg per day for five days, repeated monthly for three months and followed by the same single day dose every. After the entire IVIg cycle,

no effects of EDS and cataplexy were observed during or after the entire IVIg treatment. CSF hypocretin level was still below 40 pg/ml.
Conclusion: Several factors may account for the lack of significant effects of IVIg in our patients. First, CSF hypocretin-1 was already undetectable, suggesting thatautoimmune destruction of hypocretin neurons was already complete when IVIg therapy was started. Second, the treatment protocol might be not sufficient. At last, our patients were older at disease onset. Further efforts on a well selected large group of NC patients are needed to assess their spectrum of efficacy in this disease.

PO-1-179

MOOD, ACTIVITY, AND QOL IN PATIENTS WITH BEHAVIORALLY INDUCED INSUFFICIENT SLEEP SYNDROME AND NARCOLEPSY AS DETERMINED BY POMS AND QOL26

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Introduction: The sleeping time of Japanese adults has been decreasing every year, and is now estimated to be less than 6 hours per night on average. Insufficient sleep may cause excessive daytime sleepiness, which in turn influences mood, daytime activity, and quolity of life (QOL). And we have seen an increasing number of patients with behaviorally induced insufficient sleep syndrome (BIISS) at our sleep disorders outpatient clinic. This study sought to determine the incidence of sleep disorders among medical college students.
Subjects and Methods: We investigated the mood, daytime activity, and QOL of 93 medical college students by using the Profile of Mood States (POMS), the Quality of Life 26 (QOL26) scale, the Pittsburg Sleep Quality Index (PSQI), and Epworth score. For those subjects who were found to have BIISS and narcolepsy on assessment, we additionally conducted the multiple sleep latency test (MSLT).
Results: Among the 93 subjects, 38 were found to have BIISS (male: 22, female: 16; mean age: 21.8 years), 20 had narcolepsy (male: 10, female: 10; mean age: 24.3 years), and 35 had no sleep disorders (male: 24, female: 11; mean age: 24.1 years). For subjects found to have BIISS and narcolepsy, the respective MSLT results were 60.2% and 81.3% for sleep efficiency, 453.2 s and 206.5 s for sleep latency, and 1 and 2.7 for number of REM periods. The Epworth score was markedly higher among the groups with sleep disorders than the healthy group, and likewise scores on the POMS indicated poorer mood profiles for those with sleep disorders.

PO-1-180

FALSE-POSITIVE CASES IN MSLT BY ACCUMULATED SLEEP DEFICIENCY

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Introduction: MSLT is usually performed as objective assessment of sleepiness. It is performed on the following day after PSG. In most clinics and hospitals, patients are required to stay for a couple of days. However, if patients have chronic insufficient sleep, the accumulation of their sleep insufficiencies may affect MSLT results. Even if they get enough nocturnal sleep during the PSG, their sleep insufficiencies would not be fully recovered (Janjua T. 2003). In the present study, we compared each sleep latency by examining it with MSLT twice. First session is 0 or one hospitalized night with the following MSLT, and second session is three or more hospitalized nights with the following MSLT.
Methods: Ten males and one female (31.8 ± 14.2 yrs) who performed MSLT twice were enrolled in our study. They complained about sleep-wake disorders in our hospital from 2004 to 2010. Initially, we examined these cases using standard PSG and MSLT procedure, however, their results were doubtful compared with sleep logs and other symptoms. Therefore, we examined these doubtful cases for the second examination with two or more previous hospitalized nights and following PSG and MSLT procedure (total three or more hospitalized nights).
Result: Mean sleep latency was 6.4 min in '0 or one night' group and 14.8 min in 'three or more nights' group. There was a significant difference between these two groups ($p < 0.001$).
Conclusion: Sleep latencies of '0 or one night' group were shorter than those of 'three or more nights' group. This may produce false-positive results at diagnosis when patients were examined by standard PSG and MSLT procedures. It is thought that the effects of insufficient sleep affect these procedures, consequently, shorten sleep latencies. Therefore, we need to consider the hospitalized durations before PSG and MSLT procedures.
Reference:
Janjua T. et al. Clinical caveat: prior sleep deprivation can affect the MSLT for days. Sleep Med. 2003; 4(1): 69–72.

PO-1-181

NOCTURAL ASPECT OF CENTRAL HYPERSOMNIA PATIENTS. ANALYSIS OF SELF-COMPLETED QUESTIONNAIRE

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Introduction: Symptoms other than excessive daytime sleepiness are not always evaluated well in patients with hypersomnia of central origin. In order to elucidate the nocturnal characteristics of hypersomnia, we performed questionnaire-based survey to study the prevalence of nocturnal sleep problems and their correlates.
Methods: Subjects are 358 hypersomnia patients (216 narcolepsy with cataplexy; NA, 31 idiopathic hypersomnia with long sleep time; IHS, 111 essential hypersomnia; EHS) recruited in Japan Somnology Center and 292 non-hypersomnia controls. Self-completed questionnaire asking the frequency of nocturnal sleep problems and related symptoms were collected.
Results: Most hypersomnia patients tend to fall asleep in a short time, but the percentage of sleep initiating problems are similar among groups. Number of nocturnal awakenings is frequent in NA. Dreaming at nocturnal awaking is frequent in NA (44%) compared to Control (23%). 15% of NA experience difficulty in resuming sleep at nocturnal awakenings. Time required to be fully awake in the morning is characteristically longer in IHS. NA can wake up more easily than Control. Prevalence of hypnagogic hallucination is high in NA (78%), EHS & IHS (40%) compared to Control (7%). Note that REM sleep related phenomena are not rare in IHS. Modality of hypnagogic hallucination content shows similar pattern across groups; more visual than auditory hallucination. Tactile hallucination is common in NA and feeling of

floating/flying is common in all the subjects with the experience. Frequent nocturnal eating with half asleep condition is reported from 7% of NA. Body temperature dysregulation is common among hypersomnia patients: Raynaud phenomena in IHS (25%) and excessive sweating in NA (53%). Two thirds of IHS suffered from fatigue.
Conclusion: Nocturnal sleep of hypersomina patients shows characteristic pattern, especially in the process of waking up in the morning, which could be partly REM-related. It is clinically important to ask hypersomnia patients for nocturnal sleep problems besides daytime sleepiness.

PO-1-182

POST INFLUENZA A/H1N1 HYPERSOMNOLENCE: REPORT OF 2 CASES AND REVIEW OF THE LITERATURE

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We present 2 patients who complained for excessive daytime sleepiness after Influenza A/H1N1 infection. First case is a 42 year old woman who experienced excessive daytime sleepiness and cataplexy 10 days after the remission of suspected acute Influenza A/H1N1 infection. HLA-DQB1*0602 was negative. The diagnosis of narcolepsy with cataplexy was confirmed following extensive investigations including polysomnography and multiple sleep latency test (MSLT). Second case is a 16 year old male adolescent who had Influenza A/H1N1 confirmed by RT-PCR. Three months after his recovery, the patient developed monthly hypersomnolent attack with 5 days of mean duration. He was also accompanied by memory loss and hyperphagia. Polysomnographic recordings in between attacks showed relatively normal sleep structure. 2 SOREMPs appeared and sleep latency was 5.8 min in MSLT. These findings provide support for association of Influenza A/H1N1 infection with hypersomnolence.

PO-1-183 / AS-31 Presenter

PITOLISANT, AN INVERSE AGONIST OF THE HISTAMINE H3 RECEPTOR: AN ALTERNATIVE TREATMENT FOR SEVERE EXCESSIVE DAYTIME SLEEPINESS IN CHILDREN WITH NARCOLEPSY

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Narcolepsy is linked to a deficiency of orexins. Its clinical manifestations are often more severe in children than in adults. Narcoleptic cataplectic, NC, patients also show a deficit of histamine, HA, another hypothalamic arousal system. We have identified brain HA H3 receptor as new cerebral target for the therapy of sleep wake disorders and proposed Pitolisant, inverse agonist of H3 receptor, as a new class of anti narcoleptic drugs. In this work, we report retrospectively our experience of the off label use of Pitolisant in children followed in our sleep disorders center with severe NC with a refractory sleepiness to habitual therapy at recommended doses: modafinil, methylphenidate, mazindol, sodium oxybate. All these patients developed their disease in childhood, 12.5 plus and minus 3 years, 50 per cent boy. These treatments have been stopped for side effects, 4; and lack or partial efficacy; 2. The adolescents were 17.35 plus and minus 0.8 years old. Pitolisant treatment has been progressively increased from 10 to 40 mg. All the patients except one received the maximum dose. The treatment was rarely efficient alone; other treatment was required in association: ritaline, mazindol, sodium oxybate. In these conditions, subjective and

objective sleepiness decreased. ESS decreased from 14.35 plus and minus 1.1 to 9.25 plus and minus 2.5 and the sleep latency at Maintenance Wakefulness Test increased from 27.95 plus and minus 14.9 to 34.95 plus and minus 8.8 min. There was no habituation during the follow up, 13.55 plus and minus 7.1 months. The side effects were mild and transitory. Insomnia was the only long term side effects in 2 patients. Indeed, the polygraphic results showed a decrease in total sleep time, in percent of sleep efficiency, in percent of 3 and 4 NREM sleep and REM sleep and an increased in arousals during sleep. Pitolisant had not repercussions on blood analyses and the cardiologic evaluation. Pitolisant could be an alternative treatment with few side effects for severe excessive daytime sleepiness in children with narcolepsy. However long term follow up is required.

PO-1-184

SUSTAINED ATTENTION TO RESPONSE TASK (SART) SHOWS IMPAIRED VIGILANCE IN A SPECTRUM OF DISORDERS OF EXCESSIVE DAYTIME SLEEPINESS

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The Sustained Attention to Response Task (SART) comprises withholding key presses to 1 in 9 of 225 target stimuli; it proved to be a sensitive measure of vigilance in a small group of narcoleptics. We studied SART results in a 96 patients from a tertiary narcolepsy referral centre. Diagnoses according to ICSD-2 criteria were narcolepsy with (n = 42) and without cataplexy (n = 5), idiopathic hypersomnia (n = 37), and obstructive sleep apnea syndrome (n = 12). The SART was administered prior to each of 5 MSLT sessions. Analysis concerned error rates, mean reaction time (RT), RT variability and post-error slowing, as well as the correlation of SART results with mean latency of the Multiple Sleep Latency Test (MSLT) and possible time of day influences. Median SART error scores ranged from 8.4 to 11.1, and mean RTs from 332 to 366 ms. SART error score and mean RT did not differ significantly between patient groups. SART error score did not correlate with MSLT sleep latency. RT was more variable as the error score was higher. SART error score was highest for the first session. We conclude that a high SART error rate reflects vigilance impairment in excessive daytime sleepiness irrespective of its cause. The SART and the MSLT reflect different aspects of sleep/wakefulness and are complementary.

PO-1-185

DAYTIME SLEEPINESS AND SLEEP DISORDERS IN PATIENTS WITH ALLERGIC RHINITIS

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Background: Today, in Japan, over 20 million peoples are suffered from Hay fever caused by cedar pollen, and every year, they are disturbed with severe symptoms during season (just 2–3 mth). In clinically, there is a big problem about QOL including daytime sleepiness and sleep problems, and the medical expenses are estimated 150 billion yen. (≤1.5 billion) Recently, There are some clinical reports about correlation between allergic rhinitis and sleep disturbance. But we are not sure how to influence to Sleep or Daytime sleepiness?
Methods: Objective Study: 22 patients with hey fever caused by cedar Pollen were enrolled. We evaluated sleep architecture and objective sleepiness between before the season & on season using PSG and MSLT.
Results: WASO (wake time after sleep on set) showed significantly increase during on season rather than before season: (from 16.4 to 29.7 min). AHI does not change for the worse during on season. (total nasal resistance >0.3 pa/cm^3/sec) The highest accuracy rate is 72.7% using this statistical model. In 10 patients with nasal obstruction (total nasal resistance >0.3 pa/cm^3/sec) out of 22, REM-sleep decreased (from 24.4 to 21.1%) and mean MSLT decreased (from 12.9 to 8.4 min) significantly. Especially 4 out of 11 showed severe sleepiness that was recognized as disease (MSLT < 5 min) on season. Three following hypotheses are considered as likelihood, however, Pathology of allergic rhinitis affecting sleep is still not known. 1, Nasal obstruction will cause sleep disordered breathing. 2, Nasal obstruction will directly affect on sleep. 3, Chemical mediators in allergic diseases will affect on Sleep/Wake Center. Further studies are needed.
Conclusion: There are strong associations between nasal symptom especially nasal obstruction, sleepiness and sleep quality. But cause and effect is unknown. We need further study about allergic rhnitis and sleep disorders.

PO-1-186

MONOZYGOTIC TWINS CONCORDANT FOR RECURRENT HYPERSOMNIA

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Recurrent hypersomnia is a rare sleep disorder occuring during adolescence. It is characterized by intermittent periods of excessive sleepiness, cognitive disturbances and behavioral abnormalities. The pathogenesis of recurrent hypersomnia is not yet known. Although most cases of recurrent hypersomnia are sporadic, there may be a genetic predisposition, since nine familial cases have been described. However, no case of twins affected with recurrent hypersomnia has been reported.
Here we describe monozygotic twins who both affected with recurrent hypersomnia. In both cases, infection of influenza virus was followed by the onset of the first episode. Actimetry recording showed that during attacks, activity in day was decreased compared to asymptomatic periods, on the other hand, the activity during night was significantly higher in symptomatic periods. Polysomnography (PSG) revealed decreased slow wave sleep and frequent awakenings during symptomatic period. Human leukocyte antigen (HLA) typing revealed there are no existence of DQB1*02 loci. Our observations suggest that the possible presence of genetic and autoimmune processes, although association with HLA remains controversial.

PO-1-187

SLEEPY AND AGITATED-KLEINE-LEVIN SYNDROME MISDIAGNOSED AS BIPOLAR DISORDER: A CASE REPORT

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Case report: The patient, a 16 year-old Taiwanese teenager, had the disease onset when he was 11. He had regressive behavior, bursts of crying and irritability after flu-like symptoms. Post-infectious encephalitis was initially impressed. After steroid pulse therapy, the condition remitted. But condition recurred and he was hospitalized for steroid pulse therapy three times within 3 months. Each episode lasts for 1–2 weeks. He manifested visual hallucinations, emotional lability, irritability, increased activity, excessive talking, distractibility, drowsiness and hyperphagia. Then he was brought to another hospital and was diagnosed as bipolar disorder. No more steroids was given. He was hospitalized in psychiatric ward twice during a 18 month period with poor adherence to lithium treatment. Due to lithium intoxication, his medications were shifted to valproic acid and lorazapam. He still had episodes of sleepiness and agitation. A typical episode which happened once to twice per year included intermittent hypersomnolence, behavioral and cognitive disturbances which resulted in 8–10 days of hospitalization. His brain imaging results, biochemistry data and thyroid function were normal during these episodes. No epilepsy was seen. He was drowsy with a total sleep time of 13 hours a day, but when he got off bed, he would become argumentative, agitated, shouted and had many goal-directed behaviors. Between episodes, he had normal daily activities with almost no symptoms. There were episodes with abrupt onset despite fair drug compliance and with-in drug level, which is not often seen in bipolar patients. The recurrences were mainly in winter and autumn, and none of them were in summer. After exclusion and discussion, diagnosis of Kleine-Levine syndrome was established. We keep treatment with anticonvulsants with no antipsychotics. There were longer interspersed lucid periods within the recurring episode.
Conclusion: KLS can have typical manifestations of bipolar disorder. However, the disease course pattern and hypersomnic symptoms help differentiate the two disorders.

PO-1-188

UNUSUAL CIRCADIAN RHYTHM AND DIABETES MELLITUS IN MUTANT CRYPTOCHROME1 TRANSGENIC MICE

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Cryptochrome proteins (CRYs) play indispensable roles as inhibitive components of the transcriptional-translational negative feedback loop in the molecular model underlying mammalian circadian rhythm. We generated transgenic (Tg) mice ubiquitously expressing CRY1 having a mutation in the dipeptide motif of cysteine and proline that is conserved beyond evolutional divergence among animal CRYs: cystein 414 of the motif was replaced with alanine (CRY1-AP protein). Mice overexpressing CRY1-AP (CRY1-AP Tg) showed anomalous circadian behavior, and also symptoms of diabetes mellitus characterized by early onset, non-obese, and beta cell dysfunction (Neurosci Lett. 451, 246–251, 2009; Eur J Clin invest., 40, 1011–1017, 2010). In order to clarify yet uncovered pathogenesis of diabetes mellitus, in which the mutant CRY1 is involved, we examined the characteristic aspects of islets in CRY1-AP Tg mice. In the mature stage of the Tg mice (about 20 weeks of age), glucagon-positive cells were distributed throughout the islets, indicating abnormal islet architecture. Massive apoptosis was induced in the islets of the mature Tg mice. Also at this stage the size of the islet was significantly smaller than that of wild-type mice. In accordance with these results, expression levels of some transcription factors, which are known to play important roles in the function of islet, decreased in the islets of the mature Tg mice. These results suggest that CRY1 is crucial to the maintenance of the function of pancreatic islet.

PO-1-189

LOW BIRTH WEIGHT BY UNDERNUTRITION DURING PREGNANCY ELICITS ANXIETY AND DEPRESSION IN MALE OFFSPRING MICE

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Undernutrition during pregnancy is known as one of the crucial risk factors of low birth weight (LBW) caused in infants. LBW accompanied by catch-up growth (CUG) are increased risk for type 2 diabetes and metabolic syndrome. Type 2 diabates elicit various of sleep disorders caused by alternation of sleep architecture and quality. However, it remains unclear whether the LBW accompanied by CUG would affect higher brain function including sleep, anxiety and/or depression. We developed a mouse model of LBW with CUG by caloric restriction (CR) to pregnant female mice. We selected the CR rate for 0% (control), 20% and 50%. Pregnancy was dated with vaginal plugs (day 0.5), then pregnant female mice were performed CR from days 12.5 to 18.5. After the parturition, dams were assigned to ad libitum chow. We performed sleep recording, behavioral test to evaluate anxiety and depression in the LBW model and control mice (8–14 weeks of old). In this study, we found that 50% CR mice showed LBW and a marked increase in anxiety and depression compared with control mice. Meanwhile, 50% and 20% CR mice showed a remarkably low activity compared with control mice during dark period. Furthermore, in 50% CR mice, NREM sleep during dark period tended to be increased. These results indicate that LBW with CUG by CR during pregnancy would be a crucial risk factor of anxiety, depression and other behavioral abnormality.

PO-1-190

THE RELATIONSHIP BETWEEN CIRCADIAN RHYTHM SLEEP DISORDER AND MELATONIN SECRETION IN ANGELMAN SYNDROME

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Angelman syndrome (AS) is characterized by mental retardation, seizures and gait ataxia, and is associated with abnormalities of chromosome 15q11-q13 region. In AS, sleep problems have been reported to frequently occur. However, characteristics of sleep problems in AS still

remain unclear. The aim of this study was to investigate the sleep-wake patterns of patients with AS and its relation to melatonin secretion pattern.
This study was approved by the ethics committee of Neuropsychiatric Research Institute. Fifteen consecutive AS patients having abnormality of chromosome 15q11-q13 (5 males and 10 females aged 16.3 ± 7.1 years) participated in the study. Age-matched controls who had been diagnosed as nonspecific mental retardation were selected from the same facilities where subject AS patients lived. Eight of the AS patients had circadian rhythm sleep disorder, which was confirmed by their sleep logs (irregular sleep-wake type; n = 4, delayed sleep phase type; n = 2, free-running type; n = 2). Serum melatonin levels in AS patients were measured every four hours throughout twenty-four hours, and the values were compared to the controls. Six AS patients having circadian rhythm sleep disorders took a daily dose of 1 mg melatonin at 8 PM for three months.
As a result of two way repeated ANOVA, secretion level of melatonin of AS patients was significantly lower than that of controls ($F(1, 27) = 12.6$, $p < 0.01$). However, there was no significant difference in secretion of melatonin between AS patients with and without circadian rhythm sleep disorder. The post hoc test showed that during night times (at 8 PM to 4 AM) secretion of melatonin of the AS patients were significantly higher than that of the controls. After the treatment with melatonin, nocturnal sleep patterns were improved in four of the AS patient.
The results of this study suggest that sleep problem, especially circadian rhythm sleep disorder, is highly frequent among AS patients. Low secretion levels of melatonin was thought to underlie the mechanism of circadian rhythm sleep disorder in the AS patients.

PO-1-191 / AS-27 Presenter

NOT CURRENT, BUT RECENT WEATHER IS ASSOCIATED WITH SUICIDAL ATTEMPTS IN TRAINS IN JAPAN

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Introduction: Seasonal affective disorder (SAD) is closely associated with circadian rhythm disorder and classified into depression in the DMS-IV. Blight light is the most effective therapy for SAD, and also effective for non-seasonal depression. Clinical response to the blight light therapy is usually observed within 1 to 2 weeks. Suicides are known to be committed not at the worst time of the depressive symptom, but during the recovery from the worst. We hypothesized that recent weather condition, especially hours of sunlight during the several days before, may affect suicidal attempts.
Methods: Three prefectures (Tokyo, Kanagawa and Osaka) were chosen as the target areas, because the numbers of suicide by train were largest in them. Databases of railway delay and of weather from 2001/10/01 to 2007/11/30 were analyzed (6816 dayprefecture).
Results: 1220 suicidal attempts were reported in the database. More than two suicides were attempted in the 108 dayprefecture. Multiple suicidal attempts were not associated with seasons ($p = 0.592$), day of the week ($p = 0.107$) nor weather condition of the attempted day (such as hours of sunlight ($p = 0.461$), cloud cover ($p = 0.388$), precipitation ($p = 0.465$) and humidity ($p = 0.112$)). There was a significant association between *average of hours of sunlight among one to five days before the suicidal attempts* and *multiple suicidal attempts*, even after adjustment of season, hours of sunlight and day of the week of the attempted day ($p = 0.005$).
Conclusion: Suicide by train is associated with the recent weather condition (average of hours of sunlight among several days before the suicidal attempts), and not with the weather conditions of the attempted day.

PO-1-192

MELATONIN AND SLEEP EFFECTS ON HEALTH, BEHAVIOR PROBLEMS AND PARENTING STRESS

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In children with sleep onset insomnia and delayed Dim Light Melatonin Onset (DLMO), melatonin treatment not only improves sleep but also health, behavior and parenting stress[1]. An important question concerning the effectiveness of melatonin is whether melatonin has a direct effect on these outcomes or whether the effect of melatonin is dependent on (improved) sleep. To our knowledge this is the first study addressing this question. 41 Children (24 boys, 17 girls; mean age = 9.43 years; mean DLMO = 20:57 h.) entered melatonin treatment (1–maximum 5 mg) for three weeks and then discontinued treatment by first taking a half dose for one week and then stopping completely for another week. Sleep was measured with sleep diaries filled in by parents and with actometers. There was a positive effect of sleep duration on health. Immediately after three weeks treatment health was better for children with longer sleep durations. This effect disappeared at the end of the stop week. In general, health decreased from directly after treatment to the end of the stop week. Behavior problems decreased from baseline to the end of the stop week and this decrease was stronger for children with an earlier DLMO. These results show that the effects of melatonin on health and behavior problems may partly be dependent on improved sleep.
Reference:
Maanen A van, Meijer AM, Smits MG, Oort FJ. Termination of short term melatonin treatment in children with Delayed Dim Light Melatonin Onset: Effects on sleep, health, behavior problems and parenting stress. Sleep Med. In press 2011.

PO-1-193 / AS-30 Presenter

SLEEP IN CHILDREN WITH ASTHMA: RESULTS OF THE PIAMA STUDY

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Asthma is a chronic inflammatory disorder of the airways, affecting approximately 5–15% of children (Sadeh, Horowitz, Wolach-Benodis, & Wolach, 1998). From the children between 2–15 years, 4–12% suffers from shortness of breath and 5–20% suffers from wheezy breathing (Smit, Boezen, & Poos, 2010).
Children with asthma have worse general health and a lower quality of life than children without asthma. Studies investigating sleep in children with asthma have not yielded clear results. More information is needed concerning the question whether sleep problems are more prevalent in children with asthma and to what extent children with less serious asthma differ from children with more serious asthma with regard to sleep.
In the present study we investigated frequency of sleep problems in Dutch children (10–12 years old) with asthma and we examined relations between asthma symptoms and different aspects of sleep (time in

bed, sleep latency, nighttime awakenings, sleepiness, tiredness). Both children and parents reported about sleep and asthma, and different diagnostic groups (doctor diagnosis, parental-reported asthma symptoms, and parental-reported frequent asthma symptoms) were distinguished and compared with healthy children.
Results of 2735 children, participating in the PIAMA (Prevention and Incidence of Asthma and Mite Allergy) birth cohort showed that children with frequent asthma symptoms reported more sleepiness or tiredness during the day ($x2$ (4) = 10.218, p = .037). For all other sleep aspects, children with asthma in all diagnostic groups did not differ from healthy children. Implications for clinical practice will be discussed.

PO-1-194

LONG-TERM SLEEPINESS AND FATIGUE SYMPTOMS FOLLOWING MODERATE/SEVERE TRAUMATIC BRAIN INJURY

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Daytime sleepiness and fatigue are often cited among the most prevalent consequences after traumatic brain injury (TBI). Despite a recent increase in scientific interest, the literature is still limited as most studies have focused on the acute recovery phase and/or have been conducted in heterogeneous samples in terms of injury severity. The aim of this study was to document long-term sleepiness and fatigue after moderate/severe TBI.
Participants were 22 adults with moderate/severe TBI (mean age = 37.5 years, 22.7% women, mean time since injury = 53 months) and 22 matched healthy controls (CTL; mean age = 37.0 years, 22.7% women). They underwent four 40-minute Maintenance of Wakefulness Tests (MWT), and completed the Epworth Sleepiness Scale (ESS), Functional Outcome of Sleepiness Questionnaire (FOSQ), Multidimensional Fatigue Inventory (MFI) and a 14-day sleep diary (SD). Groups were compared using t tests.
Groups did not differ on mean sleep onset latency on the MWT (TBI = 31.6 min vs. CTL = 35.1 min). Sleep onset REM periods were observed in two TBI participants. Subjective sleepiness was similar between groups (ESS total score: TBI = 7.8 vs. CTL = 7.6) but TBI participants reported greater consequences of sleepiness on daily life compared to CTL (FOSQ total score: 17.6 vs. 18.7; p = .04). Subjective fatigue was higher in TBI participants on the MFI composite score (49.4 vs. 38.0; p = .003). Sleep diary data revealed that TBI participants spent more time in bed at night (514.5 vs. 484.2 min; p = .03), and napped more frequently (3.3 vs. 1.3 naps/week; p = .006) and for a longer time (213.1 vs. 72.0 min/week; p = .009) during the day.
As a group, individuals with moderate/severe TBI do not seem to be pathologically sleepy when assessed at least one year after the injury. On the other hand, TBI patients could be more vulnerable to detrimental effects of sleepiness on daytime functioning. Additionally, they appear to use compensatory strategies such as increasing nighttime and daytime sleep opportunities.
This study was supported by the Canadian Institutes of Health Research.

PO-1-195 / AS-5 Presenter

TIMING NON-ADHERENCE IS ASSOCIATED WITH CHRONOTYPE IN RENAL TRANSPLANT RECIPIENTS

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Background: Chronotype refers to an individual's preferred sleep-wake cycle timing within the 24-hour day. The aims of this study were to describe chronotype distribution in adult renal transplant (RTx) recipients and to explore associations with sleep quality, sleepiness, anxiety, depression, stress and medication adherence.
Methods: Using a cross-sectional design, we included a convenience sample of 423 RTx outpatients (37.6% women; time since RTx: 9.33 ± 7.15 years; mean age: 58 ± 12.36 years) transplanted at a single European transplant centre. Chronotype was assessed with the modified Horne-Oestberg morningness-eveningness questionnaire; medication adherence with the BAASIS, sleep quality with the PSQI, and sleepiness with the ESS; psychological symptomatology with the DASS-21. Descriptive statistics and Spearman's correlation were used.
Results: The prevalence of timing non-adherence (NA) (deviation from dosing schedule >2 h) was 43.3%, poor sleep quality 48.9% (PSQI > 5) and daytime sleepiness 43.3% (ESS > 6); 19.9% reported depressive symptomatology, 25.1% anxiety and 17.7% stress. Patients were classified into five chronotype groups (morning type 13.9%, moderate morning type 42.1%, middle type 40.9%, moderate evening type 2.4% and evening type 0.7%). There were no significant gender differences between groups (Chi^2: 52, 66 (df:47); p: 0.264). Eveningness was significantly correlated with younger age (Spearman's rho: 0.27; $p < 0.01$) and higher frequency of not taking the medication on time (timing NA) (Spearman's rho: −0.11; p: 0.03), while other variables such as NA itself, sleep quality, daytime sleepiness, anxiety, stress and depression did not significantly correlate with chronotype in our cohort.
Conclusion: Morningness is highly prevalent in RTx recipients. Eveningness is rare, but is associated with higher timing NA and younger age, suggesting that the assessment of chronotype could help counseling to enhance adherence. RTx could be instructed to take their drugs later and consequently come away from the 8 am–8 pm schedule.

PO-1-196

A CROSS-CULTURAL META-ANALYSIS OF SLEEP PATTERNS AND PROBLEMS DURING ADOLESCENCE

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Introduction: Many adolescent sleep surveys have been performed within countries over the past decade. However, direct comparisons are rare. The present study conducted direct statistical comparisons of

adolescent sleep patterns and problems (ie, insomnia, daytime sleepiness) across 5 continents.
Method: Adolescent sleep surveys were included if they sampled 300+ participants aged 11–18 yrs, and were recently published (1999–2011). To increase the number of statistical comparisons, the authors' unpublished Australian ($N = 385$) and African ($N = 426$) data were included. Using these criteria, 41 published studies and 2 unpublished datasets were included. Sleep patterns were related to age ($p < .0001$), thus meta-analyses involved ANCOVAs with age as a covariate. Age-adjusted means are presented, with the exception of African data (N = 1, mean age = 16.5 yrs). Differences are reported if significance was detected or effect sizes were moderate-to-large.
Results: School-night sleep data showed variability between continents. Asian adolescents went to bed later (11:20 pm) than other adolescents (Europe = 10:40 pm; Australia = 10:19 pm; North America = 10:09 pm) except Africa (1:25 am), yet it was North American adolescents who obtained significantly less sleep (7.4 hrs) than their European and Australian peers (both 8.4 hrs). This was partly due to North American adolescents having earlier rise times (6:34 am) compared to their peers (Europe = 6:58 am; Australia = 7:05 am; Africa = 9:33 am). Weekend sleep data showed a similar pattern of differences, albeit a systematically later sleep scheduling across all continents ($p < .0001$). Difficulty falling asleep was commonly reported across samples, being experienced by 16% of teens. However, slightly more teens report a sleep latency >30 mins (25%). Daytime sleepiness was also common, with variable prevalence (5–53%) due to variations in measures used.
Conclusion: Culture is an influential extrinsic factor on adolescents' sleep. Considerable work is needed to conduct simultaneous comparisons to understand such cultural influences.

PO-1-197

MULTI-FOCUSED STUDY OF SLEEP DISORDER IN FUNCTIONAL DYSPEPSIA

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Backgrounds: Patients suffering from Functional Gastrointestinal Disorders often have complaints of sleep problems. According to the previous study, it has been reported that 20% of general population with sleep disturbance have gastric symptoms like functional dyspepsia (FD) (Santhi et al., 2000).
However, the pathological relationship between FD's symptoms and its sleep disturbances is so complicated that it has not been clarified at this time. Therefore, we performed multi-focused study to clarify the considerable clinical factors impacting on development of sleep disorders in FD.
Subjects and Methods:
1) Subjects:
FD group 30 (M/F 17/13, mean age 32.9 ± 8.9 y), who met the criteria of FD in Rome II.
Control group (CL) 45 (M/F 38/7, mean age 31.4 ± 6.3 y)
2) Measurements:
   a) Pittsburgh Sleep Quality Index (PSQI)
   b) Gastro-intestinal symptom rating scale (GSRS)
   c) Gastric emptying study (GE; ^{13}C-acetate breathe test)
   d) Drink test (DT; Visceral hypersensitivity test; drink 10 ml/kg of water for 5 minutes at equal rate)
   e) Psychological test (STAI, SDS, SCL90R, MMPI, SF36)

Results
1) Thirteen cases (43.3%) had over 5.5 points in total PSQI score in FD.
2) The sub items of PSQI were significantly higher than those of CL in sleep quality, sleep latency, and sleep difficulty in FD.
3) In terms of the correlation between total PSQI score and each items in FD group,
   a) The value of Tmax (the time to the maximum concentration of ^{13}C in breathe) in GE was not correlated.
   b) The DT score was not correlated.
   c) STAI-1 score (r = 0.457) and SDS score (r = 0.487) were significantly correlated.
   d) The scores of hypochondriasis, paranoid, and hypomania in MMPI were significantly correlated.
   e) Constipation score of GSRS was significantly correlated (r = 0.418). The abdominal pain score was correlated with sleep quality.

Conclusions: From our results, it was suggested that the gastric symptoms such as constipation and abdominal pain and mental condition may be responsible for the sleep disorder in functional dyspepsia.

PO-1-198

ASSOCIATIONS BETWEEN SLEEP AND AFFECTIVE LABILITY IN ADOLESCENTS WITH A BORDERLINE PERSONALITY DISORDER

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Introduction: A bidirectional association exists between sleep quality and mood regulation. Many recent adult studies have shown sleep abnormalities in Borderline Personality Disorder (BPD), which is characterised by hostility and severe affective lability, including depressive mood. However, little is known about sleep in adolescent BPD. This study had two objectives: to characterise sleep patterns in an adolescent euthymic BPD group and to determine whether these characteristics were associated with dimensional measures of mood.
Methods: Fourteen euthymic BPD adolescents (13–17 years old; 12 girls/2 boys) wore an actigraph and filled out a sleep diary (in order to validate actigraphy data) for at least nine days, including two weekends. They also completed self-reported questionnaires assessing mood instability (Affective Lability Scales; ALS), depressive state (Beck Depression Inventory), and hostility (Buss-Durkee Hostility Inventory) on the first day of actigraphy recording. Non parametric correlation analyses (Spearman Rank Correlation Coefficient) were performed to examine the association between sleep and mood.
Results: Preliminary results show that BPD adolescents without concurrent DSM-IV Depressive Disorders experience poor sleep efficiency (weekdays: 77.92 ± 7.67%; weekends: 76.55 ± 9.27%), and shorter total sleep time (weekdays: 430.67 ± 57.80 minutes; weekends: 459.16 ± 101.15 minutes) compared to published norms (i.e., 540–600 minutes per night). Percentage of time scored as sleep during the sleeping period was negatively correlated with ALS total raw score (r = −0.53): mood was less stable as total sleep time got shorter. Duration of wakefulness (in minutes) was also correlated with ALS total score (r = 0.56) during the sleep period.
Discussion: These results suggest that sleep quality and affective instability are interrelated in euthymic adolescent BPD. To confirm these preliminary findings, a greater sample size and a comparison control group (healthy adolescents) are needed.

PO-1-199

PROSPECTIVE ANALYSIS OF SLEEP PROBLEMS IN CHRONIC RHINOSINUSITIS

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Objectives: Chronic rhinosinusitis (CRS) is commonly encountered by ENT doctors. In recent years, various studies have been conducted regarding the effects of CRS on the patient's quality of life (QOL). However, few reports of its effects on the quality of sleep have been reported. The purpose of this study was to investigate the incidence of sleep problems associated with CRS and examine which factors are involved in sleep problems.

Study design: Multicenter prospective study

Subjects: 685 patients who were diagnosed with CRS between April 2007 and March 2008 were analyzed.

Methods: All of patients completed a QOL questionnaire using a scoring system 0~6 that included items regarding nasal symptoms and sleep. In addition, data were compiled for various background parameters; for example, the peripheral eosinophil count and the presence/absence of allergic rhinitis. The patients were stratified into two groups on the basis of sleep score results: 4 and over, and less than 4. Then the two groups were compared in regard to the data for above-described parameters. Logistic regression analysis was performed using the high sleep score group (4 and over) as explanatory variable and background parameters as dependent variables.

Results: The high sleep score was seen in 148 patients (21.6%). The scores for each of the nasal symptoms were significantly higher in the high sleep score group. The sleep score was significantly higher in the patients with a complication of allergic rhinitis and high peripheral and tissue eosinophil counts. Logistic regression analysis found that nasal congestion, cough and ear fullness were nasal symptoms that contributed to a high sleep score.

Conclusions: Some patients who have CRS experience sleep problems. In addition to nasal symptoms, inflammatory conditions such as allergic rhinitis and eosinophilic inflammation also have the potential to directly affect sleep problems. Subjective symptoms such as nasal congestion, cough, etc., are closely related to sleep problems.

PO-1-200

THE ROLE OF SLEEP DISTURBANCE AND DEPRESSION IN PATIENTS WITH TYPE 2 DIABETES

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Little is known about the relationship among sleep disturbance, depression and type 2 diabetes. The goal was to evaluate the role of these indices for the quality of life (QOL) in patients with type 2 diabetes. In the present study, 270 patients were recruited from the Shiga Prospective Observational Follow-up Study for Diabetic Complications. Depressive symptoms, sleep disturbance, and QOL were assessed using Zung Self-Rating Depression Scale (SDS), Pittsburgh Sleep Quality Index (PSQI), SF-8, respectively, following evaluation of their metabolic control and complications. Furthermore, 141 patients were completed the same study after 6–12 (mean 7.3) months. Significant correlations were found among sleep disturbance, depression and QOL in the patients with type 2 diabetes. The patients with insulin therapy showed significantly higher SDS scores, meaning more depressive symptoms, than that of the patients without insulin therapy. The patients with painful neuropathy had higher PSQI and SDS scores and lower physical component of the QOL score than those of the patients without painful neuropathy. In the follow-up observation, it was found that the presence of neuropathy and elevated HbA1c level were predicting factors for increasing PSQI score and SDS score, respectively. Furthermore, presence of painful neuropathy became the risk factor for sleep disturbance of type 2 diabetic patients. Sleep disturbance or depressive symptoms were significantly correlated with the QOL scores in the patients with type 2 diabetes, suggesting the importance of these indices for the better management of the diabetic patients.

PO-1-201

THE RELATIONSHIP BETWEEN DIGESTIVE SYMPTOMS AND SLEEP DISORDERS IN OUTPATIENTS OF PSYCHIATRIC CLINICS

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Aim: Sleep disorders is very common in psychiatric patients. Most of them also have several complaints of digestive symptoms, such as abdominal pain, nausea, constipation, and diarrhea.Concerning mechanisms of these abdominal symptoms, they may be influenced by

psychiatric symptoms, pharmacological treatments, and eating behavior based on primary mental disorders.However, little epidemiological study clarified the frequency of digestive symptoms in patients with mental disorders. Therefore, the aim of this study was to reveal the rate of patients having digestive symptoms and the correlation with sleep disorders in psychiatric patients.

This study was conducted with the approval of the Ethical Committee of Jikei university school of Medicine.

Subjects and methods:

1) Subjects: 128 outpatients (mean age 50.2 ± 12.5 y, M/F 73/55, ICD-10:F2/F3/F4/F5/others 22/45/41/18/2) who attended the Jikei university hospital and its three related facilities.

Control group (CL) 45 (mean age 31.4 ± 6.3 y, M/F 38/7)

Measurements:

(1) The rating scale for digestive symptoms
   a. Gastro-intestinal symptom rating scale (GSRS)
   b. Questionnaire for the diagnosis of reflux disease (QUEST)
   c. Frequency scale for the system of GERD (gastroesophageal reflux disease) (FSSG)

(2) The rating scale for Sleep, psychiatric symptoms, and QOL
   a. PSQI
   b. SCL-90-R
   c. SF-8™

Results:

(1) GSRS total score (1.9}0.8 points) was higher than that of normals (1.5}0.5). Concerning sub items of GSRS score, constipation score was significantly higher.
(2) 48 patients (37.5%) got 4 and above in QUEST.
(3) GSRS score was significantly correlated with PSQI score ($r = 0.396$, $p < 0.01$). In terms of the sub items of GSRS, all scores except diarrhea score had significant correlations with PSQI score ($p < 0.01$), and constipation score had the most striking correlation with it ($r = 0.387$, $p < 0.01$).

Conclusions: From our results, it was suggested that 40% of outpatients in psychiatric clinics might have GERD. Moreover, various digestive symptoms might be associated with the development of sleep disturbance, especially in constipation.

PO-1-202

THE INTERRELATIONSHIP BETWEEN HEADACHE AND SLEEP

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Objectives: This study investigated the relationship between headache and sleep by evaluating sleep quality, daytime sleepiness, and specific features related to sleep breathing disorders(SBD).

Method: 101 subjects suffering from headache, and 128 healthy controls without headache were enrolled. Headache group were diagnosed by using ICHD-II criteria and completed MIDAS questionnaire. All subjects were evaluated for the subjective quality of sleep by using PSQI and ESS. In addition, randomly selected 28 subjects of each group were evaluated of sleep features(including AHI, prevalence of SBD, nocturnal SaO2, ODI) by portable sleep monitoring device.

Results

1. PSQI and ESS scores were significantly higher in headache group than control ($p < 0.0001$). Also, the prevalence of poor sleeper (Global PSQI > 5) and daytime sleepiness (ESS > 10) were significantly higher in headache group ($p < 0.0001$).
2. The severity of headache, which was estimated by using NRS ($p = 0.03$) and MIDAS ($p = 0.001$), showed significant association with sleep quality. Chronicity of headache also showed significant association with sleep quality ($p = 0.003$) and prevalence of daytime sleepiness ($p = 0.03$). But, presence of morning headache did not show significant association with sleep quality and daytime sleepiness.
3. There were no significant differences in AHI, ODI, prevalence of SBD and nocturnal SaO2 between headache group and control. Also, there were no significant differences according to presence of morning headache.

Conclusion: There is a significant association between headache and sleep. Among various characteristics of headache, severity and chronicity were significantly associated with sleep quality and daytime sleepiness, while no statistically significant association was evident between headache and nocturnal hypoxia or SBD. A limitation of this study was that it was not based on polysomnography (PSG), but based on self-reported subject information about headache and sleep. Therefore, further study applying PSG will be needed.

PO-1-203

SLEEP, DEPRESSIVE BEHAVIOR AND INFLAMMATION IN A POST MYOCARDIAL INFARCT MODEL IN THE RAT

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Introduction: Myocardial infarction (MI) in humans is followed by depression in 15–30% of cases. Here we report the data obtained in a rat model upon chronic sleep recordings and biochemical analyses, before and after antidepressant treatment.

Methods: Sleep was recorded for 24 h in 40 rats. MI was then induced in 20 rats while the 20 others were sham controls. Escitalopram (10 mg/kg/day, i.p.) was administered to 10 MI rats and 10 controls while all other rats received saline; sleep was recorded again after 14 days. In 19 other MI rats and 20 sham rats, escitalopram was followed by tests of social Interaction, forced swimming sucrose preference; circulating levels of proinflammatory cytokines were measured after sacrifice.

Results: MI rats showed signs of impaired social interaction, behavioral despair and anhedonia; this was blocked by escitalopram. MI rats displayed prolonged sleep latency, short total sleep time, short latency to but short duration of Paradoxical Sleep (PS); escitalopram did not affect sleep in MI rats but decreased PS in controls. We found less choline acetyltransferase (ChAT)-positive neurons in the pedunculopontine tegmentum (PPT) area of MI rats compared to controls while the laterodorsal tegmentum (LDT) was intact. TNF-alpha, PGE2 and corticosterone plasma levels were higher in saline-treated MI rats compared to controls; escitalopram decreased TNF-alpha, IL-beta, and PGE2 levels in both groups of rats while IL-6 showed no differences whatsoever.

Conclusion: MI induces a behavioral syndrome compatible with signs of depression in humans. These behavioral impairments are reversed by the antidepressant escitalopram through a mechanism that could involve a reduction of pro-inflammatory cytokines. Sleep disorders of MI rats are compatible with depression in humans, paralleled by decreased brainstem cholinergic neurons, but not affected by escitalopram; this could suggest alternate pathophysiological pathways.

PO-1-204

SLEEP/WAKE REGULATION IN PPARƒ¿-KNOCKOUT MICE

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Peroxisome proliferator-activated receptor alpha (PPARƒ¿) is a transcriptional factors belonging to the nuclear receptor family that has an important role in controlling gene expression related to glucose/lipid metabolism. PPARƒ¿ is known for its role in promoting hepatic fatty acid oxidation and ketogenesis in response to fasting. Recent studies have shown that energy metabolism affects sleep regulation and sleep loss is also associated with impairments in glucose/lipid metabolism. Therefore, manipulations changing PPARƒ¿ likely affect sleep and other physiological phenotypes. In the current study, we examined the role of PPARƒ¿ in sleep/wake regulation using PPARƒ¿-knockout (KO) mice. Sleep, body temperature, locomotor activities, blood pressure and heart rate were recorded in PPARƒ¿-KO mice and their wild-type littermates (WT) fed ad lib at baseline, with 5-hr sleep deprivation (SD) and fasting for 24 hrs starting at light-phase onset. PPARƒ¿-KO and WT mice were identical in basal amount of wake/sleep, body temperature, blood pressure and heart rate. PPARƒ¿-KO mice showed decreased the amount of NREM sleep in the latter half of dark period and tended to have decreased locomotor activity. In addition, PPARƒ¿-KO mice demonstrated much higher EEG delta power in NREM sleep compared with WT. However, 5-hr SD induced similar rebound response of delta power in both PPARƒ¿-KO and WT mice. In response to fasting, during hours 17–24 of the fasting day, the amount of wake and blood pressure of PPARƒ¿-KO mice were suppressed in comparison to the WT. During that period, heart rate and body temperature decreased by fasting in both WT and PPARƒ¿-KO mice. These results suggest that PPARƒ¿ gene is required for the normal integration of sleep and blood pressure regulation in mice.

PO-1-205

LOWER THETA AND ALPHA ELECTROENCEPHALOGRAPHIC ACTIVITY IN YOUNG ADULT FEMALE SUBJECTS WITH SLEEP BRUXISM: A CASE CONTROL ANALYSIS

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Aims: Sleep bruxism subjects often report transient morning pain in the first hours after an awakening. Jaw muscle pain has been observed to be gender specific with a higher prevalence in females. Middle-aged female patients with chronic widespread musculoskeletal pain (e.g. fibromyalgia) have been reported to present a gender specific reduction of sleep electroencephalographic (EEG) slow wave activity. The objective of this study was to compare sleep EEG activity of young healthy subjects and SB subjects with or without transient morning pain to assess if any gender specificity could explain female susceptibility to report pain.
Methods: A retrospective analysis on sleep laboratory data (second night) collected from 62 sleep bruxism-tooth grinding (SB) subjects and 19 age- and gender-matched control individuals (CTRL) was performed. Prevalence and intensity of morning jaw muscle pain, orofacial pain, and sleep disruption were assessed by questionnaires. EEG delta to beta power activities were quantitatively analyzed across four consecutive non-REM and REM sleep cycles. Statistical comparisons between CTRL and SB subjects with or without transient morning pain were conducted according to gender distribution.
Results: 71% of SB subjects reported transient morning jaw muscle pain. Among them, no gender difference was noted in pain reports. From the quantitative analysis, the EEG power for each frequency bands were not different between CTRL and SB, whether or not transient morning pain was present. However, female SB subjects, with and without morning pain, had a lower power of theta and alpha EEG activities in comparison to female CTRL subjects ($p = 0.03$).
Conclusion: Young SB female subjects had a lower power of theta and alpha EEG activity during sleep, whether or not they presented morning transient muscle pain. Sleep of SB patients does not seem to be influenced by the onset of muscle pain. (Supported by CIHR)

PO-1-206

TREATMENT OF BIPOLAR DEPRESSION ASSOCIATED WITH COMORBID DEVELOPMENTAL DISORDER IN ADULTS. EFFECTS OF THE LIFE RHYTHM THERAPY TARGETED AT SLEEP DISTURBANCES

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Introduction: Bipolar depression tends to be refractory to treatment and takes a prolonged course. Its atypical symptoms such as hypersomnia or hypersensitivity to rejection makes patients difficult to go out, preventing their rework. We have already stressed that certain vulnerability of sleep-wake rhythm associated with developmental disorder is involved in prolongation of disease phases of mood disorder.
Subjects and Methods: The subjects were five adults with developmental disorders who had comorbid bipolar disorder (age 30–40 Male n = 1 Female n = 4). All the subjects showed irregular sleep-wake rhythm disturbances corresponding to episodes. The subjects had more episodes of irritability, impulse, dissociative symptoms, personality change, and criminal behaviors during the periods of manic-depressive mixed state. Combined administration of mood stabilizers and atypical antipsychotic agents relieved these symptoms. Sleep disturbances were treated with co-administration of modafinil, melatonin, and Chinese herbal medicines such as TJ-35 and TJ-83. Meanwhile, the subjects were instructed to keep sleep logs to monitor their daily sleep-wake rhythm. Furthermore, structurization of lifestyle cycle was attempted

by setting daily routines referring to SPELL developed by the National Autistic Society in the UK and the therapeutic concept based on treatment methods of patients with affective psychosis at Sanatorium Bellevue in Switzerland at the end of 19th century.
Results: The five adults with developmental disorder tended to show sleep-wake rhythm disturbances induced by interpersonal stress or the lost of daily routine. As the patients became to do daily routines efficiently, their depressive mood and malaise were improved. Furthermore, it was suggested that stabilization of sleep-wake rhythm may play a role in preventing recurrence of episodes.
Discussion: Both SPELL and traditional Bellevue methods may be useful for stabilizing sleep-wake rhythm by structuring lifestyle cycle of patients with developmental disorder.

PO-1-207

THE CLINICAL PRESENTATION OF ADOLESCENTS WITH DELAYED SLEEP PHASE DISORDER

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Introduction: Adolescents typically display a pattern of delayed sleep timing, but in extreme cases this develops into Delayed Sleep Phase Disorder (DSPD). Few data exist regarding the clinical characteristics of adolescents who present for treatment for their DSPD. The objective of the present study was to provide information on the clinical presentation of adolescents with DSPD.
Methods: Data were obtained from 49 adolescents (14.6}1.0 yrs, 53% males) diagnosed with DSPD. Diagnosis was made via a 1-hr clinical sleep history interview with the adolescent and at least one parent, as well as a 7-day sleep diary and simultaneous wrist actigraphy recording. Adolescents also completed sleepiness, fatigue and depression questionnaires.
Results: 100% of adolescents reported a gradual onset of their sleep problem, occurring at ~10 yrs. 100% reported their schooling was affected by their sleep disorder, with 16% not attending school. All reported insomnia symptoms, including difficulty falling asleep and waking, as well as cognitive arousal in bed (eg, mind racing). Interestingly, adolescents misperceived their sleep onset time by 14 min, however this difference was driven by gender with females misperceiving more than males. Once asleep though, no misperception of sleep time occurred. In terms of sleep hygiene, 89% possessed electronic media in their bedroom (eg, cell phone), 35% consumed caffeine in the afternoon, 33% took frequent longs naps, and 14% used social substances (ie, alcohol, THC). In terms of emotional functioning, 5% had a diagnosis of a mood disorder, however overall, the frequency of depression symptoms was surprisingly low. In contrast, daytime sleepiness and fatigue were moderate-to-high.
Conclusions: Adolescents presenting with DSPD possess a number of clinical characteristics that may factor into the maintenance of their sleep disorder. These include poor sleep hygiene and insomnia symptoms. Consideration of these factors is warranted when treating adolescents for their DSPD.

PO-1-208

SLEEP QUALITY IN THE ELDERLY POPULATION WITH DIABETES MELLITUS, HYPERTENSION AND HYPERLIPIDAEMIA

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Introduction and objective: The elderly are known to have poor quality sleep. In individuals with diabetes mellitus, hypertension and hyperlipidaemia, this might be a result of obstructive sleep apnoea, which they are more susceptible to developing. The objective of this study was to evaluate the various demographic factors, co-morbidities (other than diabetes, hypertension and hyperlipidaemia), and lifestyle factors so as to identify risk factors and protective factors of poor sleep quality.
Materials and methods: This cross-sectional study was conducted in the primary healthcare setting (Outram Polyclinic) in Singapore. bidities were identified. The responders' sleep quality were then assessed with the Pittsburgh Sleep Quality Index (PSQI) questionnaire. Additional information on demographics, co-morbidities and lifestyle practices were collected. The study population was then divided into those with good quality sleep and those with poor quality sleep, based on the PSQI score. We then applied univariate, bivariate and multivariate analyses on the risk factors and protective factors studied.
Results: 199 patients out of the 226 patients identified responded to the questionnaire, obtaining a response rate of 88.1%. Using cox regression analysis, nocturia (prevalence rate ratio 1.542, 95% confidence interval 1.056–2.251) was found to be associated with an increased risk of poor sleep quality.
Conclusion: Nocturia is a prevalent problem in the geriatric population and it has been found to be associated with poor sleep quality in our study. Hence it is imperative to address this issue, whether by means of lifestyle modification or good control of co-morbidities, especially diabetes.
Acknowledgement: We would like to thank Dr Daniel J. Buysse for permission to use the Pittsburgh Sleep Quality Index questionnaire in our study.

PO-1-209

QUANTITATIVE EEG ABNORMALITIES IN IDIOPATHIC REM SLEEP BEHAVIOUR DISORDER

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Idiopathic REM sleep behaviour disorder (iRBD) is considered as a risk factor for synucleinopathies, such as Lewy body dementia (LBD) and Parkinson's disease (PD). A slowing of the electroencephalogram (EEG) during wakefulness has already been reported in LBD and PD. The objective of the study was to compare the EEG during a resting state between a relatively large group of iRBD patients and healthy controls.

A total of 45 iRBD patients (mean age, 66.7} 9.0 years) and 45 healthy subjects (mean age, 63.8} 10.9 years) were studied. Quantitative analyses of the absolute and relative spectral power were performed for five frequency bands, namely delta (0.75–4.0 Hz), theta (4.0–8.0 Hz), alpha (8.0–13.0 Hz), beta1 (13.0–22.0 Hz) and beta2 (22.0–32.0 Hz) in five cortical regions: frontal, central, parietal, occipital and temporal. The ratio of the absolute power of delta and theta over beta1 and beta2 (D+T)/(B1+B2) was calculated as a specific index of cortical slowing. Between-group differences on absolute and relative power were assessed by mixed ANOVAs (Group by Band) for each region while between-group differences on the ratio was assessed by a mixed ANOVA (Group by Region).
iRBD patients showed a higher delta and theta absolute power in central, parietal, occipital and temporal regions, a higher theta and lower beta1 relative power in parietal, occipital and temporal regions, in addition to a lower alpha relative power in the occipital region in comparison with control subjects. The analyses also showed that iRBD patients had a higher (D+T)/(B1+B2) ratio than controls in the five cortical regions.
This study indicates the presence of a diffuse slowing of the EEG during wakefulness in iRBD patients similar to that reported in some neurodegenerative diseases like PD and DLB.

PO-1-210

REM SLEEP BEHAVIOR DISORDER IN PSYCHIATRIC PATIENT: A CASE-CONTROL STUDY

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Objective: REM sleep behavior disorder (RBD), a parasomnia commonly occur in elderly population, has been increasingly reported in patients taking antidepressants, and was commonly regarded as "secondary RBD". However, there was limited literature to document its clinical and polysomnographic features.
Method: A case-control study consisting clinical and polysomnographic assessments. We recruited 21 psychiatric RBD patients and matched them with two control arms: 1) age, sex and psychiatric diagnosis matched control subjects from psychiatric clinic, 2) Typical idiopathic RBD of elderly population from sleep clinic.
Result: Psychiatric RBD patients were found to have comparable clinical features and degree of sleep-related injuries to that of typical RBD of elderly population. Comparing to the matched psychiatric controls, who were also prescribed with antidepressants, psychiatric RBD subjects had significantly more nightmares, dream enactment and resultant sleep-related injuries. They also had higher REM related EMG activities compared to psychiatric controls. A dosing effect was observed in REM EMG tonic activities across typical RBD, psychiatric RBD and psychiatric controls.
Conclusion: Psychiatric RBD is comparable to typical RBD in terms of the high prevalence of sleep-related injuries and personal distress. Our study suggests that RBD in psychiatric patients is not solely contributed by antidepressant. The presence of excessive REM-related tonic EMG activities may suggest a potential early neurodegenerative process as an aetiological component in psychiatric RBD. Further neuropsychiatric assessment and prospective follow-up is needed to clarify the relationship between RBD among psychiatric patients and typical elderly population, also its neurodegenerative outcomes.

PO-1-211

PRECLINICAL SUBSTANTIA NIGRA DYSFUNCTION IN IDIOPATHIC RAPID EYE MOVEMENT SLEEP BEHAVIOR DISORDER PATIENTS

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Introduction: REM sleep behavior disorder (RBD) is a parasomnia characterized by dream-enacting behaviors, unpleasant dreams and lack of muscle atonia during REM sleep. RBD may be idiopathic or related to neurological diseases. An increased risk of developing Parkinson's disease (PD) in patients with idiopathic RBD (iRBD) was reported. Transcranial sonography (TCS) has been shown to reveal hyperechogenicity of the substantial nigra (SN) in PD and in about 10% of healthy subjects. It is hypothesized that SN hyperechogenicity in healthy subjects and iRBD patients is a vulnerability marker for PD.
Methods: To assess nigrostriatal function in iRBD, TCS and 6-[^{18}F] FMT-PET were performed in 19 males with polysomnography-(PSG) confirmed iRBD (mean 66.4 years of age; mean estimated RBD duration 3.5 years).
Results: Nine of the iRBD patients were found to have SN hyperechogenicity (SN+), but the remaining 10 iRBD patients did not have SN hyperechogenicity (SN-). FMT uptake at the putamen and caudate was significantly lower in patients with iRBD (SN+) than in patients with iRBD (SN-). However, no correlation was found between SN echogenicity and FMT uptake.
Conclusions: Pathological hyperechogenic alterations in the area of the SN in iRBD may suggest the existence of preclinical substantia nigra dysfunction as determined by FMT-PET.

PO-1-212

PERSONALITY TRAIT IS NOT RELATED WITH THE OCCURRENCE OF REM SLEEP BEHAVIOR DISORDER

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Rapid eye movement sleep behavior disorder (RBD) occurs idiopathically (iRBD) and frequently represents a prodromal phase of Parkinson's disease (PD). Previous reports have suggested that patients with PD premorbidly show personality traits such as industriousness, inflexibility, cautiousness, and lack of novelty seeking. Additionally, psychological stress often causes aggravation of RBD symptoms. These phenomena encouraged us to investigate personality traits in iRBD patients.
53 patients with iRBD (M : F = 41 : 12, age 65.5 ± 6.3) and 49 age and sex matched healthy controls (HC) (M : F = 33 : 16, age 64.7 ± 4.6) were enrolled in this study. The new revision of the NEO Personality Inventory (NEO-PIR) were used to measure personality of these subjects, and the 5 domains and the 30 facets of the NEO-PIR were compared between the two groups. Among iRBD group, association between RBD variables; e.g. proportion of REM sleep without atonia (RWA/REM), length of RBD morbidity, frequency of vocalization or abnormal behavior, and the variables of NEO-PIR was investigated.

Domain level analyses revealed that no significant differences were found between the two groups. Facet-level analyses revealed that only the Fantasy facet was significantly higher in iRBD group than the HC group; however, the scores of this facet in both of the two groups were within normal level. In iRBD group, neither the domains nor the facets showed differences between the patients with and without stress related aggravation of RBD symptoms. Among the clinical descriptive RBD variables, RWA/REM showed significant but weak correlations with frequency of vocalization ($r = .289$, $p < 0.05$), the score of Neuroticism ($r = .338$, $p < 0.05$) and its subscales; Angry Hostility ($r = .299$, $p < 0.05$), Self-Consciousness ($r = .290$, $p < 0.05$), and Vulnerability ($r = .272$, $p < 0.05$). The present result suggests that patients with RBD have no noticeable personality traits, which may underlie the development of PD.

PO-1-213

COMPARISON OF POLYSOMNOGRAPHIC FINDINGS AND REM SLEEP BEHAVIOR DISORDER BETWEEN PATIENTS WITH PROGRESSIVE SUPRANUCLEAR PALSY AND THOSE WITH PARKINSON DISEASE

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Purpose: REM sleep behavior disorder is a strong indicator of underlying synucleinopathies. However, the frequency of REM sleep behavior disorder in tauopathies such as progressive supranuclear palsy remains unclear. In this study, we compared REM sleep behavior disorder related symptoms and polysomnographic findings between patients with progressive supranuclear palsy and Parkinson disease.
Methods: We conducted clinical interviews on 20 patients with progressive supranuclear palsy, 93 patients with Parkinson disease and their caregivers regarding REM sleep behavior disorder related symptoms. In addition, we made polysomnographic recordings on all the subject patients. We then compared the patients clinical backgrounds, parameters of Polysmnographies, and frequency of REM sleep behavior disorder related symptoms between the two groups.
Results: Patients with progressive supranuclear palsy had more severely disturbed nocturnal sleep than those with Parkinson disease. progressive supranuclear palsy group showed a significantly smaller number of patients with REM sleep without atonia than in those with Parkinson disease group. None of the progressive supranuclear palsy patients were experiencing REM sleep behavior disorder related symptoms, while 20 Parkinson disease patients had REM sleep behavior disorder related symptoms.
Conclusion: The existence of REM sleep wihtout atonia on polysomnographic findings and REM sleep behavior disorder related symptoms on interviews were less frequent in patients with progressive supranuclear palsy than in those with Parkinson disease.

PO-1-214

EVALUATION OF CONTRIBUTING FACTORS TO RESTLESS LEGS SYNDROME IN MIGRAINE PATIENTS

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Backgrounds: Recent studies have provided evidence for a positive association between migraine and restless legs syndrome, although the exact mechanisms and factors remain unclear.
Methods: A cross-sectional, case-control study was conducted, including patients with migraine (n = 262) and headache-free control subjects (n = 163). Restless legs syndrome was diagnosed based on four essential criteria as described by the International Restless Legs Syndrome Study Group. A total of 210 blood samples were collected to correlate various parameters with restless legs syndrome.
Results: Frequency of restless legs syndrome was significantly greater in patients with migraine than in controls (13.7% vs. 1.8%). Migraine patients with restless legs syndrome had high scores for Migraine Disability Assessment questionnaire, Beck Depression Inventory-II, Pittsburgh Sleep Quality Index, and Epworth Sleepiness Scale compared with those without restless legs syndrome. In addition, migraine patients with restless legs syndrome had a high rate of smoking and family history of restless legs syndrome, as well as increased levels of serum phosphorus and urea nitrogen compared with those without restless legs syndrome. In migraine patients, logistic regression analysis revealed that positive family history of restless legs syndrome, depressive symptoms, daytime sleepiness, and increased serum phosphorus levels were significant predictors for restless legs syndrome.
Conclusion: Our study confirmed a positive association between restless legs syndrome and migraine. Comorbidity of restless legs syndrome in migraine patients was associated with insomnia, daytime sleepiness, depressive symptoms, headache-related disability, and increased serum phosphorus levels. These findings may provide a better understanding of restless legs syndrome pathogenesis in migraine.

PO-1-215

APPEARANCE OF PERIODIC LIMB MOVEMENTS DURING SLEEP ON THE NIGHT OF CONTINUOUS POSITIVE AIRWAY PRESSURE IN OBSTRUCTIVE APNEA SYNDROME

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Objectives: Periodic limb movements during sleep (PLMs) sometimes newly appear on the night of continuous positive airway pressure (CPAP) titration in patients with obstructive sleep apnea syndrome (OSAS). To ascertain the incidence of and causative factors for this phenomenon, we investigated differences in the prevalence and associated factors for new appearing and persistence of PLMs on CPAP titration night.
Method: We retrospectively analyzed 997 consecutive OSAS outpatients who received CPAP titration. On the basis of changes in periodic limb movements index (PLMI) values (cut off level <= 15/h) from baseline PSG to CPAP titration PSG, patients were assigned to the persistent, CPAP emergent, CPAP disappearance, or non-PLMs group.
Results: The rate of the number of the patients was 6.7% in the persistent group, 8.0% in the CPAP emergent group, 4.0% in the CPAP disappearance group, and 81.2% in the non-PLM group. Multiple logistic regression analysis revealed that CPAP emergent PLMs were associated with a higher apnea-hypopnea index score (<= 30/h) on baseline PSG and aged <= 47 years and that persistent PLMs were associated with being female and aged <= 47 years.
Conclusion: A significant number of OSAS patients may develop CPAP emergent PLMs. Both CPAP emergent PLMs and persistent PLMs appear

to be age-dependent phenomena. Additionally, CPAP emergent PLMs were associated with OSAS severity. These findings provide some clues for predicting the occurrence of PLMs during CPAP titration.

PO-1-216

SEASONAL OR TEMPERATURE CHANGE COULD AFFECT SENSORY SYMPTOMS OF RESTLESS LEGS SYNDROME (RLS)

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Background: Restless legs syndrome (RLS) is a neurological disorder characterized by an urge to move of the legs and most RLS patients experience uncomfortable sensation of the legs. Change of the severity of RLS symptoms related to seasonal or temperature change is clinically experienced, however, this phenomenon has not been analyzed in detail.
Objectives: The aim of the study was to elucidate whether the seasonal or temperature change could affect the severity of RLS symptoms.
Methods: Fifty-two consecutive RLS patients (21 males and 31 females, mean age: 59.1 SD 16.0) who consulted Hiroshima Sleep Center were included in the study. Difference in sensory symptoms of RLS related to season or temperature conditions, and dose of medical treatment for RLS related to the seasonal change were investigated.
Results: Sensory symptoms worsened at summer in 19% of the RLS patients and worsened at winter in 17% of the patients. Patients with summertime worsening experience relief of the symptom in cooler condition in 60% and worsening of the symptom in warmer condition in 40%. Patients with wintertime worsening experience relief of the symptom by bathing in 33% and worsening of the symptom in warmer condition in 44%. Among the 14 patients with seasonal worsening under medication followed up for at least one year, increased dose of medication was required in 8 patients when their symptoms were worse due to seasonal change.
Conclusions: Severity of RLS symptom could be affected by seasonal or temperature difference. Seasonal worsening of the symptoms may mimic augmentation and should be differentiated.

PO-1-217

SLEEP AND LIFE QUALITY IN UNTREATED PATIENTS WITH PRIMARY RLS

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This study investigates the sleep architectures by polysomnography (PSG) and the quality of life in untreated patients with symptoms of RLS. We enrolled consecutively 69 untreated RLS patients that met the RLS criteria of ICSD2. All patients completed the overnight polysomnography (PSG), Restless Leg syndrome Quality of Life questionnaire (RLSQOL), International RLS scale (IRLSS), Beck Depression Inventory (BDI), Epworth Sleepiness Score (ESS), Stanford Sleepiness Score (SSS), and Suggested Immobilization Test (SIT). According to RLS severity, patients were divided to 3 groups (mild, moderate and severe).We excluded the 14 comorbid patients with obstructive sleep apnea (OSA) (AHI more than 10 per hr) because of considerable effects on sleep architectures and daytime consequences and the 13 patients with incorrect or incomplete data. Total 42 patients were analyzed (mean age, 54.6 yrs, 26 females). The mean duration of RLS was 12.7 years. Mean ESS was 8.1 and SSS was 2.8. Mean IRLSS for severity was 22.7 and mean SIT score was 25.7. Mean RLSQOL was 65.8 and BDI score was 11.3. All patients complained the sleep onset insomnia due to RLS symptoms, but their mean sleep latency was within normal range (17.7 min). But, they showed sleep maintenance problem (increased wakefulness after sleep onset, mean 79.2 min). Also twenty seven patients had periodic limb movement during sleep (mean PLMS index, 24.1 per hr, movement arousal index, 4.1 per hr). The RLSQOL, SIT score, and BDI score were significantly different between mild, moderate, or severe RLS group. RLSQOL and SIT score were significantly correlated RLS severity (p less than 0.01). Total sleep time and arousal index were significant correlated with RLS severity. RLS patients had poor quality of sleep and RLS severity was well correlated with RLSQOL, SIT, and BDI scores.

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ASSOCIATION BETWEEN IRRITABLE BOWEL SYNDROME AND RESTLESS LEGS SYNDROME IN GENERAL POPULATION

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Background and Objectives: The association of restless legs syndrome (RLS) with gastrointestinal disorders has been reported. The aim of this study is to document the association of RLS with irritable bowel syndrome in general population.
Methods: We recruited 3,425 Korean adult population aged 44 to 73 years who participated in a comprehensive health examination and on-site interviews as the third stage of evaluation of Korean Genome and Epidemiology Study performed from March 2005 and November 2006. The diagnosis of RLS was based on the criteria proposed by International RLS Study Group and IBS was defined according to the Rome II criteria. The prevalence of each condition was defined and their association was checked by multiple logistic regression analysis. Age, gender, renal function, depressive mood, use of RLS provocating drugs and iron or vitamin supplements, and alcohol drinking and smoking status were adjusted.
Results: The prevalence of RLS and IBS was 4.5% and 10.9%, respectively. RLS subjects had shorter nocturnal sleep (6.5 ± 1.4 vs. 6.8 ± 1.4, $p = 0.04$), lower hemoglobin concentration (13.7 ± 1.5 vs.14.1 ± 1.6, $p = 0.003$), more insomnia (44.4% vs. 28.3%), higher Epworth Sleepiness Scale (6.5 ± 3.8 vs. 5.8 ± 3.4, $p = 0.01$) and depression (27.5% vs. 12.6%, $p < 0.001$) than subjects without RLS. There was no difference in renal function, cardiometabolic status, and use of iron or vitamin supplement between two groups. IBS was significantly prevalent in the RLS group compared with subjects without RLS (23.5% vs. 1.4%, $p < 0.001$). The adjusted odds ratio of RLS in relation to IBS was 2.56 [1.72, 3.80; $p < 0.001$].
Conclusions: This study broadens the spectrum of RLS associated conditions and indicates that RLS needs to be screened in all patients with IBS.

PO-1-219

PREVALENCE OF RESTLESS LEGS SYNDROME AMONG PATIENTS WITH OBSTRUCTIVE SLEEP APNEA BEFORE AND AFTER CPAP TREATMENT, COMPARED TO THE GENERAL POPULATION

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Objectives: To compare the prevalence of reported restless legs syndrome (RLS) between subjects with obstructive sleep apnea (OSA) and a randomly chosen sample from the general population as well as possible changes with CPAP treatment.
Materials and Methods: The OSA subjects (n = 822) were a part of the Icelandic Sleep Apnea Cohort. They were newly diagnosed with moderate or severe OSA (665 males, 157 females). The control subjects (n = 742) were randomly chosen Icelanders (394 males, 348 females) who participated in another epidemiological study (www.boldcopd.org). Measurements included a standardized RLS rating scale, questions about sleep and the Epworth Sleepiness scale. The change with CPAP treatment was assessed after 2 years (n = 538).
Results: Among OSA males 23.3% reported RLS but 12.9% of control males ($p < 0.001$). 35.8% of OSA females reported RLS but 24.4% of control females ($p = 0.03$). Both among OSA patients and controls those with RLS more commonly reported insomnia, daytime sleepiness, nocturnal sweating, snoring and gastro esophageal reflux ($p < 0.05$). They were more likely to be females and to have a smoking history. No relationship was found between RLS and age, BMI, hypertension or respiratory disease in a logistic regression adjusting for the presence of OSA and the other factors mentioned. No relationship was found between RLS and sleep apnea severity. Subjects using CPAP had a decreased prevalence of RLS from 25.7% to 13.8% while no change was observed in those subjects not using CPAP ($p = 0.04$ for difference between groups). Subjects that had persistent RLS were older on average and had a lower physical quality of life at baseline.
Conclusions: RLS is more prevalent among OSA patients than controls. No relationship was found with sleep apnea severity or BMI. CPAP treatment of OSA decreases RLS symptoms significantly. RLS symptoms are significantly related with insomnia and daytime sleepiness in both OSA subjects and controls.

PO-1-220

DAYTIME SOMNOLENCE IN PATIENTS WITH RESTLESS LEG SYNDROME

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Background: Restless legs syndrome (RLS) is known to induce sleep fragmentation. However, subjective daytime sleepiness scale was reported lower in RLS patients compared to patients with other sleep disorders. To investigate the daytime sleepiness in RLS patients, we performed the polysomnography (PSG) and Multiple Sleep Latency Test (MSLT).
Methods: We enrolled consecutively 125 untreated RLS patients who met the RLS criteria of ICSD-II. But we excluded 29 co-morbid patients with obstructive sleep apnea (OSA) or two or more sleep onset REM periods because of the possibility of having co-morbid narcolepsy. Total 96 patients were analyzed (mean age 55.1 years, 66 females). We performed Epworth Sleepiness Score (ESS), Stanford Sleepiness Score (SSS), and Suggested Immobilization Test (SIT) in all patients. International RLS scale (IRLSS) was performed in 86, PSG in 71, and MSLT in 45.
Results: Mean ESS was 7.2 and SSS was 3.0. Most of RLS patients have moderate to severe symptoms on IRLSS (more than 5). Of them only 17 patients reported moderate to severe daytime sleepiness (ESS more than 11). Mean IRLS score for severity was 23.1 and mean SIT score was 26.7. SIT scores were not significantly correlated with ESS but were correlated with RLS severity (p less than 0.01). On MSLT, their mean sleep latency was 9.8 min and less than or equal to 8 min in 15 patients.
Conclusions: Although most RLS patients did not report daytime sleepiness, their mean sleep latency on MSLT was definitely shorter in about half of them. These findings suggest that daytime sleepiness of them may be related to the concentration and memory deficit and mood disturbances, which were frequently found in RLS patients.

PO-1-221

TRANSCUTANEOUS CARBON DIOXIDE LEVELS DURING NOCTURNAL PERIODIC LEG MOVEMENTS

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Conflicts of Interests: None
Keywords: Transcutaneous carbon dioxide, periodic leg movements, sleep, autonomic nervous system, vascular function, sympathetic activity
Objective: Periodic leg movements are associated with sympathetic activation. The purpose of the study was to compare the characteristics of those periodic leg movements (PLM) that do associate or do not associate with phasic or tonic sympathetic outflow to the skin.
Methods: The sympathetic outflow to the skin was detected as variable transcutaneous carbon dioxide partial pressure below the nocturnal tcCO2 plateau level, resulting from vasoconstriction of the cutaneous vessels. The high and stable tcCO2 plateau indicated a parasympathetic state with absence of vasoconstriction or sympathetic influence. The PLM characteristics and their ECG responses were analyzed during periods of either low and unstable or high and stable tcCO2 levels in 111 cardiorespiratory sleep recordings.
Results: PLM with high intensity appeared during periods on low and unstable tcCO2, whereas PLM with lower intensity occurred, when the tcCO2 had reached high and stable levels, characteristic for slow-wave sleep. Heart rate responses were associated with majority of the PLM, irrespective of the tcCO2 conditions.
Conclusions: High intensity PLMs are associated with tonic and phasic vasoconstriction of the skin arteries indicating increased sympathetic outflow to the cutaneous vascular bed. PLM with lower intensity appeared during the vasodilated state, suggesting less sympathetic intrusion and sleep disturbance.

PO-1-222

ACTIGRAPHIC ASSESSMENT OF PERIODIC LEG MOVEMENTS FOR PATIENTS WITH RESTLESS LEGS SYNDROME

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Background: The diagnosis of restless legs syndrome relies on the essential diagnostic criteria. Supportive criteria including response to dopaminergic treatment and periodic leg movements on polysomnography enhance diagnostic sensitivity. Restless legs patients who do not fulfill the supportive criteria may need an alternative treatment.
Methods: We retrospectively included 25 consecutive patients fulfilling the essential criteria for restless legs and 17 healthy controls. All subjects underwent actigraphy over three nights, and patients started treatment with dopaminergic drugs thereafter. We examined the association between the response to dopaminergic treatment and the periodic limb movement index as assessed with actigraphy.
Results: Responders had significantly higher periodic limb movement index than non-responders. Periodic limb movement was significantly lower in control subjects.
Conclusions: Periodic limb movement as assessed with actigraphy over three nights may predict the response to dopaminergic treatment in patients who fulfill the four essential criteria of restless legs.

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HYPOCRETIN (OREXIN) LOSS IN ALZHEIMER'S DISEASE

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Sleep disturbances in Alzheimer's Disease (AD) patients are associated with the severity of dementia and are often the primary reason for institutionalization. These sleep problems partly resemble core symptoms of narcolepsy, a sleep disorder caused by a general loss of the neurotransmitter hypocretin. AD is a neurodegenerative disorder targeting different brain areas and types of neurons. In this study, we assessed whether the neurodegenerative process of AD also affects hypothalamic hypocretin/orexin neurons. The total number of hypocretin-1 immunoreactive neurons was quantified in post-mortem hypothalami of AD patients (N = 10) and matched controls (N = 10). In addition, the hypocretin-1 concentration was measured in post-mortem ventricular cerebrospinal fluid of 24 AD patients and 25 controls (including the 10 patients and 8 controls in which the hypothalamic cell counts were performed). The number of hypocretin-1 immunoreactive neurons was significantly decreased by 40% in AD patients (median (25th-75th percentiles); AD 12,935 neurons (9,972–19,051); controls 21,002 neurons (16,439–25,765); p = 0.049). Lower CSF hypocretin-1 levels were found in 24 AD patients compared to 25 controls (AD: 275 pg/ml (197–317); controls: 320 pg/ml (262–363); p = 0.038). Two AD patients with documented excessive daytime sleepiness showed the lowest CSF hypocretin-1 concentrations (55 pg/ml and 76 pg/ml). We conclude that the hypocretin system is affected in advanced AD. This is reflected in a 40% decreased cell number, and in 14% lower CSF hypocretin-1 levels.

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NOCTURNAL DISTURBANCES IN PARKINSON'S DISEASE: A VALIDATION STUDY OF PARKINSON'S DISEASE SLEEP SCALE-2 JAPANESE VERSION

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Backgrounds: Sleep disturbances are common, but often difficult to be evaluated in Parkinson's disease. Very recently, revised version of Parkinson's disease sleep scale, Parkinson's disease sleep scale-2, has been developed for assessing nocturnal disturbances. The aim of this study was to assess a validity and reliability of the Japanese version of Parkinson's disease sleep scale-2 and to evaluate nocturnal disabilities by this new scale.
Methods: A cross-sectional, case-control study was carried out consisting of patients with Parkinson's disease (n = 90) and age- and gender-matched control subjects (n = 90). Parkinson's disease sleep scale-2 Japanese version was used for evaluation of nocturnal disturbances, Pittsburgh Sleep Quality Index for insomnia and Epworth Sleepiness Scale for daytime sleepiness. Motor function and complication of treatment were rated with the Unified Parkinson's Disease Rating Scale part 3 and 4, respectively. Quality of life was evaluated with the Parkinson's Disease Quality of Life questionnaire and depressive symptoms was assessed with Beck Depression Inventory-II, respectively.
Results: Parkinson's disease patients had significantly impaired scores of Parkinson's disease sleep scale-2 compared with control subjects. A satisfactory internal consistency and test-retest reliability were demonstrated. Parkinson's disease sleep scale-2 was correlated with Pittsburgh Sleep Quality Index and Epworth Sleepiness Scale. Also, a significant correlation was found with depressive symptoms, quality of life and motor function.
Conclusion: Our study confirmed a usefulness of new version of the scale, Parkinson's disease sleep scale-2 Japanese version, that enables comprehensive assessment in nocturnal disturbances in Parkinson's disease.

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SLEEP ALTERATIONS IN LONGITUDINALLY ASSESSED ALZHEIMER'S DISEASE PATIENTS

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Sleep disturbances are commonly found in Alzheimer's disease (AD) patients as well as in the elderly population. The most common disturbances are reduced sleep maintenance and longer sleep latencies. Despite common misperception, the amount of sleep is rarely affected by old age. Cholinergic medication [cholinesterase inhibitors or ChEIs] is available to delay memory degradation in AD patients however there are reports of sleep also being affected. Here the longitudinal assessment of sleep in ChEI-naive healthy elderly controls, mild cognitive impairment (MCI), early AD and moderate AD patients is presented. On commencement of the study baseline observations were made using

actigraphy and polysomnography (PSG) to assess sleep. These assessments were repeated 6 weeks after ChEI initiation.
Pre-medication significant differences in sleep characteristics between the controls and the AD patients were found, including time spent in bed, with patients staying in bed nearly three hours longer [$p < 0.05$]. Furthermore total activity levels were much lower for the AD patients [$p < 0.05$]. Activity levels were also found to be reduced in early AD patients in comparison to controls [$p < 0.05$] and differences in baseline PSG were found between all groups. Post-medication, in comparison to controls, the moderate AD patients spent more time in bed, had less sleep efficiency and more fragmentation of sleep [$p < 0.05$]. Alterations in PSG were also found with changes in rapid eye-movement and slow wave sleep most noticeable.
This is the first study to longitudinally assess the sleep and circadian rhythmicity of healthy controls, MCI, early AD and moderate AD patients. The moderate AD patients showed distinct sleep alterations after six weeks of ChEI treatment. This is important as sleep disturbances are a common reason for terminating ChEI treatment and the primary reason for institutionalisation. A better understanding of the alterations of sleep in AD patients could prolong the use of ChEI medication and consequently increase time spent at home before institutionalisation.

PO-1-226

SLEEP CHARACTERISTICS IN MILD TRAUMATIC BRAIN INJURY PATIENTS

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Introduction: Sleep disturbance, along with fatigue and pain, is one of the top three complaints following Mild Traumatic Brain Injury (MTBI). Earlier reports aimed at studying sleep in MTBI, yet no consensual results were found to describe and understand sleep disruption. Many reasons may explain these discrepancies, including sample heterogeneity, multiple traumas, confounding factors . . . In this study, we aim to look at sleep self quality report, macrostructure and spectral analysis in a homogeneous MTBI patients sample in comparison to healthy control subjects.
Methods: The diagnostic of MTBI was confirmed by a trauma neurosurgeon. 33 MTBI and 16 healthy subjects slept for two nights in a hospital based laboratory. 9 MTBI were excluded from the study for failure to comply with protocol. The final sample consisted of 24 MTBI (15M/9F; mean age = 38,3 y.o. SD = 11,4) and 16 healthy subjects (6M/12F; mean age = 31,9 y.o. SD = 9,4). The first night is for habituation and the second night is used for analysis. The Pittsburgh Sleep Quality Index (PSQI) was administered. Visual Scoring was performed according to the R&K scoring rules. Off-line spectral analysis was performed using Wavemetrics (IgorPro 6.12) on an artefact free signal.
Results: The global score on the PSQI was higher in the MTBI (mean = 8,9 SD = 4,9) than the healthy subjects (mean = 2,8 SD = 1,7) as well as for all the subscores. There were no significant differences in sleep macrostructures between the two groups for the following sleep parameters: latency (min), duration (min), efficiency (%), stages 1,2,3&4, REM (%), REM latency (min) and REM efficiency. Spectral EEG analysis is still underway.
Conclusion: The PSQI, which measures subjective sleep quality for the past month showed that the MTBI group do report a worst sleep quality than healthy subjects. Even though sleep disorders are the major complaint following a MTBI, no significant difference is observed in sleep macrostructure. FFT spectral results may provide the answer to the sleep disturbance reported by this population. Supported by: QPRN, FRSQ and CIHR

PO-1-227

RELATIONSHIP BETWEEN POLYSOMNOGRAPHIC AND ACTIGRAPHIC ASSESSMENT OF SLEEP VARIABLES IN ADULTS WITH LATE-LIFE NEUROPSYCHIATRIC OR NEURODEGENERATIVE DISORDERS

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Introduction: Although actigraphically determined sleep-wake variables provide robust sleep-wake differentiation in healthy subjects, the concordance between actigraphy and polysomnographic assessment of sleep have not been conducted in older clinical samples. Such studies are required given the increasing use of actigraphy in clinical samples.
Method: Fifty-nine patients with mild cognitive impairment (19M, age = 64.7 ± 11.1) and Parkinson's disease (23M, age = 64.0 ± 7.2) and 17 age-matched controls (7M, age = 63.4 ± 8.0) completed 2-weeks of actigraphy and 2 consecutive in-lab overnight PSG studies. Variables from the second night of PSG assessment were analysed. Agreement between the two measures was analysed using t-tests and regression.
Results: There were no significant differences in sleep-wake variables between the two groups. Average rest onset and rest offset times determined by actigraphy were significantly later than PSG determined sleep onset (mean difference = 21.3 ± 56 min, $t = 3.3$, $p < 0.05$) and offset times (mean difference = 20.5 ± 50.0 min, $t = 3.6$, $p < 0.05$). Actigraphy underestimated wake duration compared to PSG wake duration (WASO) (mean difference = –67.2 ± 60.2 min, $t = –9.7$, $p < 0.05$). Greater duration of PSG WASO was associated with greater underestimation of actigraphically defined wake time ($b = -0.869$, $r = –0.893$, $p < 0.05$).
Discussion: Although sleep-wake parameters from the two procedures were not equivalent, the differences were not profound. The underestimation of actigraphically determined wake time is consistent with previous findings where quiet wakefulness is typically scored as sleep. In this older sample, we have demonstrated that actigraphically defined wake time corresponded to 87% of PSG WASO consistently. These findings suggest that actigraphy is of significant clinical utility in some aspects of sleep-wake monitoring, and initial determination of sleep-wake disturbances that may subsequently require further, more detailed investigation in these groups.

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NEW EEG MARKERS OF ALZHEIMER'S DISEASE FOR THE ELDERLY

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This study develops new markers of the Alzheimer's disease for the elderly based on the all-night EEG of a single channel. The sleep EEG

is transformed into 5 power time series corresponding to the delta, theta, alpha, sigma and beta frequency bands. Then, the mutual information and wavelet coherence are adopted to develop a measurement for the similarity between the power time series of a frequency band pair, denoted as the half phase variance (PV). The PV values are used as markers of the Alzheimer's disease for the elderly.
In this study, the sleep EEG from electrodes C3, C4, O1 and O2 have been recorded for 7 dementia's patients (including AD patients and non-AD type patients), 19 age-matched normal controls, and 5 normal young people as baseline. It is found that the PV of theta and alpha band power time series prominently increases in dementia's patients as compared with the controls in the C3 and O1 channels with p-value < 0.001, especially for AD patients. In addition, it also increases significantly in dementia's patients in the C4 channel with p-value < 0.01. These PV values seem to be able to reflect neurophysiological degeneration and thus may serve as a marker to identify AD patients. Compared with conventional approach, this method is advantageous because only one channel measurement is required.

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COMPARISON OF SLEEP ARCHITECTURE AMONG ALZHEIMER'S DISEASE, DEMENTIA WITH LEWY BODIES AND MILD COGNITIVE IMPAIRMENT

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Objective: Previous studies have suggested that sleep quality of patients with dementia may be poorer than that of the elderly subjects without cognitive impairment. This study aims to compare sleep architecture among Alzheimer's disease (AD), dementia with Lewy bodies (DLB), mild cognitive impairment (MCI) and age-matched controls.
Methods: Clinical evaluation, cognitive screening test and polysomnography were carried out. Diagnoses of MCI, AD and MCI were made with standard guidelines. Polysomnography variables such as total sleep time (TST), sleep efficiency, sleep latency, time spent in stages slow wave sleep (SWS) and REM sleep and periodic limb movement during sleep (PLMs) were compared among MCI, AD, DLB and control groups. All subjects gave informed consent according to institutional guidelines and tenets of the Declaration of Helsinki. This study was approved by local Institutional Research Board.
Results: TST and time spent in the stages of SWS and REM sleep in the AD and DLB groups were decreased compared to those in MCI and the control group. There were significant differences in the amount of time spent in stage REM sleep among these groups. The rank order of time spent in REM sleep was control group > MCI, DLB, > AD group. PLMs index in DLB was increased compared with those in the other groups.
Conclusion: Subjects with dementia had significantly shorter TST, SWS and REM sleep. An increase in PLMs was significant in patients with DLB. Time spent in stage REM sleep was shortest in the AD group. Subjects with MCI demonstrated a significantly shorter time spent in stage REM sleep compared with the control, yet they do not meet currently accepted criteria for dementia.
Acknowledgement: This study was supported by a Grant-in-Aid for Scientific Research.

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PRECIPITATING FACTORS FOR SOMNMABULISM: A VIEW FROM PATIENTS' PERSPECTIVE

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Sleepwalking is a common arousal parasomnia affecting up to 4% of adults. Underlying pathophysiological mechanisms remain unclear, but factors that intensify or disrupt sleep can facilitate episode occurrence in predisposed individuals. Other variables have been described as facilitating episodes, but supporting evidence is scarce. Surprisingly, sleepwalkers' views on such factors have not been systematically investigated. Participants were 70 consecutive patients referred to our Sleep Disorders Clinic and diagnosed with sleepwalking. All participants underwent a clinical interview, overnight polysomnography, and completed a questionnaire assessing various aspects of their sleepwalking. One section covered a wide range of precipitating factors, including stress (3 items), dreams (2 items), sleep schedule and habits (4 items), use of psychoactive substances (4 items), and various endogenous (5 items) and environmental (6 items) factors. Each item was rated for the degree to which it contributed to their experiencing episodes using a scale from 1 (never) to 5 (always). We present the percentage of patients who responded with often or always to highlight their most salient factors.Consistent with previous literature, most sleepwalkers (68.5% of patients) considered stress to be a significant precipitating factor for their episodes. Dreams were the second most frequently reported factor (45.7%), a finding that underscores the importance of assessing phenomenological experiences in arousal parasomnias. Sleep deprivation was third with 31.4%. Surprisingly, endogenous and environmental stimuli were identified as significant factors by less than 10% of sleepwalkers. This contrasts with reports suggesting that alcohol, caffeine, sudden sounds or being touched constitute important contributing factors. These data reveal that sleepwalkers consider stress, sleep mentation, and sleep deprivation as the factors most susceptible of increasing their likelihood of experiencing episodes of somnambulism.

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DISCRIMINATING BETWEEN VIOLENT AND NON-VIOLENT SLEEPWALKERS: SENSITIVITY AND SPECIFICITY OF STAGE 4 SLEEP

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Introduction: Somnambulism (sleepwalking) is considered a disorder of arousal characterized by motor activity, impaired judgment, misperception and relative unresponsiveness to environmental stimuli, and variable retrograde amnesia. Although somnambulism can give rise to violent sleep related behaviors, little is known about why some sleepwalkers repeatedly experience violent episodes. Having less than 2% of stage 4 sleep has been identified as one potential marker of violent somnambulism. We report a follow-up study of this polysomnographic marker.
Method: All sleepwalkers were referred to our Sleep Disorders Clinic by a physician. Overnight polysomnographic recordings were

performed on 7 adult sleepwalkers (4 Men, 3 Women) reporting a history of violent episodes of somnambulism and on 54 sleepwalkers (20 Men, 34 Women) without violent episodes. The two groups did not differ significantly in terms of their age (33.3 vs 32.7 years).
Results: Violent sleepwalkers had significantly less stage 4 sleep than non-violent sleepwalkers (1.53% vs 4.65%, p = .008) and six out of seven violent sleepwalkers (86%) had less that 2% of stage 4 sleep compared to 25 of the 54 non-violent sleepwalkers (46%). A Chi square test indicated that these group proportions were significantly different (p = .036). No other polysomnographic measure differed significantly between the two groups.
Conclusion: Our findings indicate that although having less than 2% of stage 4 sleep shows good sensitivity for violent sleepwalkers, its specificity is relatively low as it also occurs in almost 50% of non-violent sleepwalkers.

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SLEEP AND EXECUTIVE FUNCTIONING IN CHILDREN WITH EPILEPSY

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Background: Sleep disturbance is commonly reported in childhood epilepsy, although few studies have quantified this using objective sleep measures. We have previously demonstrated in typically developing (TD) children that less sleep time is associated with poorer neuropsychological performance, particularly tasks measuring Executive Functioning (EF). To our knowledge, no studies have examined whether children with epilepsy are at risk of neurocognitive deficits associated with sleep disturbance.
Method: The sample consisted of 23 children diagnosed with idiopathic epilepsy (with no significant learning difficulties) and 53 TD children. Children were aged 6–13 years, with no significant differences between the two groups in age or gender. Sleep was measured for one week using wrist-worn actigraphs (AMI). Neuropsychological tests were administered measuring attention, working memory, planning, verbal fluency, inhibition, and processing speed (PSI). An aggregate score of EF (AEF) was calculated from standardised residuals (not including PSI) to measure the overall effect of sleep disturbances on EF.
Results: Although children with epilepsy slept (M = 459.91 minutes, SD = 64.62), on average, for 20 minutes less compared to TD children (M = 479.42 minutes, SD = 57.06), this difference failed to reach statistical significance (F = 2.52, p = .087). Sleep efficiency was similar between the groups: M = 84.92 (SD = 8.12) in the TD group, M = 82.38 (SD = 10.53) in the Epilepsy group. However, children with epilepsy had significantly poorer AEF compared to TD children (F = 11.86, p < .01). Furthermore, PSI was significantly lower in children with epilepsy (t = 2.82, p < .01). Conclusion: These results need further investigation but in this study are not apparently related to measures of sleep quality.
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ASSOCIATION BETWEEN SHORT TOTAL SLEEP TIME AND HYPERTENSION- THE SKARA SLEEP COHORT

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Objective: To investigate the relationship between total sleep time (TST) and hypertension in a gender-balanced community-dwelling cohort of hypertensive patients and normotensive controls (Skara Sleep Cohort).
Methods: All participants (n = 344, males 173, age 61[7] years, body mass index [BMI] 29[5] kg/m^2) underwent ambulatory home polysomnography. Hypertension was defined as supine systolic BP >= 140 mmHg and/or diastolic BP >= 90 mmHg or with ongoing hypertensive medication. A multivariate logistic regression model was used to address the association between hypertension status and anthropomorphic/sleep variables. Odds ratios (ORs) are expressed as the relative risk over the interquartile range [25% vs. 75%] of the predictor with 95% confidence intervals.
Results: The mean age, BMI, apnea/hypopnea index and TST in hypertension (n = 224, males 109) and control (n = 120, males 64) groups were 63(6) vs. 59(7) years, 29(5) vs. 27(4) kg/m^2, 29(24) vs. 20(23) n/h and 360(76) vs. 395(67) minutes, respectively (p < 0.01). Logistic regression analysis demonstrated that the number of apnea/hypopnea events (47 vs. 218 events), TST (331 vs. 426 minutes), BMI (25 vs. 31 kg/m^2) and age (56 vs. 67 years) all independently contributed to hypertension (OR 1.89 [1.1 : 3.2], 0.58 [0.4 : 0.8], 1.96 [1.4 : 2.8] and 2.25 [1.7 : 3.9], respectively).
Conclusion: Short sleep time is associated with hypertension independent of age, BMI and apnea/hypopnea events in this population-based cohort.

PO-1-234

SLEEP-RELATED EATING DISORDER: A SLEEP DISORDER OR MENTAL DISORDER? A CASE REPORT EXPLORING SRED AND THE IMPORTANCE OF SUCH DISTINCTION

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This is the case of a 32 year old woman who has been living with Sleep-Related Eating Disorder (SRED) for 25 years. She experiences the typical picture of recurrent arousals from sleep associated with compulsive ingestion of food, impaired levels of consciousness and amnesia. Currently, 50% of her nights are affected by the disorder, with 2–3 episodes each night. Until recently this disorder was considered distinct from Nocturnal Eating Syndrome (NES), where subjects are fully aware of their feeding, much of which may take place before the patient goes to sleep. However, the 2005 revision of the International Classification of Sleep Disorders has blurred the boundaries between the two conditions by in effect subsuming NES into SRED. This report describes some of the difficulties a young mother has experienced in living with and managing the disorder. It raises specific issues in three areas: the clinical

and psychosocial importance of understanding and maintaining the distinction between SRED and NES; the prevalence and problems associated with increased weight in SRED patients; the limited options and efficacy of treatment in SRED.

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THE SINGLE DOSE PHARMACOKINETIC AND PHARMACODYNAMIC PROFILES OF SUVOREXANT (MK-4305), A DUAL OREXIN RECEPTOR ANTAGONIST, IN HEALTHY MALE SUBJECTS

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Introduction: Orexin neuropeptides play a critical role in regulating the transition between wake and sleep. Suvorexant (MK-4305), a potent dual orexin receptor antagonist, represents a potentially new approach to treating insomnia.
Methods: This first-in-human study of suvorexant was a multi-part pharmacokinetic and pharmacodynamic study in healthy young men. Part I was a randomized, double-blind, single rising-dose study to evaluate the safety, tolerability, and pharmacokinetics of suvorexant (n = 16). Part II was a 4-period crossover study to evaluate the effects of suvorexant on quantitative EEG (qEEG) (n = 12).
Results: Suvorexant was generally well tolerated in healthy young men up to 120 mg with the most frequently reported adverse experience being somnolence. Following AM administration, suvorexant was rapidly absorbed with a median Tmax of 1.0–2.0-hour and apparent terminal T1/2 of 8.5–15-hours. Night-time administration did not affect AUC0-, but slightly decreased Cmax and median Tmax was delayed by 1-hour. The increases on AUC0- and Cmax appeared less than dose proportional from 4 to 120 mg. There was a dose-dependent and time-limited increase in sleepiness on Karolinska sleepiness scale and decrease in alertness on Bond-Lader VAS, which were consistent with the desired pharmacodynamic effects. Following AM administration, single doses of 20 and 80 mg produced a dose-dependent increase in delta band power spectral density on qEEG suggesting sleep promoting effects. The effect of suvorexant on qEEG disappeared at 8 and 12-hour post-dose indicating no long-lasting effect which may cause next-day residual effects.
Conclusions: Suvorexant was well tolerated and demonstrated pharmacokinetic and pharmacodynamic profiles that supported its development as a hypnotic.

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A DUAL OREXIN RECEPTOR ANTAGONIST, MK-6096, IN PATIENTS WITH PRIMARY INSOMNIA: RANDOMIZED, CONTROLLED, CROSSOVER POLYSOMNOGRAPHY STUDY

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Objectives: Orexinergic activity originating in the lateral hypothalamus plays a critical role in sleep/wake regulation. Drugs that influence orexinergic tone may be useful in the treatment of sleep disorders. We evaluated MK-6096, a potent and selective dual orexin receptor antagonist (DORA), for the treatment of primary insomnia in adults.
Methods: A randomized, double-blind, placebo-controlled, adaptive, 2-period (4-weeks per treatment period, separated by a 2-week washout) cross-over polysomnography (PSG) global study was performed to assess the efficacy and tolerability of MK 6096 (2.5, 5, 10, and 20 mg) orally-administered 30 minutes before bed time in the treatment of primary insomnia. PSG was performed on Night 1 and at the end of Week 4 of each period. The primary outcome measure was sleep efficiency.
Results: 324 patients were randomized and administered at least one dose of study medication: 318 received MK-6096 (2.5 mg N = 79, 5 mg N = 78, 10 mg N = 80, 20 mg N = 81) and 315 received placebo. All doses of MK-6096 were superior to placebo (p-values < 0.002) for the co-primary endpoints of difference from placebo in change from baseline sleep efficiency at Night 1 (LS mean [95% CI]: 2.5 mg = 8.4% [5.3,11.6], 5 mg = 10.0% [6.9,13.2], 10 mg = 10.7% [7.7,13.8], 20 mg = 13.4% [10.3,16.4]) and end of week 4 (2.5 mg = 4.6% [1.8,7.4], 5 mg = 4.5% [1.7,7.3], 10 mg = 9.7% [6.9,12.5], 20 mg = 8.6% [5.8,11.4]). Significant dose-related effects were also observed for sleep induction and maintenance parameters. MK-6096 was generally safe and well-tolerated.
Conclusions: Treatment for 4-weeks with the DORA MK-6096 is efficacious and well-tolerated in adults with primary insomnia. Support: Merck Research Laboratories.

PO-1-237

PRECLINICAL EFFICACY OF SUVOREXANT AND OTHER OREXIN RECEPTOR ANTAGONISTS

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Introduction: Orexins are neuropeptides which promote wakefulness by activation of two G-protein coupled receptors, Orexin 1 Receptor (OX1R) and Orexin 2 Receptor (OX2R). Antagonism of Orexin Receptors provides a novel therapeutic approach for primary insomnia and

is supported by both genetic and pharmacological data. Merck has led the discovery and development of Dual Orexin Receptor Antagonists (DORAs) as a novel treatment for primary insomnia, with the lead compound Suvorexant (MK-4305) currently in Phase III clinical studies.
Methods: The detailed pharmacological characterization of Suvorexant and a series of other small molecule DORAs will be presented. Studies included in vitro binding and functional assays, ex vivo receptor occupancy studies, as well as in vivo locomotor assessment, multi-species PSG and quantitative EEG in wild-type and transgenic animals. Comparisons with other sleep-promoting medications were also conducted.
Results: Equivalent in vitro binding affinities and potencies for orexin receptors from mice, rats, rabbits, dogs, rhesus and humans were observed. In vivo studies with Suvorexant and DORAs from distinct structural classes showed dose-dependent receptor occupancy, reduced homecage locomotor activity and proportionally increased REM and NREM sleep in multiple species. These sleep effects fundamentally differ from sedating GABAergic drugs, and unlike zolpidem and diazepam, DORAs do not impair rotarod performance even when administered at >10-fold above sleep-promoting doses. Examination of sleep architecture and qEEG patterns showed consistency and dose-dependence in mice, rats, and dogs, with modulation of low and high frequency spectral power bands.
Conclusion: Suvorexant and other dual orexin receptor antagonists effectively promote sleep across species and provide a novel approach for the treatment of primary insomnia.
Support: This project was supported by Merck.

PO-1-238

CHARACTERIZATION OF MK-6096: A NOVEL DUAL OREXIN RECEPTOR ANTAGONIST FOR THE TREATMENT OF INSOMNIA

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Introduction: Orexin/Hypocretin is a neuropeptide responsible for regulating arousal in mammals, acting through Orexin 1 Receptor (OX1R) and Orexin 2 Receptor (OX2R) to promote wakefulness. Genetic and pharmacological studies demonstrate that blockade of orexin receptor signaling reduces wakefulness and could provide benefit for insomnia. MK-6096 is a potent and selective Dual Orexin Receptor Antagonist (DORA) developed by Merck Research Laboratories, and has recently completed PhIIb studies as a treatment for primary insomnia.
Methods: This presentation will focus on the preclinical characterization of MK-6096, including data from in vitro receptor binding, calcium release and specificity assays, and in vivo receptor occupancy, locomotor, sleep and quantitative EEG (qEEG) assays. MK-6096 in vitro and in vivo activities were examined across species including mice, rats and dogs.
Results: MK-6096 and other DORA compounds effectively block orexin-induced locomotor activity, demonstrate receptor engagement in an ex vivo occupancy assay and dose-proportionally promote sleep in multiple species. MK-6096 and other DORAs reduce wake activity and proportionally increase both slow wave sleep (SWS) and rapid eye movement (REM) sleep to increase total sleep time. Dose-dependent and translational qEEG effects were observed across preclinical species. Sleep architecture and qEEG patterns were consistent and dose-dependent across DORAs from distinct structural classes, and differ from studies using GABA modulators. Orexin receptor antagonists modify sleep architecture by consistently increasing deep sleep states at the expense of wakefulness.
Conclusion: MK-6096 is a potent and selective DORA that effectively promotes sleep in multiple species, and provides a new therapeutic approach for the treatment of insomnia.
Support: This project was supported by Merck.

PO-1-239 / AS-22 Presenter

RELATIVE CONTRIBUTION OF OREXIN-1 AND OREXIN-2 RECEPTORS TO THE SLEEP EFFECTS INDUCED BY A DUAL OX1/2R ANTAGONIST

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Introduction: In accordance with the prominent role of orexins in the maintenance of wakefulness via activation of orexin-1 (OX1R) and orexin-2 (OX2R) receptors, various dual OX1/2R antagonists have been shown to promote sleep. We have demonstrated that blockade of OX2R is sufficient to initiate and prolong sleep, and that simultaneous blockade of OX1R attenuates the NREM but enhances the REM sleep promoting effects of a selective OX2R antagonist in rats. The differential role of these receptors in sleep-wake modulation was further investigated using mice deficient for either the OX1R or the OX2R treated with a dual OX1/2R antagonist.
Methods: Four separate groups of mice (OX1R KO and WT; OX2R KO and WT) were implanted with telemetric devices for recording EEG/EMG signals, locomotor activity and body temperature. Following 24 h baseline sleep evaluation, animals were orally dosed with a dual OX1/2R antagonist (compound A, 30 mg/kg) or vehicle at dark onset and recordings were analyzed during the 12-h dark phase.
Results: In baseline conditions, sleep-wake parameters were similar in OX1R KO and WT mice. OX2R KO mice displayed elevated sleep fragmentation and more NREM sleep time than WT mice during the dark phase. The OX1/2R antagonist produced an increase in NREM and REM sleep time in WT mice. The REM sleep promoting effect, concomitant with SOREM, was more pronounced in OX1R KO than in WT mice. In contrast, NREM but not REM sleep was rather decreased and direct wake to REM transitions (DREM) were observed in OX2R KO mice.
Conclusion: The data indicate that sleep patterns can be differently affected by simultaneous transient (pharmacological) and permanent (knockout) inhibition of either OX1R or OX2R in mice. These results further extend our investigation on the relative contribution of each orexin receptor to the sleep effects induced by a dual OX1/2R antagonist, and reinforce the view that selective OX2R antagonists are more suitable for the treatment of insomnia.

PO-1-240

MK-6096, A DUAL OREXIN RECEPTOR ANTAGONIST, ENHANCES SLEEP ONSET AND MAINTENANCE AS MEASURED BY PSG IN HEALTHY MALE SUBJECTS

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Introduction: Orexin neuropeptides play a critical role in regulating the transition between awake and sleep. MK-6096, a potent orexin receptor antagonism, represents a potentially new approach to treating insomnia.
Methods: Double-blind, placebo-controlled 5-period cross-over study to evaluate the effect of MK-6096 on sleep parameters via polysomnography (PSG) in healthy male subjects. EFollowing a habituation night in the sleep lab, each subject received 3 doses of MK-6096 (5, 20 and 60 mg) and placebo in Periods 1–4. PSG recording started 1-hr post-doseafter dosing and lasted for 8 hours. Pharmacokinetic samples were collected in a 5th period.
Results: All 3 doses of MK-6096 significantly decreased latency to persistent sleep (LPS) and wake after sleep onset (WASO) ($p < 0.05$). The effects were dose-dependent. Mean LPS was decreased by 63%, 85% and 94% at 5, 20 and 60 mg of MK-6096, respectively. Mean WASO was reduced by 39%, 45% and 51% at 5, 20 and 60 mg of MK-6096, respectively. A corresponding significant increase in sleep efficiency was observed ($p < 0.05$). While no statistically significant change in percentage of non-REM sleep was detected, a small increase in percentage of REM sleep occurred. MK-6096 did not show evidence of clinically significant residual effects at 5 and 20 mg, as assessed by subjective (e.g. Leed's Sleep Evaluation Questionnaire) and objective (e.g. reaction time and digit symbol substitution test) measurements. The most frequently reported adverse event was headache.
Conclusions: Single doses of MK-6096 at 5–60 mg demonstrated significant enhancement of sleep onset, maintenance and efficiency in healthy male volunteers. MK-6096 was safe and well tolerated at all doses tested.

PO-1-241 / AS-25 Presenter

ESSENTIAL ROLES OF GABA TRANSPORTER-1 IN CONTROLLING RAPID EYE MOVEMENT SLEEP AND INCREASED SLOW WAVE ACTIVITY AFTER SLEEP DEPRIVATION

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GABA transporter subtype 1 (GAT1) constructs high affinity reuptake sites for GABA in the CNS and regulates GABAergic transmission. Compounds that inhibit GAT1 are targets for epilepsy treatment. Sedation has been reported as a side effect of these agents, indicating possible sedative or hypnotic potential. To elucidate the role of GAT1 in sleep-wake regulation, we characterized the spontaneous sleep-wake cycle and responses to sleep deprivation in GAT1 knock-out (KO) mice. Under baseline conditions, GAT1 KO mice exhibited dominant theta-activity across all vigilance stages, including wakefulness, rapid eye movement (REM), and non-REM (NREM) sleep. During the light period, the KO mice spent longer time in REM sleep and shorter time in NREM sleep. They also showed more state transitions from NREM to REM sleep, more numbers of longer REM bouts, and less numbers of longer NREM bouts than the WT mice. During the dark period, the KO mice exhibited fragmented REM sleep, although no difference was observed in the amount of each stage between these two genotypes. After the mice were subjected to 6-h sleep deprivation, both NREM and REM sleep rebounds were found in both genotypes. However, compared to the baseline, the slow wave activity of NREM sleep was briefly elevated in the WT mice but remained completely unchanged in the KO mice for 6 h after sleep deprivation. These results indicate that GAT1 plays a critical role in the regulation of REM sleep and homeostasis of NREM sleep. On the other hand, NO-711, a selective GAT1 inhibitor could mimic the major phenotypes of GAT1 KO mice. These results indicated that GAT1 plays an essential role in sleep-wake regulation.

PO-1-242

RESIDUAL SEDATIVE EFFECTS ON NEXT-DAY ALERTNESS AND PSYCHOMOTOR PERFORMANCE OF BEDTIME ADMINISTERED ANTIHISTAMINE-RANDOMIZEDCONTROLLEDTRIAL-

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Antihistamines are frequently used in various clinical settings for reliving symptoms of allergic diseases. Sedation is a most common side effect of the antihistamines, which effect was frequently utilized for the treatment of insomnia caused by allergic symptoms such as skin itching. The main aim of the present study is to examine the feature and impact of residual sedative effect of antihistamines and zolpidem administered at bedtime. The study considered of 4 experimental sessions with at least 7-day intervals conducted by a double-blind, placebo-controlled, crossover study design. In each period, 22 healthy male young volunteers (mean age±SE: 22.2 ± 0.8 years) took either zolpidem 10 mg, diphenhydramine 50 mg, ketotifen 1 mg or placebo orally at bedtime and underwent polysomnography. Next-day residual sedative effects were evaluated by the multiple sleep latency test, alpha attenuation test, visual analog scale, and several psychomotor performance tests conducted in both the morning and afternoon. No significant difference was observed in the sleep architecture among 4 experimental sessions. Both the subjective/objective sleepiness and psychomotor deterioration were significantly enhanced in the order of ketotifen and diphenhydramine sessions. Contrastingly, zolpidem showed no significant next-day residual effects. These results strongly disapprove of the alternative use of sedative antihistamines for insomnia in patients with allergic diseases.

PO-1-243 / AS-11 Presenter

EFFECTS OF TRIAZOLAM WERE INFLUENCED BY CIRCADIAN TIMING OF ADMINISTRATION

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To determine whether effects of triazolam are influenced by circadian timing of administration, chronopharmacological study have done. Fourteen healthy young Japanese volunteers participated, and they repeated 40 min nap trials and 80 min enforced wakefulness for 50 hours from 1400 hours on day 1 to 1600 hours on day 3, to minimize effects of sleep debt. Polysomnogram was recorded during nap trials, and was scored manually according to international criteria. Saliva melatonin concentrations, simple reaction time, equilibrium of body were measured during enforced wakefulness. Subjective sleep duration, subjective sleep latency and subjective sleep depth during prior nap trial, and subjective sleepiness during enforced wakefulness were obtained by questionnaire and visual analogue scale. Opaque capsules were administered 30 min before every nap trial. One capsule contained 0.25 mg of triazolam, and the others contained placebo. Subjects were separated into two groups, and administered triazolam 1730 hours or 2330 hours on day 2 by double-blind randomized manner.

In both groups, triazolam enhanced objective sleep for 5 hours after administration. Subjective sleep parameters were deteriorated 8–13 hours after administration possibly due to acute withdrawal effect. Different effects of triazolam by administration time were observed in subjective and objective sleep parameters at 0.5 and 4.5–8.5 hours after administration. Hypnotic effects and withdrawal effects were stronger when administered at 1730 hours.

Insomniacs may regard their symptoms have become more serious when they had taken ultra-short acting hypnotics at early evening due to stronger acute withdrawal effects.

PO-1-244

THE RISE AND FALL OF ZOLPIDEM IN AUSTRALIA

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Background: The hypnotic zolpidem is marketed in Australia as Stilnox and as Ambien in the United States. During 2007–8 zolpidem was subject to sustained negative media attention causing a large stimulated reporting event (SRE) in spontaneously reported adverse effects data collected by the Therapeutic Goods Administration. We aimed to quantify the prescription rates for zolpidem for insomnia in Australia since 2000, the size of the fall in popularity following the 2007–8 SRE, and what drugs might have replaced it.

Methods: Analysis of the BEACH study (Bettering the Evaluation And Care of Health), a continuous representative cross-sectional sampling of primary care activity across Australia (9,842 GPs recording 984,200 patient-encounters). We quantified weighted average prescription rates associated with insomnia problems for the leading hypnotics (temazepam, nitrazepam, oxazepam, diazepam and zopiclone) for each 12 month period from April 2000 to March 2010.

Results: Across the years, between 93–99 medications per 100 insomnia problems were prescribed, supplied or advised for over-the-counter purchase. Zolpidem prescription per 100 insomnia problems rose from 0.04 in 2000–01 to a peak of 15.4 in 2006–07 before falling to 7.3 by 2009–10. Throughout this period temazepam has been by far the leading hypnotic and the fall in prescriptions for zolpidem has largely been associated with an increase in temazepam prescriptions which had previously dropped as zolpidem popularity rose in 2001–05.

Conclusions: A stimulated reporting event associated with zolpidem in Australia has resulted in about a halving of prescribing of zolpidem. Prescribing of temazepam has largely replaced the vacated market share.

PO-1-245

THE EFFECTS OF ZOLPIDEM AND TRIAZOLAM, RAMELTEON THE PHYSICAL AND COGNITIVE FUNCTIONS IN HEALTHY, ELDERLY PERSONS

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Introduction: Many problems have been reported on the use of hypnotics on the elderly, such as balance disorders, falling, and memory disorders. A safer use of hypnotics is being anticipated. We investigate the effects of a single dose of Zolpidem and Triazolam, Ramelteon on the physical and cognitive function in healthy, elderly persons.

Methods: We performed a double-blind crossover trial on 14 healthy elderly subjects (mean age 64.5 years) in order to investigate the residual effect of a single administration of Zolpidem (5 mg) and Triazolam(0.125 g), Ramelteon(1 mg). The subjects were given either hypnotics or a placebo at 23 o'clock before going to bed. Objective assessments Critical Flicker Fusion Test (CFF), Total Sway pass, Functional Reach Test (FRT), Timed Up and Go test (TUG), Simply Discriminatory Reaction test (SDR), Short-Term Memory test (STM) were conducted at 22 o'clock before the subjects took the hypnotic, and at 4, 6, 10, and 14 o'clock the next day. This experiment protocol was approved by Akita University Ethical Committee. The ANCOVA with a grouping factor (placebo vs. drug sessions) for objective assessments was conducted to verify main effects and interactions of time and/or drug. A p-value less than 0.05 was considered significant.

Results: The CFF and FRT, the result of Zolpidem were significantly better than those of placebo($p = 0.02$) or Ramelteon($p = 0.02$). And, the SDR, the results of Ramelteon and Triazolam were significantly better than those of placeb($p = 0.01$).

Discussion: It is known that clinical parameters FRT, TUG, which focus on the dynamic balance are more useful rather than those which focus on statistic balance in order to evaluate the accidental falls in the elderly. This study suggests that Zolpidem may decrease the risk of falling down because this hypnotic keep the dynamic balance. Triazolam and Ramelteon showed effects on the cognitive functions on the following day when given to healthy elders.

PO-1-246

LONG-TERM USE OF HYPNOTICS IN JAPAN

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Objectives: The occurrences of long-term benzodiazepines use in the general population were approximately 2–7.4%. Prior research generally indicated that there appears to be a strong relationship between age and the occurrence of benzodiazepines use. This study aimed at revealing the current status of long-term hypnotics use and the risk factor accounting for long-term use among Japanese, with the use of large-sized health insurance data.
Methods: Data were derived from medical fee receipts of approximately 330,000 people enrolled in multiple health insurance associations in Japan. We selected adult patients who were prescribed at least one hypnotic for the first time between April 2005 and March 2008. Follow-up period was extended to March 2009. To reveal the risk factor of long-term use of hypnotics, we performed Cox regression analyses with time-dependent variables in those patients who were followed up for up to 12 months, considering discontinuing prescription hypnotics as event, while patients who withdrew from health insurance associations during the study period were defined as censored cases.
Results: A total of 3,981 patients (M: 2,382 F: 1,579, 40.3 ± 12.4) were prescribed hypnotics first time during the study period. Each of the following variables had significant association with lower risk of discontinuing prescription hypnotics in univariate time-dependent analysis: combined use of another psychotropic drug (anxiolytics, antidepressants or antipsychotics); prescribed hypnotics at the department of psychiatry in the first month; high dosage of hypnotics; female; and high age. All variables were taken as candidates in multiple time-dependent Cox regression analyses.
Conclusion: The present results showed that combined use of antidepressants, high dosage of hypnotics and high age were each associated with higher risk of long-term benzodiazepines use in the Japanese population.

PO-1-247

HYPNOTIC DRUGS IMPROVE THE FIRST-NIGHT EFFECT" OF MICE AFTER CAGE CHANGE"

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First night effect (FNE) is a well-known phenomenon in human sleep research, which is characterized by decreased total sleep time and longer sleep latency. We established an animal FNE model and used this model to evaluate the hypnotic effects drugs, i.e., zolpidem, diazepam, dopamine D1 receptor antagonist SCH 23390, dopamine D2 receptor antagonist raclopride, or histamine H1R antagonist pyrilamine. After C57BL/6 mice were surgically implanted with sleep recording electrodes, we investigated spontaneous sleep and the effect of cage changes on sleep. When mice were moved to clean or dirty cages, the sleep latency was longer for clean cages than for dirty cages. Therefore, the pharmacological studies were performed under clean cage-change conditions. When mice were pretreated with zolpidem, raclopride, diazepam, and pyrilamine, non-rapid eye movement (NREM) sleep latency was decreased, whereby zolpidem, raclopride, and diazepam were most effective in our FNE model. Zolpidem, raclopride, or diazepam significantly increased NREM and REM sleep, but diazepam-pretreated mice showed a drastic decrease in the delta power (1.25–3.75 Hz) for NREM sleep in the electroencephalogram between 1 and 6 h after cage change. Our results suggest that a mouse model with cage change is suitable to mimic human FNE and that zolpidem and raclopride are potential drugs to prevent FNE.

PO-1-248

TRENDS IN THE USE OF SLEEP MEDICATIONS BY AUSTRALIAN ADULTS

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Objective: People report achieving less sleep than in previous years, although the time allocated to sleep appears unchanged over recent decades. Changes in sleep quality may be responsible for subjective reports of lack of sleep. The prevalence of sleep medication use was investigated in Australian adults as a proxy for secular changes in sleep quality.
Design: Secondary analysis of data from Australian National Health Surveys conducted from 1977 to 2007.
Participants: Community-dwelling individuals aged 15 to 65 and over.
Measurements and Results: Self-reported use of sleep medications in the previous 2 weeks was the main variable of interest. Unadjusted rates of sleep medication use was 3.3% in 1977, 4.8% in 1983, 6.1% in 1989, 1.7% in 1995, 4.3% in 2001, 5.3% in 2004, and 1.2% in 2007. Logistic regression models with age and gender as the covariates show that the odds of sleep medication use fluctuate considerably over time. Compared to 1977, use of sleep medication was more likely in 2007 (AOR 1.43; 95% CI 0.79–2.57). Across all years, women (2.11; 1.56–2.85) and the elderly (23.67; 6.97–33.00) were more likely use sleep medications. However, there appeared to be a trend of decreasing medication use by middle-aged and elderly groups over time.
Conclusions: Likelihood of sleep medication use appears to have increased in the Australian population and supports a trend of decreasing sleep quality over recent years. However this increase seems limited to younger age groups. It was not possible to explore the influence of availability and access to medications but the findings contribute to the growing literature on secular changes in population sleep.

PO-1-249

SLEEP PROBLEMS AND SUBSEQUENT PSYCHOTROPIC MEDICATION: A REGISTER-LINKED STUDY WITH 5-YEAR FOLLOW-UP

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Introduction: Sleep problems and mental disorders are associated. Studies examining the association between sleep problems and psychotropic mediation using register-based data are lacking.

Data and methods: Participants were 40–60-year-old employees of the City of Helsinki, Finland (77% women). Data on sleep problems – difficulties in initiating and maintaining sleep and non-restorative sleep – and covariates were derived from surveys conducted in 2000–2002 (response rate 67%). Follow-up data were derived from the Social Insurance Institution's registers of prescribed medication (consent to register linkages 74%, data analysed N = 5336). All purchased psychotropic medication (ATC-coded, mainly antidepressants, hypnotics, and sedatives) 5–7 years prior to and 5 years after baseline were included. Sleep problems were assessed with the Jenkins Sleep Questionnaire. Logistic regression analysis was used to calculate odds ratios (OR) with 95% confidence intervals (CI), adjusting for a large number of covariates.
Results: Frequent sleep problems were reported by 19% and no sleep problems by 14%. During the follow-up 22% of the participants purchased psychotropic medication. Adjusted for age, gender, and prior psychotropic medication, the ORs for psychotropic medication were 1.39 (95%CI 1.05–1.83) among those with rare sleep problems, 2.10 (95%CI 1.60–2.75) among those with occasional problems, and 3.49 (95%CI 2.63–4.63) among those with frequent problems, compared to those with no sleep problems. The associations were similar in both genders, as well as for groups of psychotropic medication examined. Adjusting for other covariates had a negligible effect on the associations.
Conclusion: Sleep problems are associated with subsequent psychotropic medication, with a clear gradient.

PO-1-250

THE RELATIONSHIP BETWEEN SELECTIVE SEROTONIN REUPTAKE INHIBITOR AND PERIODIC LIMB MOVEMENT SYNDROME IN DEPRESSIVE PATIENT

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Objective: To investigate the relationship between Selective Serotonin Reuptake Inhibitor (SSRI) and Periodic Limb Movement Syndrome (PLMS) in depressive patients.
Methods: 31 depressive patients in SSRI treatment were recruited from the polysomnography database. Two comparing groups were recruited at the same time: 27 depressive without any pharmacological treatment and 31 normal controls. According to the AASM Manual, we evaluated the stage of sleep, events in sleep and PLMS.
Results: compared to no treatment group (5.3 ± 1.4) and normal control group (4.1 ± 1.1), SSRI group (13.7 ± 2.6) experienced more Periodic Limb Movement Index (PLMI) ($p < 0.001$). The prevalence of PLMS in SSRI group (41.9%) was much higher than no treatment group (11.1%) and normal control group (6.5%) ($p < 0.001$). Furthermore, the logistic regression revealed that higher SSRI dosage, longer REM latency, and higher arousal index were risk factors for PLMS in SSRI group.
Conclusion: SSRI could increase the risk of PLMS in the depressive patients. It could make a lot of arousals in sleep, and these arousal could make sleep fragment and reduce the slow wave sleep. All in all, this phenomenon was an very important side effect in SSRI treatment.

PO-1-251

THE EFFECT OF SELECTIVE SEROTONIN REUPTAKE INHIBITOR ON THE MUSCLE TONE OF RAPID EYE MOVEMENT SLEEP IN DEPRESSIVE PATIENT

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Objective: To investigate the effects of Selective Serotonin Reuptake Inhibitor (SSRI) on the muscle tone in depressive patients.
Methods: 21 depressive patients in SSRI treatment were recruited from the polysomnography database. Two age- and sex-matched comparing groups were recruited at the same time: 21 depressive without any pharmacological treatment and 21 normal controls. According to Lapierre & Montplaisir criteria, we reevaluated the tonic and phasic electromyogram (EMG) in every Rapid Eye Movement (REM) sleep.
Results: compared to no treatment group and normal control group, SSRI group experienced more tonic EMG (10.1 ± 9.4% VS 3.3 ± 3.7% & 2.8 ± 3.4%, $P < 0.001$) and phasic EMG (submental: 11.5 ± 6.8% VS 6.3 ± 4.1% & 5.0 ± 3.7%, $P < 0.05$; Anterior tibialis: 18.8 ± 13.2% VS 10.3 ± 7.2% & 9.8 ± 5.5%, $P < 0.05$) in REM sleep. In SSRI group, both tonic and phasic EMG in REM sleep correlated with REM latency positively and correlated with percentage of REM sleep negatively.
Conclusion: SSRI could increase EMG activity in REM sleep, and might produce some symptomatic REM sleep behavioral disorder (RSBD). Because it do not have neurological basis, so it could be cured by quitting SSRI.

PO-1-252

THE CHANGE OF COGNITIVE FUNCTION ON THE NEXT MORNING AFTER TAKING MIRTAZAPINE 15 MG IN NORMAL MALE VOLUNTEERS

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Mirtazapine (MIR) sometimes induces sleepiness. We have examined the characteristics of the sleepiness induced by MIR employing placebo controlled double blind cross over design. 14 male right-handed normal volunteers participated in the study. This study was approved by Kyorin University Ethical Committee and all gave informed consents. The sleep wake patterns of volunteers were observed actigraphically for more than one week before examination to exclude the irregular sleep wake patterns. MIR 15 mg or placebo was in a white capsule not to discriminate visually. 7 volunteers took MIR 15 mg first followed by more than one week washout interval, then they took placebo secondly. Another 7 volunteers took drugs using inverse schedule. The order of taking drugs was controlled by envelope method. On the day when taking drugs, volunteers gathered at 1800 h, eating dinner at 1900 h, taking bath at 2000 h. They took drugs just at 2300 h and went to bed under less than 5 lx illumination. On the next day, they woke up at 0700 h. After daily morning habit, examinations started from 0900 h. Attachment the electrodes for electrophysiological examinations and flicker test were carried out at 0900 h. Assessment of subjective feeling with visual analogue scale and sleep latency test were performed at 0940 h. Acquisition of electroencephalogram (EEG) at waking state for examining power spectral analysis and event related potential (ERP) were done at

1020 h. At last Kreapelin test was examined before 1200 h. In ERP, visual P300 was examined. Red circle (target) and yellow circle (non-target) were randomly showed (stimulus time 100msec, visual angle 2 degree, target 20%/ non-target 80%, inter stimulus interval 1sec). EEG (from Fz, Cz, Pz, C3, C4, O1, and O2, A1+A2 as reference by 10–20 method) was acquired when target emerged up to 30 times. The P300 latency in MIR showed significant increase compared with placebo. The changes in P300 amplitude and the result of Kreapelin test did not reach the significance level. MIR may decrease the processing speed, which does not have effect on performance representing Kreapelin test.

PO-1-253

THE CHANGE OF SLEEPINESS AND SLEEP LATENCY ON THE NEXT MORNING AFTER TAKING MIRTAZAPINE 15 MG IN NORMAL MALE VOLUNTEERS

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Mirtazapine (MIR) sometimes induces sleepiness. We have examined the characteristics of the sleepiness induced by MIR employing placebo controlled double blind cross over design. 14 male right-handed normal volunteers participated in the study. This study was approved by Kyorin University Ethical Committee and all gave informed consents. The sleep wake patterns of volunteers were observed actigraphically for more than one week before examination to exclude the volunteers having irregular sleep wake patterns. MIR 15 mg or placebo was in a white capsule not to discriminate visually. 7 volunteers took MIR 15 mg first followed by more than one week washout interval, then they took placebo secondly. Another 7 volunteers took drugs using inverse schedule. The order of taking drugs was controlled by envelope method. On the day when taking drugs, volunteers gathered at 1800 h, eating dinner at 1900 h, taking bath at 2000 h. They took drugs just at 2300 h and went to bed under less than 5 lx illumination. On the next day, they woke up at 0700 h. After daily morning habit, examinations started from 0900 h. Attachment the electrodes for electrophysiological examinations and flicker test were carried out between 0900 h and 0940 h. Assessment of subjective feeling including sleepiness with visual analogue scale (VAS) and sleep latency test (SLT) were performed between 0940 h and 1020 h. Acquisition of electroencephalogram at waking state for examining power spectral analysis and event related potential were done between 1020 h and 1100 h. At last Kreapelin test was examined before 1200 h. In SLT, sleep onset was defined by following criteria: a. the time when sleep stages except for stage 1 or stage wake is observed. b. the initial time when consecutive 150 sec stage 1 sleep was observed. SLT did not show the significance. On the contrary, sleepiness by VAS and alertness by Flicker test showed the significant sleepiness and the significant decrease in MIR compared with placebo. The sleepiness induced by MIR may have different characteristics from other sleepiness because SLT did not reflect the subjective sleepiness.

PO-1-254

DOPAMINE D_2 RECEPTORS ARE ESSENTIAL IN THE MAINTENANCE OF WAKEFULNESS

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Dopamine (DA) is critically involved in regulating processes responsible for the generation of complex movements and emotions, cognition, reward processing, and drug addiction. In contrast, the role assigned to DA in sleep-wake cycle has been relatively limited, because the activity of DA neurons in the ventral tegmental area and substantia nigra pars compacta is not significantly modulated by the sleep-wake state. The main DA receptors (R) in the brain are D_1R and D_2R. To clarify the roles of DA receptors in the sleep-wake regulation, we used D_2R knockout (KO) mice and pharmacological manipulation. We found that the D_2R blockade could reduce the sleep latency and increase amounts of non-rapid eye movement (non-REM, NREM) sleep. Modafinil is the most potent wake-promoting medicine for enhancing the extracellular DA level in the nucleus accumbens and the prefrontal cortex, and for increasing wakefulness. By using D_2R KO mice and D_1R antagonist, we demonstrated that D_1R and D_2R are essential for the arousal effect of modafinil, with D_2R being the receptor of primary importance. Compared with wild-type (WT) mice, D_2R KO mice exhibited a significant decrease in wakefulness, with a concomitant increase in NREM and REM sleep, especially during the first 4 h after lights off. When the KO mice were subjected to a cage change, the latency to sleep in the KO mice decreased to half of the level for WT mice. The D_2R antagonist raclopride mimicked these effects in WT mice. When GBR12909, a DA transport inhibitor, was administered intraperitoneally, it induced wakefulness in WT mice, but its arousal effect was attenuated to one-third in the D_2R KO mice. These results indicate that D_2R plays an essential role in the maintenance of wakefulness.

PO-1-255

KETAMINE MODIFIED MELANIN-CONCENTRATING HORMONE IN RAT BRAIN

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Anesthesia disturbs sleep. Ketamine, a NMDA antagonist, is a widely used intravenous anesthetics. Ketamine is a dissociated anesthetics that depresses cerebral cortical activity but activates subcortical structures. Therefore, unpleasant dreaming or hallucination could be developed with ketamine. We previously reported that endogenous sleep-wakefulness related substance such as orexin1) and neuropeptide-S2) decreased ketamine anesthesia time. These results suggest various sleep-related endogenous substances could be involved in anesthetic process of ketamine. Melanin-Concentrating Hormone (MCH) is one of them that potentiates REM sleep. We tested if ketamine would affect MCH level in several brain regions responsible for sleep process. After obtaining approval from ethical committee of Hirosaki University, a total 4 male SD rats were used. They are housed with 12 h light-dark cycle (lights on at 08:00) and could access food and water freely. The rats received 100 mg/kg ketamine ip. Anesthesia time was defined a

duration from loss of righting reflex through regain it. Mean anesthesia time was 32 ± 5 min. Measurement of MCH levels of the cerebral cortex, hypothalamus, pons, hippocampus, and serum are done with ELIZA at pre-anesthesia, 20, 60 and 120 minutes after ketamine administration. Pre-anesthesia values of MCH in each regions are 5.057 ± 1.506 pg/mg tissue (pons), 7.632 ± 0.001 (hypothalamus) pg/mg tissue, 3.446 ± 0.001 (hippocampus) pg/mg tissue, 2.048 ± 0.001 (cerebral cortex) pg/mg tissue, 233.125 ± 53.771 pg/ml (serum).Ketamine increased MCH level of the hypothalamus (17.485 ± 6.565 pg/mg tissue) at 20 minutes after ketamine anesthesia ($p < 0.01$). This increase was continued throughout all time point after ketamine administration. At 120 minutes after ketamine administration, MCH levels were increased in hippocampus (7.123 ± 0.001; $p < 0.01$) and cerebral cortex (6.190 ± 0.896; $p < 0.05$)Ketamine had different effect on the MCH levels. These effects would be involved in process of unique property of ketamine anesthesia.

PO-1-256 / AS-24 Presenter

DIFFERENTIAL ROLES OF OREXIN RECEPTOR-1 AND -2 IN THE REGULATION OF NON-REM AND REM SLEEP

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Orexin-A and orexin-B are hypothalamic neuropeptides that play critical roles in the maintenance of wakefulness. Intracerebroventricular (ICV) administration of orexin-A has been shown to promote wakefulness and suppress both rapid eye movement (REM) sleep and non-REM (NREM) sleep through the orexin receptor-1 (OX1R) and orexin receptor-2 (OX2R). Here, we elucidated the differential roles of orexin receptors in the regulation of sleep and wakefulness by comparing the effects of ICV orexin-A administration in wild-type, OX1R-/- and OX2R-/- mice. The effects of orexin-A on wakefulness and NREM sleep were significantly attenuated in both knockout mice as compared to wild-type mice, with substantially larger attenuation in OX2R-/- mice than in OX1R-/- mice. These results suggest that although the OX2R-mediated pathway has a pivotal role in the promotion of wakefulness, OX1R also plays additional roles in promoting arousal. In contrast, suppression of REM sleep by orexin-A administration was slightly and similarly attenuated in both OX1R-/- and OX2R-/- mice, suggesting a comparable contribution of the two receptors to REM sleep suppression. Histological studies demonstrated differential distributions of each receptor subtype in distinct neuronal populations with specific neurotransmitter identities in brainstem cholinergic/monoaminergic neurons. In the laterodorsal tegmental and pedunculopontine tegmental nuclei especially, cholinergic neurons exclusively expressed OX1R mRNA, but OX2R mRNA was expressed mainly in GABAergic putative interneurons. Thus, each orexin receptor subtype plays differential roles in gating NREM and REM sleep, through distinct neuronal pathways.

PO-1-257

SLEEP FORENSICS- A WALK ON THE WILD SIDE…OR AN AVENUE FOR POST-MARKETING ANALYSIS OF ZOLPIDEM?"

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First defined at WorldSleep07, Sleep Forensics is a growing investigative field most often associated with the sleepwalking defense. For 5 years (8/1/06 to 6/1/11), the sleep forensics team at the Minnesota Regional Sleep Disorders Center were contacted by attorneys to place their cases (Total # Cases = 210) in consideration for a formal review to assess whether a sleep disorder may have been involved. As anticipated, Parasomnias were the most prevalent sleep disorder subtype implicated (N = 97). Surprisingly, Pharmaceutical Toxicity was the second most common subtype (N = 82) with Zolpidem accounting for the majority (N = 79) for which DWI was the most common associated criminal complaint (N = 43). We learned there was an unmet need to review medico-legal cases perhaps involving sleep disorders or altered levels of awareness. We found that Sleep Forensics was much more than a walk alongside Parasomnias and for many in the legal community it was a call for an investigation into the adverse consequences of Zolpidem. The high prevalence of Zolpidem legal cases in our experience raises several questions. Are such adverse consequences unique to Zolpidem or is this reflective of the popularity of the medication given its widespread use? Our case review reveals that the possible adverse effect of Zolpidem is most often associated with the criminal complaint of DWI. Is this indicative of an unusual and rare side effect (i.e. sleepdriving) or is this reflective of inadequate counseling concerning appropriate use of a seemingly-safe non-benzodiazepine medication? Conceivably, investigative pursuits in the emergent field of Sleep Forensics can provide insight into medications such as Zolpidem- for if the adverse effect is one that involves a behavior that takes the individual out of the bedroom, then the adverse effect has now become a public safety concern for which we all share in this responsibility.

PO-1-258

CAN MINOCYCLINE REVERSE MORPHINE-INDUCED RESPIRATORY DEPRESSION IN OBSTRUCTIVE SLEEP APNEA PATIENTS?

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Background: Recent animal studies suggest that the antibiotic minocycline reverses morphine-induced respiratory depression, while enhancing morphine-induced analgesia. We conducted a proof of concept double-blind, cross-over, placebo-controlled clinical trial, testing this combination of drugs on mild to moderate obstructive sleep apnea (OSA) patients.

Methods: After a screening polysomnography (PSG) study, 10 OSA patients underwent 2 overnight PSG sleep studies separated by an

interval of at least 1 week. The patients took a 3 day course of either active or placebo minocycline (100 mg twice a day), in random order, before the two PSG studies. They also took 30 mg oral control-release morphine 4 hrs before the start of each PSG study. Ventilatory chemoreflexes were tested just before sleep.
Results: Compared to baseline, the administration of 30 mg morphine alone did not cause significant respiratory depression in all key PSG parameters (all $p > 0.05$). However, compared to the use of morphine alone, the combination use of morphine and minocycline tended to have worse mean SpO2 nadir (83.5 ± 7.3 vs 78.9 ± 8.6 SD%, $p = 0.13$) and sleep time with SpO2 < 90% (6.5 ± 6.9 vs 13.7 ± 16.3 SD mins, $p = 0.12$). Mean heart rate was also reduced during awake (73.0 ± 16.4 vs 62.9 ± 15.4 SD/min, $p = 0.06$), during non-REM sleep (57.6 ± 9.1 vs 53.2 ± 8.1 SD/min, $p = 0.088$) and during REM sleep (62.1 ± 9.6 vs 57.1 ± 8.0 SD/min, $p = 0.1$). Compared to baseline, mean central chemosensitivity was reduced either using morphine alone or in combination with minocycline (2.2 ± 1.3 vs 1.5 ± 0.8 SD, 2.2 ± 1.3 vs 1.4 ± 0.5 SD, l/min/mmHg; $p = 0.18$, $p = 0.09$). Basal minute ventilation was particularly reduced with the combination minocycline (10.4 ± 3.6 vs 12.6 ± 5.3 SD l/min baseline, $p = 0.02$; 10.4 ± 3.6 vs 12.1 ± 4.3 SD l/min morphine alone, $p = 0.1$).
Conclusion: A clinically significant protective effect of minocycline on opiate-induced respiratory depression is unlikely. Conversely, the majority of outcomes tested show a trend towards greater respiratory depression with the addition of minocycline.

PO-1-259

THE EFFECT OF LOW-DOSE ORAL QUETIAPINE ON SLEEP AND COGNITIVE IN ADULTS

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To clarify the effects of quetiapine(QUE), an atypical antipsychotic drug, on sleep, we investigated polysomnographic sleep structure, subjective sleep quality and side effect. The double-blind, placebo-controlled, randomized cross-over study was carried out for 10 adult volunteers (mean age23,1 years) after one night for adaptation. Placebo or QUE 25 mg was administered orally at 10 pm every one week interval.
The efficacy and side effects were judged by Saint Mary's Hospital Sleep Questionnaire (SMH), Karolinska Sleepiness Scale (KSS), tapping test (TT), cognitive reaction test (CRT) and stabilometry. Nearly 40% of shortening of sleep stage1 ($p < 0,05$) and 10% of extention of sleep stage2 ($p < 0,05$) were observed after QUE intake compared with placebo.
Moreover, improvement of the sleep structure was remarkably observed in the subjects with higher score in Pittsburgh Sleep Quality Index (PSQI) than in those with lower score and the number of awakenings decreased in SMH and alertness in the following morning worsend in SMH and KSS in the QUE session.
Also the aggravation of the cognitive function was observed in the QUE session: the number of error and the mean latency of reaction was increased, and the amount of reaction decreased in CRT. In particular, the longer latency of reaction, the longer the duration of slow-wave sleep ($p < 0,05$).
Although, 25 mg of QUE lengthened sleep stage2 in healthy adults, the aggravation of cognitive function is a problem as side effect. The application of QUE to a large number of insomniacs would be necessary in the future.

PO-1-260

CROCIN PROMOTES NON-RAPID EYE MOVEMENT SLEEP IN MICE

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*Crocus sativus L.*Crocus sativus L. (saffron) has been traditionally used for the treatment of insomnia and other diseases of the nervous systems. Crocetin and crocin are major carotenoid pigment of saffron and a number of pharmacological studies have demonstrated that crocin and also crocetin have a wide range of neuroprotective activities against Alzheimer's disease, depression, and memory impairment. On the other hand, the effects of crocin and crocetin on sleep still remain unknown. In this study, we examined the sleep-promoting activity of crocin and crocetin by monitoring the locomotor activity and electroencephalogram after administration of these components to mice. Orally administered crocin (80 and 160 mg/kg of body weight) significantly suppressed the total amount of locomotor activity during the 12 hr by 33% and 20%, respectively, as compared with the vehicle control. Crocin (30 and 100 mg/kg of body weight) increased the total time of non-rapid eye movement (non-REM) sleep by 60% and 170%, respectively, during a 4-hr period from 20:00 to 24:00 after its intraperitoneal administration at a lights-off time of 20:00. Crocetin (100 mg/kg) also increased the total time of non-REM sleep by 50% after the administration. Compared with the vehicle-treated control, the number of non-REM sleep bouts increased by 2.2-fold and also those of wake bouts by 2.0-fold for 4 hr after the crocin treatment. Crocin increased the number of stage transitions from wakefulness to non-REM sleep and from non-REM sleep to wakefulness by 110% and 190%, respectively. There was no significant difference in EEG power density of non-REM sleep between the crocin treatment and the vehicle control, indicating crocin did not affect the EEG power density of NREM sleep. Crocin is considered to induce non-REM sleep that is very similar to physiological sleep, suggesting its potential use for the treatment of insomnia.

PO-1-261

CLINICAL TRIAL ON HERBAL TREATMENT OF PRIMARY INSOMNIA – A RANDOMIZED PLACEBO-CONTROLLED STUDY

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Objective: To evaluate the efficacy of a Traditional Chinese Medicine (TCM) herbal formula composed of Semen ziziphi spinosae, Caulis polygoni multiflori, Poria cum radix pini, Fructus tritici levis, Rhizoma anemarrhenae and Radix polygalae in subjects with primary insomnia.
Methods: This double-blind, randomized, placebo-controlled trial (RCT) enrolled 162 primary insomniac subjects who received either 4 weeks' TCM herbal formula or placebo. Efficiacy was evaluated by both subjective and objective sleep measurements (polysomnography and actiwatch).
Results: The TCM group had a nearly significant reduction in sleep latency as measured by polysomnography as compared to the placebo group ($p = 0.074$). In addition, when the adaptation night data was

excluded, there was a trend of better sleep, in terms of shorter time in bed and higher sleep efficiency in the TCM group. The subjective sleep quality improved in both groups at the end of 4 weeks' treatment but a higher percentage of the TCM group reproted "improvement of their insomnia" than the placebo group (66.2% vs. 49.3%, $p = 0.04$) as well as a marginal non-significance in the "improvement of sleep quality" item (63% vs. 47.3%, $p = 0.055$). Multivariate analysis suggested that the TCM group had a much less temporal night-to-night instability in sleep efficency as measured by actiwatch compare to the placebo group ($p < 0.05$). In addition, the TCM group had slightly more improvements in subjective sleep quality related to depth, peacefulness and refreshness when compared to that of the placebo group. The TCM herbal product was well tolerated.

Conclusion: To our knowledge, this is the first randomized placebo-controlled trial of TCM herbal formula for primary insomnia using a stringent screening process and both subjective and objective sleep measurements. Our study suggested that the TCM herbal formula provided a significant improvement of sleep in insomniac subjects when compared to the placebo group.

PO-1-262

ANTI-NMDA RECEPTOR ANTIBODY POSITIVE PATIENTS WITH VARIOUS PSYCHIATRIC AND SLEEP SYMPTOMS

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Recently, causative roles of encephalitis (EN) in major psychiatric features have been emphasized. These symptoms are often in young females with ovarian teratomas with good responses to tumor surgery and immunotherapy, and with autoantibodies to the NMDA receptor (NMDAR). We have experienced 10 these patients (pts) with various psychiatric and sleep symptoms. These pts exhibited 3 distinct clinical pictures, and we believe that the report of our cases will bring further discussions on the autoimmune-mediated atypical psychosis.The first 3 cases had typical clinical pictures of anti-NMDAR EN, beginning with psychiatric symptoms, and then seizures and disturbances of consciousness occurring. In order to examine the specificity of the anti-NMDAR Ab involvements, we also examined the Ab in other psychotic pts with hypersomnia. Narcolepsy (NA) with severe psychosis was included, because auto-Ab (Ma2, AQP4) mediated mechanisms are suspected in some secondary NA cases.We found that 3 narcolepsy pts (among 5), who had severe psychotic symptoms, were positive for the Ab. These cases were hypocretin deficient, but no significant neurological signs were noted. They were under stimulant medications, and their symptoms were unchanged when the stimulants were withdrawn. Antipsychotics and modified electro-convulsion treatment (ECT) were required to manage the psychotic symptoms. In addition, we also found 4 Ab positive pts with schizophrenia or schizo-affective disorders among 51 pts examined. The neurological symptoms were mild in these cases, and mECT was effective for 3 cases.Our results showed a high incidence of anti-NMDAR Ab positivity in a broader range of psychiatric disorders, including sleep and schizophrenia pts. Although the causative relationship between anti-NMDAR Ab positivity and psychiatric symptoms in these pts are not known, they exhibit unique demographic and clinical characteristics: Eight are female, and ovarian tumors are associated with 2 pts. Most of their symptoms are resistant to the pharmacological treatments, but responded relatively well to mECT.

PO-1-263

THE NEUROPROTECTIVE EFFECT OF MINOCYCLINE FOR ISCHEMIC INJURY IN NEURONAL CELL

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Obstructive sleep apnea (OSA) may increase this risk of transient ischemic attacks (TIA) and minor stroke.High mobil ity group box-1 (HMGB1), a nonhistone DNA-binding protein, is massively released into the extracellular space from neuronal cells after ischemic insult and exacerbates brain tissue damage in rats. Minocycline is a semi synthetic second-generation tetracycline antibiotic which has recently been shown to be a promising neuroprotective agent. In this study, we found that minocycline inhibited HMGB1 release in oxygen-glucose deprivation (OGD)-treated PC12 cells and triggered the activation of p38mitogen-activated protein kinase (MAPK) and extracellular signal-regulated kinases (ERK1/2). The ERK kinase (MEK)1/2 inhibitor U-0126 and p38MAPK inhibitor SB203580 blocked HMGB1 release in response to OGD. Furthermore, HMGB1 triggered apoptosis in a dose-de pendent fashion. Minocycline significantly rescued HMGB1-induced apoptosis in a dose-dependent manner. In light of recent observations as well as the good safety profile of minocycline in humans, we propose that minocycline might play a potent neuroprotective role through the inhibition of HMGB1-induced neuronal apoptosis in OSA.

PO-1-264

RAMELTEON INDUCES ACUTE SLEEPINESS ON THE PATIENTS WHO HAVE THE TENDENCY OF SEASONAL AFFECTIVE DISORDER

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Ramelteon, an agonist of melatonin-1 receptor, which is used for treatment of insomnia, sometimes induces the acute sleepiness. We found that the patients who complain the acute sleepiness show the seasonal patterns. Fourteen outpatients (7 males, 7 females, age 14–74 years old) who consulted our clinic and have taken Ramelteon for their insomnia participated in the present study after informed consents orally for anonymous presentation. They are comprised one schizophrenia, five mood disorders (one atypical depression, two seasonal affective disorders, two other type mood disorders), two neurosis, four insomniacs, and two sleep wake rhythm disorders. We examined their seasonality with Seasonal Pattern Assessment Questionnaire (SPAQ) (Rosenthal, 1984). To judge the intensity for seasonality by assessing the questionnaire 11. 'To what degree do the following change with the seasons?' which assess the intensity of the seasonality for following items: A. Sleep length, B. Social activity, C. Mood (overall feeling of well-being), D.

Weight, E. Appetite, and F. Energy level. Additionally, we defined the anchor point after following criteria: 4. Extremely marked change: Immediate answer for the items by the open question, 'Do you have any seasonal change about physical or mental state?' 3. Immediate answer after reading the item. 2. Spending time for answer after reading. 1. Seasonal change is uncovered in other part of the questionnaire, then confirming the seasonality. 6 patients complained the acute sleepiness after Ramelteon, the points of the seasonality was 6.67, which is significantly higher than the patients without acute sleepiness, whose seasonality points was 1.25. Ramelteon may induce acute sleepiness in the patients who have seasonal features.

PO-1-265

EFFECTS OF SYNTHETIC CANNABINOIDS, CANNABICYCLOHEXANOL AND JWH-018, ON ELECTROENCEPHALOGRAM POWER SPECTRA AND LOCOMOTOR ACTIVITY IN RATS

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Objectives: Several synthetic cannabinoids (SCs) have recently been distributed as adulterants in many herbal products on the illegal drug market around the world, on behalf of marijuana which contains psychoactive cannabinoids such as Δ^9-tetrahydrocannabinol (Δ^9-THC). However, there is a little information on pharmacology of those SCs. In this study following our previous report [Uchiyama, N. et al., Forensic Sci. Int., 2011, in press, doi:10.1016/j.forsciint.2011.05.005], we examined the pharmacological activities of two SCs, cannabicyclohexanol (CCH) and JWH-018, and Δ^9-THC by analyzing electroencephalograms (EEG) power spectra and the locomotor activity after administration to rats.
Methods: Sprague-Dawley male rats (8 weeks old) were implanted with EEG electrodes for polygraphic recording. After 10-days recovery, the EEG of each rat was recorded for 48 h. The first 24 h recording was used as a control with the vehicle-treatment. The second 24 h recording was obtained after an intraperitoneal (i.p.) administration of the above drugs at 3 doses of 1, 2.5 and 5 mg/kg. The cortical EEG signal was amplified, filtered (0.5–35 Hz), and recorded by using the analysis software SLEEPSIGN. EEG spectrum was analyzed after fast Fourier transformation. Locomotor activity of each rat was measured after the i.p. injection of each drug by monitoring with an infrared device.
Results: CCH and JWH-018 significantly increased EEG power in a frequency range of 4.5–6.0 Hz for the first 3 h in each dose. Δ^9-THC showed EEG pattern similar to those of SCs only at the dose of 5 mg/kg. In addition, CCH significantly decreased the locomotor activity in a dose-dependent manner for a longer duration than that of Δ^9-THC. JWH-018 decreased the locomotor activity for longer duration than that of Δ^9-THC at the dose of 2.5 mg/kg, but the shorter duration than that of Δ^9-THC at the dose of 5 mg/kg. However, JWH-018 had more rapid onset of the actions than CCH and Δ^9-THC.
Conclusion: These SCs significantly changed the EEG power spectra and suppressed the locomotor activity in rats.

PO-1-266

ADHERENCE AND EFFECTIVENESS OF POSITIONAL THERAPY FOR OBSTRUCTIVE SLEEP APNEA SYNDROME

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The purpose of this investigation was to explore how adherence to apositional therapy intervention affected therapeutic outcome inparticipants with positional-related obstructive sleep apnea syndrome. Eighteen adult participants identified as having positional-related obstructive sleep apnea by an initial overnight polysomnography study were recruited. Participants were instructed to use a "tennis balltechnique" positional device for three weeks at home and record their sleep habits and adherence before a final post-treatment polysomnography evaluation. A repeated measures MANOVA found significant effects of treatment between pre- and post-test on the objective polysomnography variables of Total Recording Time [$F(1,17) = 5.21$, $p < .05$, $\eta^2 = .24$], Total Sleep Time [$F(1,17)=8.59$, $p<.01$, $\eta^2=.34$], Sleep Efficiency [$F(1,17) = 5.42$, $p < .05$, $\eta^2 = .24$], Total REM sleep time [$F(1,17) = 9.91$, $p < .01$, $\eta^2 = .37$], and the Apnea-Hypopnea Index [$F(1,17) = 14.28$, $p < .001$, $\eta^2 = .46$]. Sleep onset latency was not statisticallysignificant. There were significant effects of treatment on the subjective measures of the Functional Outcome of Sleep Quality $F(1,17) = 8.92$, $p < .01$, $\eta^2 = .35$], Pittsburgh Sleep Quality Index [$F(1,17) = 11.2$, $p < .01$, $\eta^2 = .39$], Epworth Sleepiness Scale [$F(1,17) = 6.69$, $p < .05$, $\eta^2 = .28$], and the Brief Symptom Inventory [$F(1,17) = 5.14$, $p < .05$, $\eta^2 = .23$]. No significant interaction effects were found between treatment and adherence when participants were grouped post-hoc into an adherent or non-adherent categories based on their self-reported daily log data. In summary, the results of this study indicated that the positional device was efficacious for significantly improving both objective polysomnography variables and subjective variables of sleep. The results also indicated that even partially adherent participants reported significant improvements in nighttime sleep quality and quality of life after the three weektreatment period. This study found very acceptable adherence rates with this traditional positional device design.

Poster presentations 2

PO-2-001 / AS-28 Presenter

PARVALBUMIN-POSITIVE BASAL FOREBRAIN NEURONS ENTRAINS CORTICAL GAMMA OSCILLATIONS AND PROMOTES WAKEFULNESS: AN OPTOGENETIC STUDY

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The basal forebrain (BF) plays a crucial role in the modulation of cortical activity across sleep-wake cycles via cortically projecting cholinergic

and non-cholinergic neurons. Among non-cholinergic neurons, an important component consists of parvalbumin (PARV)-containing, gamma-aminobutyric acid (GABA)ergic neurons whose firing rates increase during electroencephalographic (EEG) low-voltage fast activity. However, their precise contribution to cortical activation and sleep-wake regulation is not well understood. Therefore, we sought to activate the PARV-positive BF neurons using optogenetic stimulation and determine the effect on the EEG and sleep-wake behavior. Adeno-associated viral vectors with double-floxed Channelrhodopsin2 (ChR2)-eYFP were injected stereotactically into the BF of transgenic mice expressing Cre recombinase under the control of the PARV promoter (PARV-Cre mice). Post-hoc immunohistochemistry confirmed high levels of double labeling of ChR2-eYFP (green) and PARV protein (red) (n = 2). Optical stimulation was performed through an optical fiber inserted into a guide cannula targeting the BF. Entrainment of the cortical EEG was particularly pronounced when the BF stimulation was at the gamma oscillation frequency (40 Hz) (n = 5). Notably, this entrainment could be reproducibly elicited over the course of an hour of stimulation. 20 Hz stimulation elicited a clear 40 Hz harmonic. We believe this PARV- specific solicitation of cortical gamma oscillation has not been previously reported, and may represent an important but unsuspected feature of BF activation. The effect on the sleep-wake cycle was investigated by comparing one hour of baseline EEG with that of same time of day of one hour of phasic stimulation at 40 Hz. Excluding the 5 s of stimulation, optical stimulation increased wakefulness from 9.2% to 45.2% and decreased NREM sleep from 75.3% to 43.5% (n = 1). We conclude that optogenetic stimulation of PARV-positive BF neurons entrains cortical rhythms, particularly those in the gamma range, and enhances wakefulness.

PO-2-002 / AS-28 Presenter

BOTH OREXIN AND GHRELIN DEPOLARIZE THE RAT LATERODORSAL AND PEDUNCULOPONTINE TEGMENTAL NEURONS VIA PHOSPHOLIPASE C SIGNALING PATHWAY: AN IN VITRO STUDY

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Orexin and ghrelin are newly identified neuropeptides that stimulate food intake. Orexin is produced in the lateral hypothalamus, whereas ghrelin is produced in the medial hypothalamus and peripheral organs, such as the stomach. Recent studies demonstrate that these peptides are also involved in the regulation of sleep-wakefulness. Cholinergic neurons in the laterodorsal (LDT) and pedunculopontine (PPT) tegmental nuclei play a potential role in the control of wakefulness and rapid eye movement (REM) sleep. Interestingly, both LDT and PPT neurons express receptors for orexin and/or ghrelin. Therefore, we examined the electrophysiological effects of orexin and ghrelin on LDT and PPT neurons using rat brain slice preparations. whole-cell patch clamp recording revealed that approximately 55% of LDT and PPT neurons were depolarized by both orexin and ghrelin. The percentage of neurons that were depolarized by orexin alone was 13% in the LDT and 23% in the PPT, whereas 24% of LDT neurons and 9% of PPT neurons were depolarized by ghrelin alone, indicating that LDT neurons are more responsive to ghrelin than orexin and PPT neurons are more responsive to orexin than ghrelin. When orexin and ghrelin were simultaneously applied to LDT and PPT neurons that were depolarized by each of both peptides, a depolarization that was almost equal to the addition of orexin- and ghrelin-induced depolarizations was induced. The depolarization of LDT and PPT neurons induced by orexin and ghrelin was significantly suppressed by D609, an inhibitor of phosphatidylcholine-specific phosphplipase C (PC-PLC). In addition, most of LDT and PPT neurons that responded to orexin and ghrelin were characterized by low threshold spikes and A-currents and they were cholinergic. These results suggest that orexin and ghrelin additively depolarize LDT and PPT neurons via the common PC-PLC signaling pathway, and that orexin and ghrelin may act as effective modulators on LDT and PPT neurons to mediate the hypothalamic and peripheral influences on brainstem machinery to regulate both wakefulness and REM sleep.

PO-2-003 / AS-31 Presenter

FIRING PROPERTIES OF THE NEURONS IN THE AMYGDALA DURING SLEEP AND WAKEFULNESS IN RATS

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Amygdala is known to be a center of emotion and is closely involved in the regulation of autonomic nervous system associating with emotional behavior. During REM sleep, in addition to desynchronization of EEG and rapid eye movement (REM), large fluctuation of autonomic signs such as blood pressure, hart rate or body temperature occur. It has been reported that, in human, activity of amygdale increases during REM sleep. However, little is known about the single neuronal activity in the amygdale during sleep and waking. Single neuronal activity was recorded from the amygdale in non-anesthetized, head restrained rats. About half of the neurons (9 of 19) in the basolateral nucleus of amygdala displayed the most active firing during REM sleep. Of them, five increased the firing in advance of the onset of REM sleep. In the central nucleus of amygdala, neurons active both during waking and REM sleep were recorded. Most of the amyddala neurons displayed phasic firing during REM sleep, while during slow wave sleep, neurons frequently showed burstic firing. These results suggest that the amygdale is closely related with the phasic events during REM sleep.

PO-2-004 / AS-25 Presenter

PHYSIOLOGICAL SIGNIFICANCE OF SEROTONERGIC INHIBITORY INPUTS TO OREXIN NEURONS

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The neurons producing neuropeptide orexin/hypocretin (orexin neurons) have an important role in the maintenance of arousal. It is reported that serotonergic neurons in the raphe nucleus are densely innervated by orexin neurons. These serotonergic neurons express both orexin receptors, OX1R and OX2R, and are activated by orexin. On the other hand, orexin neurons are innervated by serotonergic neurons in the raphe nucleus, and are inhibited by serotonin through the serotonin 1A receptor (Htr1a). Although these results suggest that serotonergic input forms a negative feedback circuit, its physiological role has not been completely understood.
To reveal this, expression of Htr1a mRNA is reversibly regulated in the orexin neurons by applying or removing doxycycline (DOX) from chow. Electrophysiological analysis of orexin neurons revealed that inhibitory

effect of serotonin was approximately 2-hold prolonged in *Htr1a* over expression mice compared with control mice. EEG and EMG recording from *Htr1a* over expression mice revealed that these mice showed fragmentation of wakefulness in the early dark period. DOX application for 5 days cancelled Htr1a mRNA over expression in the orexin neurons and consolidated wakefulness in the early dark period. DOX removing for 14 days over expressed Htr1a mRNA, and wakefulness was fragmented again. However, sleep/wakefulness pattern in the light period was not significantly different from control mice. These results suggest that inhibitory inputs from serotonergic neurons to orexin neurons function as negative feedback circuitry to preserve the activity of orexin neurons in moderate range in the early dark period.

PO-2-005

EXPLORING THE THALAMUS ACROSS THE NATURAL SLEEP-WAKE CYCLE AND ITS ROLE IN SOMATOSENSORY PROCESSING

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Little is known about thalamic cell activity across the natural sleep-wake cycle, especially during REM sleep (REMS), nor its correlates with neocortical activity in non-anesthetised animals. We therefore developed a new technical approach to perform intra- and extracellular single-unit recordings in the mouse somatosensory thalamus coupled with local field potentials (LFP) recordings in its cortical target, polygraphic monitoring of vigilance states and video-tracking of whisker movements. While tonically active during whisking, thalamic cells of the ventroposteromedial nucleus strongly decrease their firing during quiet wakefulness. In slow wave sleep, thalamic cells exhibit robust bursts correlated with the cortical waves, and their membrane potential is more hyperpolarised than in wakefulness and characterised by 1–10 mV membrane potential oscillations correlated with cortical slow waves and spindles. When the mouse enters REMS, thalamic neurons are suddenly depolarised and increase their firing rate. Most cells further increase their activity simultaneously with the REMS associated whisker movements and cortical desynchronisation. Between two episodes of REMS whisking, cortical LFP exhibits a low frequency oscillating activity. This study is the first characterisation of rodent thalamic membrane dynamics across physiological sleep and wakefulness. Furthermore, although cortical response to whisking behaviour has been described, our results bridge the gap between periphery and cortex. Our data reveal that thalamic membrane potential and/or firing is strongly responsive to peripheral inputs, but also tightly linked with cortical activity in each vigilance state. These original data are therefore crucial for the understanding of information processing throughout the somatosensory system.

PO-2-006 / AS-32 Presenter

ELECTROPHYSIOLOGICAL EFFECTS OF OREXIN ON LATERODORSAL AND PEDUNCULOPONTINE TEGEMENTAL NEURONS IN RATS IN VITRO

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Orexin-A (ORX-A) and orexin-B (ORX-B) act upon ORX receptor-1 (OX_1-R) and -2 (OX_2-R) in the brain, and participate in the regulation sleep-wakefulness and feeding. Although ORX-containing neurons project to the laterodorsal (LDT) and pedunculopontine (PPT) tegmental nuclei that control wakefulness and rapid eye movement sleep, the actions of ORX on LDT and PPT neurons are not thoroughly understood. Thus, we examined the electrophysiological effects of ORX on LDT and PPT neurons using rat brain slice preparations. whole-cell recording revealed that ORX depolarized LDT and PPT neurons postsynaptically and dose-dependently. The dose-response curve for ORX-A was almost overlapped to that for ORX-B in LDT neurons, whereas in PPT neurons the dose-response curve for ORX-A was shifted to the left of that for ORX-B with the EC_{50} values for these ORXs being 66 nM and 536 nM, respectively. The ORX-induced depolarization was partly suppressed in high-K^+ solution with extracellular K^+ concentration of 13.25 mM or in low-Na^+ solution in which NaCl was replaced with N-methyl-D-glucamine-Cl. Finally, the depolarization was completely abolished in high-K^+/low-Na^+ solution. Inhibitors of the Na^+/Ca^{2+} exchanger had no effect on the ORX-induced depolarization. In both LDT and PPT neurons, the reversal potential obtained from current-voltage relationships in low-Na^+ solution was approximately −90 mV. When the standard pipette solution was changed to the Cs^+-containing solution to block K^+ channels, the reversal potential was approximately −40 mV in standard external solution. Most LDT and PPT neurons that responded to ORX were characterized by low threshold spikes and A-currents and they were cholinergic. These results suggest that ORX depolarizes LDT and PPT neurons via OX_2-R and OX_1-R, respectively, and via a dual ionic mechanism including an increase of nonselective cationic conductance and a decrease of K^+ conductance. The present results also suggest that LDT and PPT neurons are involved in the cellular process through which ORX participates in the regulation of sleep-wakefulness.

PO-2-007

BURSTIC EYE MOVEMENTS DURING PALADOXICAL SLEEP WERE NOT UNDER THE CONTROL OF SUPERIOR COLLICULUS

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Rapid eye movements (REMs) are the most prominent physiological features of paradoxical sleep (PS). Although REMs during PS are analogous in shape to REMs during wakefulness (saccades), the neural mechanisms regulating REMs during PS are still unknown. In human EEG study, during PS, we have found the positive cerebral potentials following REMs over the occipital visual areas. This potential is known to represent cortical visual information processing after saccades. These results suggest that, during PS, there are voluntary driven REMs under the control of forebrain mechanism. However, it is well known that REMs during PS persist in midbrain-transected cats (without forebrain structures). In this study, we addressed the question whether REMs during PS are, like saccades, influenced by the forebrain structures. In un-anesthetized, head-restrained 7 rats, we examined the effect on the eye movements during PS of electrical lesions to the superior colliculus (SC) that is known to regulate saccade. During PS, two types of eye movements, burstic eye movements and isolated ones occurred. Burstic eye movements were observed more frequently than isolated eye movements but were not observed during wakefulness. After successful

lesion to the SC, the number of burstic eye movements during PS did not change (1.4 ± 0.9 /min in pre lesion and 1.5 ± 0.9 /min in post lesion). In addition, the duration of PS also had no clear difference (44.4 ± 15.9 min in pre lesion and 43.3 ± 12.4 min in post lesion). Our findings suggest that burstic eye movements during PS are regulated by the mechanism not under the control of SC.

PO-2-008 / AS-24 Presenter

SUBSTANCE P DEPOLARIZES SLEEP-ACTIVE CORTICAL NEURONS AND INDUCES EEG SYNCHRONIZATION

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We recently described a population of sleep-active neurons in the cerebral cortex of rodents that present Fos expression during sleep but not wake. These cells express NPY, nNOS and NK1, the receptor for substance P (SP).
To test the hypothesis that SP can modulate the activity of cortical sleep-active neurons and enhance EEG synchronization, we performed *in vitro* patch clamp recordings of cortical NK1 neurons in slices from Npy-hrGFP mice and from squirrel monkey while delivering SP and other sleep-wake related compounds to the bath. To determine the effects of cortical infusion of SP *in vivo*, we also performed multi-site cortical injections of SP in freely-behaving mice while recording EEG and EMG. Putative sleep-active neurons were identified in layers 5–6 of coronal cortical slices after 10 min of incubation in 35 nM of fluorescent TMR-SP, a ligand that is internalized by NK1-expressing neurons. The effects of SP (1–100 nM), ACh, 5-HT, NE and other neuromodulators on membrane potential were determined with and without TTX.
SP strongly depolarized all the recorded neurons that were positive for nNOS in both mice and monkeys, suggesting that SP can modulate cortical activity *in vivo*. 5-HT and NE also depolarized these cells. To characterize the effects of cortical injection of SP *in vivo*, mice were implanted with a telemetry device (DSI, Inc.) that enabled measurement of EEG and EMG in freely-behaving mice. Animals were administered 600 nl of either vehicle or SP diluted in ACSF in 8 cortical sites simultaneously via 4 pairs of bilateral cannulae (Plastics One). Cortical injection of SP evoked a strong increase in delta activity in the EEG that was not observed with vehicle injections.
Our results indicate that SP can modulate the activity of cortical nNOS neurons *in vitro* and EEG activity *in vivo*. The depolarization evoked by NE and 5-HT (which are associated with wakefulness) suggests that there must be an additional mechanism to suppress the activity of nNOS neurons during wakefulness.

PO-2-009

SLEEP DEPRIVATION AND EFFECT OF NITRIC OXIDE, ENDOGENOUS OPIOID LIGANDS, AND MELATONIN ON GASTRIC MUCOSAL DAMAGE IN RATS

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Partial sleep deprivation has been shown to induce gastric mucosal damage in rats and this effect could be due to stress responses. There were some relations among nitric oxide, endogenous opioid ligands, and melatonin with different models of stress. The aim of this study was determining the role of nitric oxide, endogenous opioid ligands, and the possible role of melatonin in gastric mucosal damage induced by partial sleep deprivation. So, 84 male rats assigned in 7 subgroups (n = 12): 3 control subgroups which slept normally and received saline, L-NAME (a non-selective nitric oxide synthase inhibitor), and naltrexone respectively; 3 subgroups had disturbed sleep and received the same drugs as control; and the last one had disturbed sleep and received naltrexone and L-NAME. Partial sleep deprivation was induced by specially designed rotating cages for 14 days. Serum melatonin was measured by ELISA technique. Gastric mucosa damage was assessed macroscopically and microscopically. The results indicated that partial sleep deprived animals have significantly more severe gastric damages than normally slept animals ($P < 0.001$), and inhibition of nitric oxide synthase or blockage of opioids did not have a significant effect on this damage. Furthermore, it was found that serum melatonin was significantly lower ($P < 0.001$) in partial sleep deprived animals than normal slept animals. In conclusion, melatonin might have a protective role in preventing gastric mucosal damage induced by partial sleep deprivation in a way other than nitrergic or opioid pathways.

PO-2-010

EFFECTS OF STIMULATION OF MEDIAN RAPHE NUCLEUS ON STRESS AND STRESS-INDUCED SLEEP ALTERATIONS

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The hippocampal theta waves (4–7 Hz) are dominant in the electroencephalograms (EEGs) during rapid eye movement (REM) sleep, exploration, orientation and anxiety. Theta oscillations has been considered as an index for anxiety level, since anxiolytics suppress the reticular formation-induced hippocampal theta oscillation. The projections from median raphe nucleus (MR) to the medial septum desynchronize the generation of hippocampal theta waves. Current study was designed to investigate whether the MR involves in the enhancement of stress-induced hippocampal theta waves and in the following sleep disturbances. Twelve times of randomized and inescapable foot electroshocks, performed within 10 minutes prior to the light period of the light : dark cycle, increased theta oscillations. After foot electroshocks, the amount of REM sleep was significantly decreased. Application of a train of 100 Hz, 40 ƒÊA electrical stimuli or microinjection of glutamate into

the MR alleviated the enhancement of footshock-induced theta oscillations and increased the time for rats spending in the open arms of elevated-plus maze (EPM), indicating the role of MR in anxiety. However, the footshock-induced reduction of REM sleep was not altered by MR stimuli. These results suggest that the underlying neuronal circuits for the theta oscillations under stress and for the stress-induced decrease of REM sleep may differ.

PO-2-011

THE MYELIN MUTANT TAIEP RAT AS A MODEL OF NARCOLEPSY-CATAPLEXY

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During the process to obtain a high-yawning subline of Sprague-Dawley rats, we obtained a myelin mutant rat with a syndrome characterized by tremor, ataxia, immobilities, epilepsy and paralysis. The acronym of these symptoms given its name taiep. The rats showed an initial hypomyelination followed by a progressive demyelination. During the immobility episodes (IEs) the cortex had a disorganized activity in the beta band, associated with theta rhythm in the hippocampus that is a REM-like sleep pattern. In the present work, we analyze the electrophysiological characteristics of IEs and its relationship with the sleep-wake cycle under basal conditions and after total sleep deprivation. The animals we maintained under standard conditions with a 12:12 light-dark schedule and free access to rodent pellets and tap water. All procedures were approved by the IACUC. The animals were implanted in three different regions of the cortex, hippocampus, nuchal muscles and right orbit with standard techniques and recording signals with Harmonie System. Our results showed that during IEs taiep rats showed three characteristic patterns of muscle tone changes. In type A there is an initial increase in the muscle tone followed by diminution until reach atonia; type B is characterized by an increase of the muscle tone in the middle of IEs and type C showed changes of muscle tone along IEs duration. Importantly all IEs showed a REM-like sleep pattern suggesting a REM sleep disorder similar to narcolepsy. Total sleep deprivation (TSD) performed manually by gently touching technique, waking rats each time they showed polygraphic signs of sleep by 3, 6, 12 and 24 h, and recording during a recovery period showed an increase in the power of SWS rebound after 24 h TSD, but not with other times used. However, a linear increased of IEs are tightly correlated with the time the rats were sleep deprivated ($r2 = 0.85$). In conclusion, IEs in taiep rats are the expression of REM sleep and are controled by homeostatic process. So, myelin mutant taiep rat is an adequate model of narcolepsy cataplexy.

PO-2-012

SHORT-TERM HOMEOSTASIS AND THE NREM/REM ALTERNATION WITHIN SLEEP ARCHITECTURE IN THE RAT

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The time course of the likelihood of entering or ending a REM sleep episode (R) can be described, respectively, as its Propensity and Volatility. Propensity is the instantaneous rate of into-REM transition throughout the interval going from the end of one R to the start of the next R. Volatility is the instantaneous rate of out-of-REM transition throughout R. In this report, we describe those two processes through the alternating sequence of NREM/REM bouts within sleep episodes. Episodes of wake (W), NREM (N) and R were detected with 5-second resolution by an automated system in the 12-hour light-phase from 43 days of recordings of Sprague-Dawley rats. Operationally, episodes within sleep were defined as lasting at least 2 epochs and intervening episodes of W, at least 6 epochs. A total of 2,228 W/sleep alternations were detected. A total of 4,732 N and of 3,056 R episodes were counted. There was a much higher probability of going out to W from the first N in a sleep episode (N1) than from later Ns (47% VS. 24%). In the first 90 seconds of N1 the rate of transiting to W was more than two-fold that of transiting to R (a W inertial effect), a relationship that was later reversed. Early transitions from N1 to W were significantly more frequent the longer the preceding W. N1s that transit to W are significantly shorter that N1s that transit to R (N priming effect). Additionally, the following R1s that transit to W are significantly longer than those that go back to N. In all Rs, the likelihood of going from R to N follows a sharp U curve with a nadir at 1.5–2.0 minutes (N inertial effect and R saturation effect); whereas that of going from R to W increases monotonically through R. Rs that transit to W are significantly longer that those that transit to N and then to W, and these, again, longer that those that transit to N and the go back to R. This suggests that R fulfillment facilitates ending a sleep episode. Characterizing the overt dynamics of sleep-wake alternation may contribute to understanding the time course of the underlying processes that are responsible for sleep architecture.

PO-2-013 / AS-18 Presenter

LOWER BRAIN ACTIVITY DURING SLEEP AND WAKEFULNESS; INDUCED BY EXPOSURE TO LONG MATERNAL SEPARATION AND CHRONIC MILD STRESS IN RATS

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Adverse events in early life can induce vulnerability to handle stressful situations later in life. Sleep disturbances and depression are widespread in victims of negative childhood experiences.
In male rats, we investigated the effects of 180 minutes (long maternal separation; LMS) early separation from the mother during the postnatal days 2–14, compared to 10 minutes (brief maternal separation; BMS). As adults, the animals were exposed to unpredictable chronic mild stress (CMS). Twelve hour EEG/EMG recording, sleep staging and EEG power spectrum analyses were performed before and after CMS exposure.
There were no differences in sleep stages between LMS and BMS offspring. Exposure to chronic mild stress increased total sleep time and time in REM sleep in LMS compared to BMS rats ($p < 0.05$). Within the LMS group, all sleep parameters were affected by CMS except for REM sleep, while CMS affected all sleep parameters in BMS group.
During wakefulness, CMS reduced EEG power in two higher frequency ranges (19.5–35 Hz $p < 0.001$; 35–60 Hz $p < 0.01$), in the theta (6–9 Hz) and in the delta (0.5–4 Hz) range ($p < 0.001$ in both) in the LMS group. Only power in 35–60 Hz frequency range was reduced ($p < 0.05$) in the BMS group.

During slow wave sleep, in both LMS and BMS group chronic stress reduced the EEG power in delta ($p < 0.001$) and theta range ($p < 0.01$). Power was also reduced in 19.5–35 Hz frequency range in BMS ($p < 0.05$), however more strongly in the LMS group ($p < 0.001$). In addition LMS group showed lower power in 35–60 Hz range ($p < 0.05$).
During REM sleep, CMS affected both groups; theta power was reduced in BMS group ($p < 0.05$), and more strongly in LMS group ($p < 0.01$), in addition to a lower power in high frequency ranges ($p < 0.001$ in all). In the BMS group there was an increase in delta power ($p < 0.05$). Long- and brief maternal separated rats responded differently to chronic mild stress. LMS showed more REM sleep. The characteristic EEG power for REM sleep and wakefulness were more strongly reduced in LMS rats. The results indicate that LMS animals are more vulnerable to stress as adults.

PO-2-014

REM SLEEP RECOGNITION BASED ON NEURONAL SYNCHRONY USING TIME-FREQUENCY INTERFERENCE ANALYSIS OF EEG RECORDINGS IN THE RAT

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REM sleep is characterized by a highly predominant, uniform, theta rhythm. During NREM sleep the characteristic large amplitude, irregular, delta-rich activity encompasses a broad spectrum that includes theta band. Since theta activity may be high in both states, EEG analysis based on FFT must additionally compute the delta to theta ratio. Here we present an alternative approach for REM sleep detection based on the direct identification of synchronous rhythms. It has been shown that, through analysis of the envelope of neuronal signals, the degree of synchrony of the underlying neuronal oscillators can be inferred (Diaz et al., J Neurosci 4512-06, 2007). It was demonstrated that combinations of asynchronous oscillators produce a signal whose envelope exhibits a characteristic interference modulation. The coefficient of variation of such signals envelopes (ECV) corresponds to the CV of the Rayleigh probability density function and it approaches sqrt (4/pi-1) or 0.523. When signals are instead produced by a population of synchronized oscillators their ECV is significantly lower. Twenty five days from five chronically implanted Sprague Dawley rats were used to obtain continuous epidural EEG and EMG recordings. States were scored with a 10-second epoch resolution, both visually and by a computer algorithm. After filtering, the theta band ECV per epoch was calculated. Theta ECV for NREM epochs approximated the 0.523 fingerprint value, indicating asynchronous activity of the involved oscillators. In contrast, the theta ECV was markedly lower during REM-sleep, in consonance with their high degree of synchrony. Plotting theta ECV versus EMG power, three very well-defined clusters corresponding to REM, NREM and W are distinguished. Since this method focuses on the signal structure, independently of the signal power, it can directly recognize REM sleep based on the remarkable synchrony of its theta rhythm.

PO-2-015

COMMON CARDIAC RESPONSE TO RESTRAINT STIMULI IN RAT AND MOUSE DURING EARLY POSTNATAL PERIOD

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Introduction: Using a piezoelectric-transducer (PZT) sensor that enabled us to measure heart rate (HR) of small newborn animals noninvasively, we compared the development of HR and the HR response to restraint stress during the first two postnatal weeks between rats and mice.
Methods: Basal HRs of rats and mice were measured by the PZT sensor at postnatal day (P) 0-P14 by simply put them on the sensor for 5 min. Then, HR response to restraint stress was measured for 5 min by restraining them with ECG electrodes which were fixed on the PZT sensor. Additionally, the same protocol was performed after autonomic blockade with atropine, metoprolol or both to evaluate the relevance between the HR response and autonomic nervous system regulation.
Results: Basal HR measured by PZT sensor (PZT-HR) in rats(mice) was 220(323) b/m at P0, which steeply increased to 330(598) b/m at P2(P5) and almost linearly increased thereafter until P14 to 470(692) b/m. In contrast to stable PZT-HR, the stress by attaching ECG electrodes significantly decreased HR of rats(mice) during 5 min at P0 [181(319) to 171(302) b/m, $P < 0.05$] through P10(P3) [427(468) to 364(436) b/m, $P < 0.05$] after an initial HR drop at 0 min, while it induced transient bradycardia at P11(P9) -P14. The transient bradycardia was abolished by parasympathetic blockade with atropine.
Conclusion: Basal HR in both newborn rats and mice increased almost linearly with changing its slope in the first postnatal week but not in S-shape curve as described in the earlier studies. The development of parasympathetic nervous system may be also similar between them because the both exhibited transient bradycardia in response to restraint stress during the second postnatal week. These similar developments of HR and autonomic nervous system seem to be a heritable trait common in rodents at least in rats and mice.

PO-2-016

PRETERM BIRTH ALTERS AUTONOMIC BLOOD PRESSURE CONTROL DURING SLEEP IN INFANCY

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Background: Preterm infants have increased risk for Sudden Infant Death Syndrome (SIDS). Impaired autonomic blood pressure (BP) control leading to an uncompensated hypotension is thought to be involved in SIDS. Assessment of BP variability (BPV) can be used to assess autonomic BP control, however, there are no data concerning BPV during sleep in preterm infants. We aimed to investigate the effects of preterm birth, sleep state and age on BPV across the first 6 months of term-corrected age (CA).
Method: Preterm (n = 25) and term (n = 31) infants were studied at 2–4 wks, 2–3 mo and 5–6 mo CA using daytime polysomnography. BP

was recorded during quiet (QS) and active (AS) sleep using a photoplethysmographic cuff (Finometer™). Using spectral analysis, 2 min BP epochs were used to establish BPV indices: Low frequency power (LF, reflects baroreflex changes and sympathetic modulation), high frequency power (HF, reflects respiratory changes and parasympathetic activity) LF/HF (reflects sympathovagal balance).
Results: Compared to term infants, preterm infants had lower LF/HF at 2–4 wks and 2–3 mo during QS ($p < 0.05$) and at 2–3 mo and 5–6 mo during AS ($p < 0.05$); lower LF power at 2–4 wks during QS ($p < 0.05$); and higher HF power during both QS and AS at all ages studied ($p < 0.05$).
Within the preterm group, LF/HF and LF power were increased in AS compared with QS at 2–4 wks CA ($p < 0.05$), and HF power was decreased in AS compared with QS at both 2–4 wks and 2–3 mo CA ($p < 0.05$). Between the ages of 2–4 wks and 5–6 mo CA, LF power decreased and HF power increased with age in AS in the preterm group ($p < 0.05$).
Conclusions: Preterm infants exhibit a profoundly altered BPV, which suggests that preterm birth provides for reduced sympathetic vascular modulation compared to term infants. Sleep state and age also have marked effects on BPV in preterm infants, suggesting heightened sympathetic vascular modulation in AS, which drops away with age. Overall, lower sympathetic modulation in preterm infants may lead to an impaired ability to appropriately respond to hypo/hypertensive challenges during sleep and may potentially lead to SIDS.

PO-2-017

POOR SLEEP AND CARDIOVASCULAR FUNCTION IN CHILDREN

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Background: Poor sleep in adults is associated with increased risk of hypertension and cardiovascular (CV) disease, but associations with CV function in children are little studied and the results are contradictory. We investigated whether actigraphic sleep quantity and quality were related to 24-hour ambulatory blood pressure (ABP) and CV reactivity to a standardized psychosocial stress test in children.
Methods and results: We studied term-born, healthy 8-year-olds (SD = 1.4 years) without sleep disordered breathing (n = 321 with 231 and 265 providing valid data for analyses on ABP and CV reactivity, respectively). Sleep was registered with an actigraph for six nights on average (SD = 1.2, Range = 3–13 nights). ABP was measured for 24-hours (41% non-school days) with an oscillometric device. The children underwent the Trier Social Stress Test for Children during which blood pressure (BP), electrocardiogram and thoracic impedance were recorded and processed offline to give measures of cardiovascular and autonomic function. Neither quantity nor quality of sleep were related to 24-hour ABP or CV reactivity after accounting for major covariates (sex, age, height, body mass index and parental education).
Conclusions: These findings in healthy 8-year-old children do not support the mainstream of epidemiological findings, derived from samples more heterogeneous in age, sociodemographic characteristics and health, suggesting that poor sleep is associated with an unhealthy CV phenotype.

PO-2-018

FRACTAL HEART RATE DYNAMICS DURING SLEEP IN PATIENTS WITH CHRONIC FATIGUE SYNDROME

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We determined whether feelings of unrefreshing sleep in patients with chronic fatigue syndrome (CFS) were associated with differences in heart rate dynamics during sleep from normal.
Beat-to-beat RR intervals during nocturnal sleep and subjective scores on visual analog scale for sleepiness were collected from 18 healthy and 17 CFS female study participants aged 25–55. Age did not differ between the groups. A short-term fractal scaling exponent of heart rate dynamics, analyzed by the detrended fluctuation analysis (DFA) method was assessed during wakefulness after sleep onset, non-rapid eye movement sleep (stage 1, stage 2, stage 3 or 4), rapid eye movement (REM) sleep (stage REM), and arousal. CFS patients were stratified into those who reported more or less sleepiness after a night's sleep (a.m. sleepier or a.m. less sleepy, respectively).
The fractal scaling index during stage 1, stage 2, and stage 3 or 4 was significantly ($p < 0.05$) higher for patients in the a.m. sleepier group than healthy controls, although standard polysomnographic measure did not differ between the groups. The fractal scaling index during stage 2 and stage 3 or 4 was significantly ($p < 0.05$) lower than that during wakefulness after sleep onset and arousal for healthy controls and patients in the a.m. less sleepy group, but did not differ between sleep stages for patients in the a.m. sleepier group.
These results suggest that autonomic nervous system activity during sleep might relate with unrefreshing sleep in patients with CFS.

PO-2-019

ALTERATION IN THE AUTONOMIC NERVOUS SYSTEM ACTIVITY OF EXTREMELY PREMATURE INFANTS DURING EARLY NEONATAL PERIOD

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Background: Although a major deficit in autonomic nervous system (ANS) activity has been reported in extremely premature infants during early neonatal period, evidences on the alteration in the ANS activity during this period is not widely available. The aim of this study was to investigate the alteration in the ANS activity in extremely premature infants from birth to 7 days of postnatal age (PNA).
Methods: Electrocardiographic recording was performed from birth to 7-days of PNA in 15-infants born within 25–27 weeks of gestational age. Time-domain and frequency-domain analysis of heart rate variability was performed using R-R intervals. As ANS activity indices, standard deviation of normal to normal R-R intervals (SDNN) and root mean square of successive R-R differences (RMSSD) were computed by

time-domain and total power (TP: 0.0–0.50 Hz), the power of low frequency (LF: 0.04–0.15 Hz), the power of high frequency (HF: 0.15–0.50 Hz) and LF/HF ratio were computed by frequency-domain analysis. Data were analyzed in various session from 3-hour (hr) to 7-days of PNA.
Results: Significant changes were not observed in SDNN and RMSSD computed by time-domain analysis until 7-days of PNA($p < 0.05$). Indices from frequency-domain analysis, TP, LF and HF were gradually but significantly increased over the week in the time-dependent manner (TP, 3-hrs: 1053.8 ± 789.4 ms^2, 7-days: 3552.2 ± 1360.9, $p < 0.01$; LF, 3-hr: 553.5 ± 412.7, 7-day: 1698.5 ± 570.3, $p < 0.01$; HF, 3-hr: 259.4 ± 248.2, 7-days: 1077 ± 456.9, $p < 0.01$) with a significant decrease in LF/HF ratio (3-hr: 2.4 ± 1.5, 7-days: 1.6 ± 0.4, $p < 0.05$). LF, indicating sympathetic nervous system (SNS) activity, was significantly higher compared to HF, a marker of parasympathetic nervous system activity, in each session (LF × HF, < 0.001, respectively), however, the increase in HF was greater than the increase in LF power.
Conclusion: The increase in the TP, LF and HF with the increase of PNA suggests a progressive development of the ANS activity after birth and LF × HF indicates the dominance of SNS in the extremely premature infants during early neonatal period.

PO-2-020

HEART RATE VARIABILITY CAN BE USED TO ESTIMATE SLEEPINESS-RELATED DECREMENTS IN PSYCHOMOTOR VIGILANCE

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Study Objectives: To assess whether heart rate variability (HRV) can be used to estimate decrements in psychomotor vigilance caused by sleepiness.
Design: In a within-subjects design, HRV measures were compared with validated measures of sleepiness derived from eyelid closures and the electroencephalogram (EEG).
Setting: Chronobiology and Sleep Laboratory, Duke-NUS Graduate Medical School Singapore.
Participants: Twenty four healthy Chinese men (mean age±SD = 25.9 ± 2.8 years).
Interventions: Subjects were kept awake continuously for 40 hours under constant environmental conditions. Every two hours, subjects completed a 10-min Psychomotor Vigilance Test (PVT) to assess sustained visual attention.
Measurements and Results: During each PVT, we examined the electrocardiogram (ECG), EEG, and percentage of time that the eyes were closed (PERCLOS). Similar to EEG power density and PERCLOS measures, the time course of ECG RR-interval power density (0.02–0.08 Hz) correlated with the 40-h profile of PVT lapses (reaction time × 500 ms). Based on receiver operating characteristic (ROC) curves, RR-interval power density performed as well as EEG power density at identifying a sleepiness-related increase in PVT lapses above threshold. RR-interval power density also classified subject performance with sensitivity and specificity similar to PERCLOS.
Conclusions: The ECG carries information about a person's vigilance state. Hence, HRV measures could potentially be used to predict when an individual is at increased risk of attentional failure. Our results suggest that HRV monitoring, either alone or in combination with other physiologic measures, could be incorporated into safety devices to warn drowsy operators when their performance is impaired.

PO-2-021

CORRELATION OF BRAIN ACTIVITY AND HEART RATE TIME COURSES DURING NOCTURNAL SLEEP: A PILOT STUDY

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Introduction: Sleep is an active process with dynamic changes in the electrophysiology of the brain and other organs, such as the heart, in various time scales. Having "sound" sleep, consequently, is important not only to patients with sleep-related disorders but also to others with comorbidities, e.g., cardiac dysfunction. Electroencephalograms (EEG) and electrocardiogram (ECG), routinely used to monitor patients during sleep studies, enable us to explore simultaneous, dynamic changes in the brain and heart. The purpose of this study is to introduce a method to examine correlations of brain and heart activity, and demonstrate its potential application in a clinical setting.
Methods: Full polysomnography (including six-channel EEG, ECG, EOG, etc) was recorded for 17 patients (8 obstructive apnea and 9 healthy controls). Each 5 s epoch of the EEG and ECG signals was examined for non-physiological artefact. Artefact-free EEG epochs were analyzed using the power spectral method and detrended fluctuation analysis (DFA), while a QRS detection algorithm was applied to 5 s ECG epochs. These values were calculated for each sleep stage. In particular, correlations between DFA scaling exponents (SE) and the RR interval (RRI) of the heart beat were explored.
Results: We found two distinct patterns of correlations between DFA SE and RRI. 15 of the 17 patients showed significant positive correlations (i.e., higher DFA SE occurs with slower heart rate, mean correlation coefficient, $r = 0.30$, $p < 0.001$), while 2 patients (one from OSA and one from controls) show significant negative correlations ($r = -0.27$, $p < 0.001$). No inter-group differences were found.
Discussion: The strong correlation between brain and heart activity suggest that our method could be a potential measure to study the comorbidity of sleep and heart-related disorders. The clinical conditions associated with the positive and negative correlations require further study.
Support: Australian Research Council, Australian National Health and Medical Research Council.

PO-2-022

HAEMODYNAMIC COUPLING OF ELECTROGRAPHIC TRANSIENTS DURING NON-REM SLEEP

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Introduction: The transit between the state of wakefulness and the stages of sleep can be assessed by way of various electrographic

phenomena. The K-complex, sleep spindles and vertex sharp waves are landmarks in the staging of sleep (Rechtschaffen and Kales., 1968). The neurophysiological origin of these sleep transients are fairly well understood, due in part to the work of Steriade and colleagues (Amzica & Steriade., 1997; Steriade et al., 1987), though their functional role is less clear. Combined EEG-fMRI is a potential tool for elucidating the functional role of these electrographic transients.
Method: The EEG-fMRI data were obtained from 14 control subjects who had undergone a night of sleep deprivation prior to scanning (3T Philips Achieva, TR = 2000 ms, 64 channel EEG, Brain Products, Munich, Germany). GLM analysis was performed using SPM5 (Wellcome Department of Imaging Neuroscience, UCL, UK).
Results: Of the 14 subjects, 4 failed to reach a sufficient state of sleep. The 10 subjects who fell asleep had one or more of the sleep transients present in the EEG, with all showing fMRI activation. Vertex sharp waves demonstrated activation in the primary somatosensory, primary visual and auditory cortex, with additional involvement of inferior frontal regions. Common activation patterns for K-complexes included superior frontal, post central regions, as well as temporal and posterior cingulate areas. Sleeps spindles showed differing activation patterns dependent on their frequency and topographical distribution.
Discussion: These findings suggest vertex sharp waves may act as priming mechanism of primary sensory systems in response to exogenous stimuli; such as sound. Robust activation was identified with K-complexes, despite previous EEG-fMRI studies concluding that, due to no associated fMRI changes, there was little metabolic demand in their generation (Czisch et al., 2009). Our findings support the observations made by Schabus et al. (2007), of the notion of two spindle types though there is some discrepancy. The potential role of these sleep transients are discussed.

PO-2-023

EFFECTS OF INTENSIVE EXERCISE ON PHYSIOLOGICAL RESPONSES DURING SLEEP

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Introduction: There have been various researches on the relationship between sleep and exercise. However, few researches have been conducted in relation to physiological responses during sleep after intensive exercise. The purpose of the present study is to examine the effect of intensive exercise on sleep electroencephalogram (EEG), heart rate variability (HRV) and rectal temperature (RT).
Method: Seven young males participated in the experimental condition consisting of three consecutive days. The first night was set for acclimatization. Subsequent two nights were set as "no exercise day (second night, control condition)" and "exercise day (third night, exercise condition)". On the exercise day, the participants performed ten sets of 5 seconds maximal pedaling exercise with 25 seconds rest periods between sets. An applied load for maximal intermittent exercise was equivalent to 7.5% of each participant's body weight. The exercise was then repeated after 30 minutes. Respiratory parameters and blood lactate concentration were measured before and after exercise. During sleep (bedtime from 23:30 to 07:30), polysomnography (PSG), HRV (heart rate: HR, low frequency: LF, high frequency: HF and LF/HF), and RT were continuously recorded.
Results: There were no significant differences in sleep variables and EEG power spectrum. However, HR, LF/HF and RT were significantly higher in the exercise condition than in the control condition ($P < 0.05$). In addition, HF was significantly lower in the exercise condition than in the control condition ($P < 0.05$).
Conclusion: Although sleep variables and EEG power spectrum did not differ between conditions, HR, LF/HF, HF and RT showed significant differences between conditions. These results suggest that intensive exercise has a strong effect on autonomic systems such as HRV and RT, but not on EEG during sleep.

PO-2-024

EFFECT OF SINGLE BOUT MODERATE INTENSITY 1-HR AEROBIC EXERCISE AT NIGHT ON FOLLOWING NIGHT SLEEP

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Although, there have been studies to investigate the effect of exercise on sleep, most of the results indicate the exercise has only little effect on sleep. However, Walker et al. (1978) reported an interesting result that exercise has strong effect on heart rate during sleep. This result may indicate that physical exercise has more effect on autonomic parameters during sleep than EEG sleep. Therefore, in this study, we aim to examine not only EEG sleep, but also other physiological parameters such as heart rate (HR), respiratory rate (RR) or core body temperature (CBT). Healthy young male subjects, who are sedentary nonsmokers, participated in the experiment consisting of two sets of two consecutive nights. The first night was adaptation night in the both sets. The second night was exercise condition in the first set and control condition in the second set. Two sets were separated by one week. Sleep time was 8 hours from 11pm to 7am. On the exercise condition, subjects performed 60-minutes cycle ergometer exercise at 60%VO2max 3.5 hours before bedtime. On the control condition, subjects relaxed by watching TV and reading books at the same time period. We recorded PSG including EEG, HR, RR, and CBT. Newly developed sheet type sensor was also used. This device was inserted under bed mattress and measured HR and RR. In addition, cortisol, blood glucose level, blood lactate level, and subjective sleep quality. We have finished a part of subjects. The results up to now indicate that WASO, HR and CBT increased exercise condition. Furthermore, heart rate variability analysis revealed that parasympathetic nervous system during exercise condition decreased. Complete results with statistical analysis will be presented at the meeting.

PO-2-025 / AS-28 Presenter

DECREASES IN CONNECTIVITY BETWEEN THE CENTROMEDIAN NUCLEUS OF THE THALAMUS AND THE NEOCORTEX DURING HUMAN SLOW-WAVE SLEEP

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The objective of this study was to extend, into humans, the finding from animal studies of a functional deafferentation between non-specific

thalamic nuclei and the neocortex during slow-wave sleep. Simultaneously collected EEG and fMRI were used in this regard. A functional connectivity analysis was conducted by calculating the correlation between fMRI activity in the centromedian nucleus of the thalamus and the rest of the brain during wakefulness and slow-wave sleep. Significant differences between wake and sleep were calculated on a voxelwise basis using Fisher's z transformation. The absolute value for each transformed correlation was used in this calculation because if a strong positive correlation during wakefulness became a strong negative correlation during sleep, this would still indicate the same magnitude of connectivity and thus the difference between the conditions would be and should be zero. Based on previous animal work, it was hypothesized that a majority of neocortical regions would show a significant decrease in the magnitude of their correlation with the centromedian nucleus during sleep. This hypothesis was supported. The neocortical regions that displayed decreased connectivity were mostly heteromodal regions (e.g., posterior cingulate/precuneus), but there were also decreases in unimodal regions (e.g., lingual gyrus). This study provides evidence of a functional deafferentation between non-specific nuclei of the thalamus and the neocortex during slow-wave sleep using a non-invasive technique in humans. The results represent a plausible mechanism that might correlate with sensory thresholds in future sleep studies and explain them based on known neurophysiological phenomena. For example, the thalamus may act like a gate where sensory signals are essentially blocked from being transmitted to the neocortex during sleep. These data may also lead to a better understanding of disorders of consciousness such as coma, which exhibit similar changes in thalamocortical connectivity.

PO-2-026

ASSOCIATION BETWEEN JAW POSITION AND MASSETER TONE DURING SLEEP

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Objectives: Muscle tone of orofacial muscles as well as other skeletal muscles is decreased during sleep. Since masseter muscle is responsible for the jaw-closing movements, the changes in masseter tone can be correlated to the amount of jaw opening during sleep. Thus, we investigated the association between masseter tone and the amount of the jaw opening during sleep.
Methods: Twelve healthy adult subjects (7M; 5F, 25.5 ± 5.7 years) were participated. They had normal occlusion and were free from sleep disorders and stomatognathic dysfunction. Masseter EMG activity and jaw movements were recorded simultaneously with video-polysomnography for two nights. Jaw movements were recorded by the six-degree-of-freedom jaw tracking device that can detect the positions of intraoral sensors attached to upper and lower teeth. The data from the second night were analyzed. Sleep stages were scored according to the R&K method. For every one second during quiet sleep period without masseter contraction and jaw movement, masseter tone and the jaw opening length were analyzed.
Results: Masseter tone significantly differed between sleep stages (Friedman test, $P < 0.001$). It was lower during Stage REM than Stages 1, 2 and 3&4 (post hoc Wilcoxon tests, $P < 0.05$). The jaw opening length was smaller during Stgae1 than other sleep stages (Friedman test, $P < 0.001$; post hoc Wilcoxon tests, $p < 0.05$). In all subjects, no obvious correlations were found between masseter muscle tone and the jaw opening length in the night (Pearson correlation coefficient < 0.3).
Conclusion: The results suggest that the changes in masseter tone are unlikely associated with the amount of the jaw opening during sleep.

PO-2-027 / AS-20 Presenter

THE PATTERNS OF CLOSE-OPEN JAW MOVEMENT DURING SLEEP IN NORMAL SUBJECTS

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Objectives: Increased jaw motor activities associated with tooth grinding are thought to be a cause of dental problems in sleep bruxism patients. Although mechanical impacts to teeth during jaw motor activities can vary with the patterns of jaw movements, there is little information on jaw movements during sleep. This study was aimed to characterize the patterns of close-open jaw movement during sleep.
Methods: Video-polysomnographic recordings with masseter EMGs were made in 8 young healthy volunteers (6M; 2F, 23.8 ± 2.2 yrs old) for two nights. Jaw movements were simulataneously recorded by the six-degree-of-freedom jaw tracking system. The data from the second night were analyzed. Masseter EMG bursts with the amplitude × 5% of maximal voluntary tooth clenching were detected. Jaw motor episodes were scored when the successive bursts were separated by × 2 seconds. Then, cycles of close-open jaw movements were selected. For each cycle, jaw movement trajectories on the frontal view were analyzed.
Results: Among 231 episodes scored (mean±SD: 28.9 ± 11.4), 121 episodes (15.1 ± 6.5) contained 371 (46.4 ± 35.4) close-open jaw movements: 33.2% of cycles were more likely vertical (Lateral jaw shift: 0.81 ± 0.70 mm) while the other cycles (66.8%) were characterized by jaw sliding movements against the upper dentition with a larger lateral jaw shift (3.42 ± 1.68 mm). Lateral jaw sliding was found to occur either during jaw-closing, jaw-opening phase, or both phases of a close-open cycle. An inter-individual difference was found for the percentage of the occurrence for the jaw movement patterns.
Conclusion: In normal subjects, jaw motor episodes were occasionally associated with close-open jaw movements. The patterns of close-open jaw movements can vary. Variations of the jaw movements during jaw motor activity suggest that teeth are exposed to a variety of mechanical load during sleep.

PO-2-028

BRAIN ACTIVITY MARKERS OF SLEEP CORRELATE WITH PERFORMANCE DURING A SUBSEQUENT EXTENDED WAKEFULNESS CHALLENGE

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Introduction: Vigilance failure due to sleep loss has a major impact on health and the economy. It is important to identify individuals at risk of vigilance failure but this is difficult in a clinical setting. Better

biomarkers of neurobehavioural dysfunction e.g. impaired driving are required. We explored the relationship between brain activity biomarkers of sleep and neurobehavioural dysfunction during a subsequent extended wakefulness challenge.
Methods: Healthy subjects completed a 3-day/night protocol with two nights of polysomnography (night 1 = baseline; night 3 = recovery) and 40 h of extended wakefulness in between. Performance testing on a psychomotor vigilance task (PVT) and driving simulator (AusEd) occurred every 2 h during wake. Baseline sleep EEG (Cz/A1) was analysed using power spectral analysis and detrended fluctuation analysis (DFA) following artefact exclusion. We explored correlations of power spectra and DFA scaling exponents (ScE) of sleep with performance measures. ScE increases with deeper sleep, is lower in REM and wake, and correlates with slow wave sleep (SWS).
Results: We assessed 9 healthy subjects (8 male) without sleep disorders (age 28 yrs, BMI 23 kg/m^2). A greater low-delta power (0.5–1 Hz) of SWS correlated with poorer vigilance (PVT mean reciprocal reaction time $r = -0.83$, $p = 0.005$; lapses $r = 0.76$, $p = 0.02$) and impaired driving (AusEd steering deviation $r = 0.73$, $p = 0.02$; crashes $r = 0.79$, $p = 0.01$) following one night of sleep deprivation (×28 h awake). The DFA ScE of SWS also positively correlated with vigilance and driving ability. Conversely, sigma power (12–15 Hz) of NREM (stages 2, 3 & 4) negatively correlated with driving ability.
Discussion: Strong relationships between brain biomarkers of baseline sleep and neurobehavioural dysfunction during extended wakefulness exist in these subjects. Increased low-delta power and ScE of SWS significantly correlated with worse performance, and increased sigma power with better performance. These biomarkers may be useful to identify those at risk of vigilance failure or monitor treatment effectiveness.

PO-2-029

FRONTAL BRAIN NETWORK ACTIVITY DEPENDS ON SLEEP

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The restorative effects of sleep or conversely, the effects of sleep loss on waking brain activity remain poorly understood. An example of sleep deprivation-induced effects is the loss of functions mediated by the prefrontal cortex. We here investigate the relationship between sleep and subsequent awake brain activity high-density EEG. We hypothesize firstly: that a night of sleep deprivation (SD) leads to less optimal functional network, described with graph theory, as compared to after normal sleep; and secondly, that the functional network changes are not uniform across the brain but show regional specificity. We obtained resting state eyes-close EEG measurements of 8 healthy subjects both after a night of normal sleep and after a night of sleep deprivation. Synchronization between the 61 electrodes was determined using synchronization likelihood, a measure of linear and non-linear coupling. From the synchronization matrix, small world network characteristics, i.e. the cluster coefficient (C) and the path length (L), were calculated for different frequency bands. A permutation analysis with a cluster correction for multiple comparisons was applied to assess significant local changes in C and L. We found that SD selectively affects the network characteristics of frontal regions. After SD, C was lower for the alpha band and L was higher in the beta and theta band compared to after sleep. These changes could not be explained by power differences. Frontal connectivity, as determined by small-world network analysis, was decreased locally after sleep deprivation in the alpha and theta band. A homeostatic restorative function of sleep would therefore be most prominent in the frontal regions. It remains to be investigated how task-related neural network activity responds to sleep deprivation: the findings fit well with the notion that specifically functions associated with the frontal cortex suffer from sleep deprivation, such as executive control and higher-order cognitive processes.

PO-2-030

THE RELATIONSHIP BETWEEN THE POLYSOMNOGRAPHIC SLEEP STATE AND THE SUBJECTIVE QUALITY OF WAKEFULNESS

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The relationship between the objective sleep state and the subjective quality of wakefulness after waking up was investigated in the normal sleep.
Subjects were twenty healthy males. PSG and the subjective feeling scores of VAS (visual analog scale) were recorded for eight consecutive nights. First two days were adaptation nights. Subjects were awakened by alarm after seven hour sleep. Sleep stages were scored by the R&K's manual every 20 seconds. EEG frequency analysis immediately before awakening for less than three minutes was made with the complex demodulation method. Spearman's correlation was calculated to analyze the relationship (*; $p < 0.05$).
In the VAS scores immediately after awakening, results showed the negative correlation ($r = -0.49^*, -0.51^*$) between the amount of Stage2 in the last quarter of sleep and the scores of energy and the total activity (average score of wakefulness, mood, energy and fatigue), and the positive correlation ($r = 0.49^*, 0.59^*$) between EEG alpha power 30 sec before awakening and the scores of wakefulness and refreshment, and the positive correlation ($r = 0.52^*, 0.59^*$) between EEG beta power 30 sec before awakening and the scores of wakefulness and refreshment.
In the VAS scores 1 hour after awakening, results showed the negative correlation ($r = -0.55^*$) between the amount of Stage2 in the last quarter of sleep and the scores of mood, and the negative correlation ($r = -0.50^*, -0.50^*, -0.46^*$) between the number of spindles in the last quarter and the scores of mood, fatigue and the total activity. However, there were no significant correlations between EEG power 30 sec before awakening and VAS scores.
It is suggested that the quality of wakefulness immediately after awakening showed stronger correlation with the sleep state immediately before awakening. On the other hand, the quality of wakefulness 1 hour after awakening showed the correlation with the sleep state in the last quarter or longer period of sleep.

PO-2-031

TOPOGRAPHICALLY ENHANCED SLOW SPINDLES IN MEDICATED DEPRESSIVE PATIENTS

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Introduction: Accumulated researches have demonstrated that sleep spindles were generated within thalamo-reticular formation and that frontal spindles observed in parietal region consisted of slower frequency, compared with those in centro-parietal region. The difference of propensities between slow spindles and fast spindles have been still under debate.
Objectives: To clarify the properties of sleep spindles between healthy subjects and medicated depressive patients, including frequency range, spectra power and the pattern of propagation.
Methods: Healthy comparison subjects (n = 20)and medicated depressive patients(n = 14)were recruited. Subjects were recorded during all night with 16 channels EEG. Recordings were analyzed for changes in EEG power spectra, power topography. In addition, we graphically demonstrated the pattern of propagation of each type of spindle, divided into fast spindle(12.5–16 Hz)and slow spindle(10.5–12.5 Hz). Ethical committee of Tokyo Medical and Dental University approved this study and written informed consent was obtained from each subject.
Results: As a result of ANOVA and multiple comparison, sleep EEG of depressive subjects exhibited statistically the highest amplitude of slow spindle in frontal pole region, compared with the other regions. On the other hand, sleep EEG of normal subjects exhibited the highest amplitude in frontal region. Slow spindles were generally dominant in whole cerebral regions in depressive patients, while fast spindles were prominent within frontal region in normal groups.
Conclusions: Sleep spindles are generated by the thalamic reticular nucleus and are modulated by corticothalamic and thalamocortical connections. The alteration in sleep spindles in medicated depressive subjects may reflect dysregulation in thalamic-reticular and thalamocortical mechanisms and could represent a recovery process on neural network, involving pharmacological modulation on synaptic function.

PO-2-032

SENSORY INPUT AND SLEEP, REVISITED

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The passive sleep theory was proposed by Bremer (1935) i.e., the lack of sensory input would be the origin of sleep. Beside, the surgical section of the olfactory, optic, statoacoustic, and trigeminal nerves, one vagus nerve and the spinal cord posterior paths in cats -quasi total deafferentation-, carried out by Vital-Durand et Michel (1971) showed that diminishing the contact with the external world. The sphinx behavior observed was associated with a peculiar occipital EEG, and a *"somnolence"* state.
Later became clear that sleep was depending on brain active processes.

The auditory is a special sense continuously open during wakefulness and also in sleep[1]. In a recent study (based on previously demonstrations in guinea pigs reported results) four implanted deaf patients were recorded during 4 nights each one; 2 nights with the implant OFF, with no auditory input, and 2 nights with the implant ON, i.e., with normal auditory input, being only the common night sounds present, without any additional auditory stimuli delivered. All of them with the implant OFF showed normal sleep patterns. When compared the night recordings with the implant ON and OFF, a new sleep organization was observed for the recordings with the implant ON, suggesting that brain plasticity may produce changes in the sleep stage percentages while maintaining the ultradian rhythm. During sleep with the implant ON, the analysis of the electroencephalographic delta, theta and alpha bands in the frequency domain, Fast Fourier Transform, revealed a diversity of changes in the power originated in the contralateral cortical temporal region[2]. Conclusions, it was showed that the auditory input in humans can introduce changes in CNS activity leading to shifts in sleep phases percentages characteristics emphasizing the relevance of the sensory input on sleep.

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PO-2-033 / AS-31 Presenter

OPTOGENETIC ACTIVATION OF PREOPTIC AREA GABAERGIC NEURONS INHIBITED ACTIVITY OF OREXIN NEURONS

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Neurons in the preoptic area (POA), especially the ventral lateral preopticarea and the median preoptic nucleus, fire rapidly during sleep and cease firing during wakefulness. These neurons carry GABA, and thought to play an important role in initiation and maintenance of sleep by sending inhibitory projections to the arousal systems that reside in the brain stem. Recently, several evidence have suggested that orexinergic neurons in the hypothalamus,which play a critical role in maintaining arousal, are also influenced by these neurons. To elucidate the roles of these neurons in regulation of orexin neurons, we optogenetically stimulate these sleep-active neurons. We used Gad1-Cre knock-in mice, in which Cre recombinase is exclusively expressed inGABAergic neurons. We used an adeno-associated viral vector to deliver channelrhodopsin-2-YFP to Cre-expressing neurons in the POA. The axonal projection of the GABAegic neurons of the POA was visualized with double-label immunohistochemistry used anti orexin antiserum combined with an anti-GFP antiserum. Rich immunoreactivities of GFP-ir projections were observed in arousal region including the LHA. Optogenetic stimulation of POA GABAergic neurons resulted in increase of NREM sleep accompanied by inhibition of activity of orexin neurons. These observations suggest that the POA GABAergic neurons are important ininhibition of arousal regions including hypothalamic orexin neurons.

PO-2-034 / AS-23 Presenter

FEEDING-INDUCED CATAPLEXY AND C-FOS EXPRESSION IN BRAIN AREAS PROJECTING TO THE BRAINSTEM IN OREXIN KNOCKOUT MICE

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Cataplexy is a sudden loss of muscle tone induced by strong emotions that occurs in people with narcolepsy. About 90% of narcoleptics with cataplexy have low or undetectable orexin/hypocretin levels, and mice lacking orexin signaling have atonia and paralysis episodes strongly resembling human cataplexy. Although orexin has an essential role in the regulation of cataplexy, the neural mechanisms that trigger cataplexy are poorly understood. To better understand these mechanisms, we first sought a stimulus to produce high levels of cataplexy. We found that chocolate markedly increases cataplexy in orexin knockout (KO) mice. Next, we microinjected the retrograde tracer cholera toxin subunit B (CTB) into ventrolateral periaqueductal gray and lateral pontine tegmentum – an area that receives orexin projections and is thought to suppress rapid eye movement sleep and cataplexy. We then mapped the distribution of neurons double immunolabeled for CTB and c-Fos, a marker of neuronal activation. Compared with orexin KO mice that received normal chow, orexin KO mice that received chocolate had higher numbers of neurons showing double labeled cells in the medial prefrontal cortex, parasubthalamic nucleus, and prerubral field. Increased activity in some of these regions may trigger cataplexy induced by highly palatable food or emotionally positive stimuli.

PO-2-035

NR6A1 REGULATES HYPOCRETIN/OREXIN TRANSCRIPTION

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Hypocretin (also called as orexin) coordinates the regulation of sleep/wakefulness and energy homeostasis. The reduction in nuclear receptor subfamily 6, group A, member 1 (*Nr6a1*) expression was shown in hypocretin neuron-ablating transgenic mice. Using a database analysis *in silico*, we identified a putative NR6A1 target sequence within hypocretin promoter. To evidence prepro-hypocretin transcription is functionally modulated by NR6A1, we performed chromatin immunoprecipitation (ChIP)-PCR, double-immunostaining, luciferase reporter assay, and *in utero* electroporation study. ChIP-PCR showed the endogenous NR6A1 binds to DNA containing putative NR6A1-binding site. Double-immunostaining indicated almost all hypocretin neurons were positive for NR6A1 immunoreactivity. Transfection with NR6A1 into SH-SY5Y cells modulated hypocretin promoter activity, an effect that was countered by using a mutated prepro-hypocretin promoter lacking a putative NR6A1-binding site. *In utero* electroporation with Nr6a1 into the fetal hypothalamus activated in hypocretin transcription compared with that of GFP-electroporation. These studies confirmed that NR6A1 works as a regulator for hypocretin transcription.

PO-2-036

OREXIN CHANGES IN EXPERIMENTALLY IMMUNIZED RATS BY TRIB2

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Narcolepsy is thought to be caused by loss of orexin neurons in the hypothalamus. The allele of the HLA (DQB1*0602 as susceptible, DQB1*0603 as protective) and the polymorphisms in T-cell receptorƒ¿ loci are strongly associated with the morbidity. It is also reported improvement of cataplexy and normalization of CSF Orexin-A by the intravenous administration of IgG. These evidences indicate the contribution of autoimmune mechanism, however, the details remain unknown. Recently, Cvetkovic-Lopes et al reported about 30% narcolepsy patients have autoantibodies to TRIB2 protein, which is highly expressed in orexin neurons. We also have confirmed the autoantibodies to TRIB2 (anti-TRIB2) in the serum of Japanese narcolepsy patients. To clarify whether 1) orexin neurons are degenerated by the attack of anti-TRIB2 or 2) anti-TRIB2 increases in the serum due to loss of orexin neurons, we investigated the changes in orexin of rats experimentally immunized with TRIB2.

Twenty-five 6 week-old female SD rats were given every other week the subcutaneous injection of keyhole limpet hemocyanin (KLH), 30ƒÊG TRIB2 conjugated to KLH (TRIB2), or saline (control). The IgG titers were also checked every other week by ELISA. After the IgG titers rose, orexin concentrations in CSF were measured by ELISA kit. The rat brains were stained immunohistochemically to investigate the change of orexin neurons.

The percent ratio to the average orexin level of age matched control group was calculated. Orexin in both KLH and TRIB2 group decreased significantly compared to the initial value. Orexin levels of 16, 18, and 20 week-old rats in KLH group are 114.16%±14.05, 61.96%±4.90, and 81.18%±10.67 (mean±SEM), respectively. Similarly, these in TRIB2 group of 16, 18, and 20 week are 97.75%±8.38, 77.56%±8.12, and 73.84%±8.65, respectively. There was no significant difference between KLH and TRIB2 group. Contrary to expectation, there was no change in orexin neurons of either group in histological study. This result may suggest that the general activation in immune system has the effect on the regulation of orexin synthesis.

PO-2-037

DOPAMINERGIC SLEEP REGULATION IN DROSOPHILA MELANOGASTER

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In mammals, dopamine regulates different kinds of cognition and behavior, such as reward, attention, motivation, sleep, working memory and learning. Neural circuit of dopamine system and dopamine receptors dissociate these functions.

Since identification of sleep in Drosophila melanogaster, the most sophisticated genetic model organism, there have been significant advances in the understanding of molecular basis of sleep. In Drosophila melanogaster, dopamine also regulates sleep, learning and memory. Dopamine transporter (DAT) mutant, fumin, shows short

sleep phenotype and poor memory retention. However, little is known about how these different functions are achieved by dopamine. Here we show that specific neural circuit and dopamine receptor regulates fly sleep. Double knock out of DAT and dDA1 receptor rescued short sleep phenotype in fumin mutant. Tissue specific knock down of dDA1 receptor in fumin background revealed the brain locus important for sleep regulation by dopamine. Activation of subsets of dopamine neuron which contribute to the formation of aversive memory showed little effect on fly sleep. We further searched sleep regulating subset of dopamine neuron by expressing thermosensitive dTrpA1 channel using mosaic analysis with a repressible cell marker (MARCM) system. The direct activation of dopamine neuron subset with dTrpA1 channel identified specific neural circuit. These results suggest that specific subsets of dopamine neuron regulates fly sleep.

PO-2-038

SLEEP ALTERATIONS IN HUMANIZED P2RX7 MICE – VALIDATING A SUSCEPTIBILITY MARKER FOR DEPRESSION

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Introduction: Biological markers for depression are of great interest due to their potential to indicate the presence of the condition. Recently, a single nucleotide polymorphism (SNP) identified in the purinergic receptor P2X, ligand-gated ion channel, 7 (P2rx7) gene has been found to be associated with depression. In search for the functional relevance of this polymorphism as a susceptibility marker for depression, we investigated sleep-wake patterns and sleep architecture in humanized mouse mutants in which the murine P2rx7 gene was substituted by the wild-type or the disease-associated variants of human P2rx7 (P2rx7h).
Methods: All mouse lines (wild-type $P2rx7^{hWT}$, heterozygote, $P2rx7^{hWT/hMT}$ and homozygote $P2rx7^{hMT}$; n = 11 each group) habituated into 12:12-h light-dark cycles were implanted with EEG-EMG electrodes for polygraphic sleep recordings. Spontaneous sleep-wake states were monitored for a 24-h light-dark cycle starting with the onset of the light period.
Results: All mouse lines exhibited a diurnal rhythm in the distribution of sleep and wakefulness, with increased amounts of sleep during the light than the dark period. The amount of wake, NREM or REM sleep did not differ between genotypes across the 24-h recording period. However, during the light period, significantly less amount of SWS2 and more frequent entries into the REM sleep episodes were demonstrated in heterozygous $P2rx7^{hWT/hMT}$ mice. Compared with two other lines, dramatic suppression of the EEG power in lower frequency bands was observed in the $P2rx7^{hWT/hMT}$ strain. In particular, the activity of slow waves during NREM sleep was decreased in $P2rx7^{hWT/hMT}$ mice during the normal resting phase.
Conclusion: In summary, only heterozygous mice carrying the humanized variant of P2rx7 gene show a reduced quality of sleep. Strong drives toward REM sleep and altered homeostasis of sleep regulation are quite unique sleep characteristics observed in heterozygous $P2rx7^{hWT/hMT}$ mice. We suggest the feasibility of this mouse line as a new depression model to study sleep disorders caused by the same variation in humans.

PO-2-039

THE INVOLVEMENT OF CRH-R1 IN STRESS-INDUCED REM SLEEP REBOUND

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Severe stress is thought to underlie the development of many psychiatric disorders such as depression. A cardinal symptom of depression is impaired sleep including changes in sleep architecture (e.g. REM sleep disinhibition). A contribution of corticotropin-releasing hormone (CRH) as a major activator of the stress axis to these sleep changes was suggested. Our study showed that a lack of the central CRH receptor type 1 (CRH-R1) prevents REM sleep rebound after a mild stressor (i.e. sleep deprivation). In this study we investigated whether these results could be replicated by applying a stronger stressor (i.e. restraint stress) to our animals. Conditional CRH-R1 knockout (CRH-R1 CKO) mice and their wildtype littermates (CL) were implanted with EEG and EMG electrodes. After recovering from surgery mice were restrained for one hour at the beginning of the light period by placing them into falcon tubes. One week later, restraint was repeated to collect blood samples to assess plasma corticosterone levels (CORT) in response to the stressor. EEG and EMG recordings were performed for 23 h one day before, during, and one day after the first restraint experiment. Under baseline conditions, no differences in vigilance states were detected between the genotypes. After the stressor, both groups showed increases in CORT levels, as well as decreased wakefulness and increased NREM sleep at the beginning of the dark period. However, in CRH-R1 CKO unlike CL animals no REM sleep rebound occurred. Previous studies report that the rebound of REM sleep induced after certain stressors is blocked by unspecific CRH receptor antagonists. Our results are in line with these observations and point towards a crucial involvement of central CRH-R1 pathways in REM sleep regulation.

PO-2-040

LACKING PURINERGIC P2X7 RECEPTOR (P2X7R) INFLUENCES BASELINE SLEEP BUT NOT RESPONSES TO SLEEP LOSS AND AN IMMUNE CHALLENGE IN MICE

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The purinergic P2X7 receptor (P2X7R) is a ligand-gated ion channel and locates on macrophages and microglia, involved in the maturation and release of inflammatory mediators such as interleukin-1β (IL-1β). Cytokines like IL-1β trigger many physiological and behavioural changes in depression. Further, many reports support that those cytokines possess sleep regulatory properties. Since sleep-wake behaviour is often altered in depressed patients, it is of our interest to know a role of P2X7R in sleep regulation. Therefore, we employed P2X7R knockout (KO) mice and analyzed sleep patterns under baseline and stress conditions. P2X7R KO mice and wild-type littermates were implanted with EEG and EMG electrodes. Baseline recordings were initiated 2 weeks after surgery, and 6-h sleep deprivation (SD) was subjected at the beginning of the light period on a following day. In a different group of animals, 10μg of lipopolysaccharide (LPS) was i.p. injected at dark

onset, and sleep responses to this immune challenge were compared between genotypes. During the light period, P2X7R KO mice spent slightly more non-REM sleep at the beginning, whereas during the dark period they showed a reduced amount of non-REM sleep, compared to wild type animals. Regarding REM sleep, attenuated levels were mostly consistent throughout the baseline day in P2X7R KO mice. In contrast, they were more awake during the dark period than wild type mice. In response to SD, however, both genotypes demonstrated similar sleep recovery. As reported in previous studies, LPS challenge increased non-REM sleep and suppressed REM sleep, but these sleep responses were similarly observed in both genotypes. Although the release of somnogenic IL-1β elicited by SD and LPS seems to be attenuated in P2X7R KO mice, the magnitude of their sleep responses, in which IL-1β should be involved, were not lower than that in wild type mice. The results suggest that lack of P2X7R influences spontaneous sleep-wake structures. Sleep responses to some stress stimuli in P2X7R KO mice, however, may be compensated by other factors.

PO-2-041

IS ENHANCED REM SLEEP IN CONDITIONAL CRH-OVEREXPRESSING MICE DUE TO CHOLINERGIC ACTIVATION?

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Objectives: Impaired sleep often associates with depression. Especially, reduced slow-wave sleep and disinhibition of rapid eye movement (REM) sleep are characteristic in those patients. Recently, we demonstrated upregulated REM sleep in two different types of conditional CRH-overexpressing mouse models suggesting that overexpressed CRH in the forebrain including limbic structures (CRH-COE-Cam) contributes to enhanced REM sleep. The present study examined a possible involvement of altered cholinergic activity by limbic CRH in REM sleep regulation.
Methods: CRH-COE-Cam mice were implanted with a guide cannula for in vivo microdialysis probe targeting the right central nucleus of amygdala (CeA). Extracellular levels of acethylcholine (ACh) and spontaneous locomotor activity were determined across 2 days. In another experiment using C57BL/6J mice, we analyzed c-fos expression after CRH (1.0 ng and 10 ng) microinjected into the right CeA.
Results: Compared with controls, homozygous CRH-COE-Cam mice showed constantly elevated ACh levels throughout 48 h whereas spontaneous locomotor activity was similarly observed in both genotypes. Microinjections of CRH at either dose increased the number of c-fos positive cells in the brainstem including the locus coeruleus and the laterodorsal tegmental nucleus but none of them were identified as cholinergic.
Conclusion: The results suggest that cholinergic activity is higher in CRH-COE-Cam mice than controls. In this model, overexpressed CRH in the amygdala may contribute to intensifying the cholinergic system, that may lead to upregulated REM sleep, although where the outcome of this stimulation ends up to elicit REM sleep still needs to be clarified.

PO-2-042

CHRONIC MILD STRESS AND ACUTE SLEEP DEPRIVATION: INTERACTIVE AND BRAIN-REGION SPECIFIC EFFECTS ON REGULATION OF TRANSLATION FACTOR AND CPEB PHOSPHORYLATION

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Restricted/disrupted sleep and/or stress trigger adaptive responses in the brain at the level of gene transcription. Here, we investigated the possible impact of chronic mild stress (CMS) and acute sleep deprivation in rats on post-transcriptional mechanisms important for memory formation and synaptic plasticity. Thirty six adult male rats were implanted with EEG and EMG electrodes. After postoperative recovery the animals were randomly separated into one CMS (4 weeks of daily exposure to mild stressors) group and one control group. Further, they were subdivided into one group of 8 h EEG/EMG controlled sleep deprivation (gentle handling) or non-sleep deprivation. Sleep was recorded prior to and after termination of CMS/control condition. Decapitation was performed immediately after sleep recording or sleep deprivation. The brain regions dentate gyrus, hippocampus and prefrontal cortex (PFC) were analysed for post-transcriptional effects. CMS exposure enhanced phosphorylation of two key translation factors, eukaryotic initiation factor 4E (eIF4E) and elongation factor 2 (eEF2) in the PFC, but not in the hippocampus and dentate gyrus. Acute sleep deprivation alone increased phospho-eIF4E expression in the PFC while decreasing phosphorylation in the dentate gyrus. In contrast, eEF2 phosphorylation was elevated in all brain regions after sleep deprivation. Thus, CMS and sleep deprivation, when separate administered, have distinct region-specific effects. The combined treatment revealed striking interactions in which prior CMS modulates the effects of sleep deprivation on translation specifically in the hippocampus proper. CMS strongly enhanced sleep deprivation-induced eEF2 phosphorylation while preventing dephosphorylation of a major regulatory RNA-binding protein, cytoplasmic polyadenylation element-binding protein (CPEB) in hippocampus. We conclude that CMS and acute sleep deprivation have interactive and brain region-specific effects on translational control of relevance to mechanisms of stress responsiveness and sleep homeostasis.

PO-2-043 / AS-23 Presenter

VESICULAR NUCLEOTIDE TRANSPORTER IS DOMINANTLY EXPRESS IN SLEEP-WAKE CENTERS OF THE CENTRAL NERVOUS SYSTEM

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The vesicular nucleotide transporter (VNUT, SLC17A9) was recently shown to partake in the vesicular storage of ATP in ATP-secreting cells. ATP is crucial as a neurotransmitter and a transmitter of signals between glial cells. Considering that VNUT may influence the availability of ATP that is released in the central nervous systems (CNS) by exocytosis,

understanding the distribution of VNUT in the brain is deemed essential. We, therefore, performed mRNA and protein profiling of VNUT in the mouse and rat CNS.VNUT was abundantly expressed in different cell groups as well as cell types throughout the CNS. VNUT was highly expressed in neurons and glial cells, particularly astrocytes. Cell groups expressing high levels of VNUT extends from the fore brain to hind brain, such as the glomerular and mitral cell layers of the olfactory bulb, different layers of the cerebral cortex, the hypothalamus, the supraoptic and paraventricular hypothalamic nuclei, substantia innominata of the basal forebrain, ventrolateral preoptic nucleus, thalamic relay nuclei, tuberomammillary nucleus, red nucleus and substantia nigra, dorsal and median raphe nuclei, and Purkinje cells of cerebellum. Interestingly, many of these cell groups are involved in sleep-wake regulation. These results imply that VNUT may control the availability of extracellular ATP acting both as a fast excitatory neurotransmitter and as a neuromodulator, both directly and via its conversion to somnogen adenosine. Considering that ATP interacts with other neurotransmitters via different receptor subtypes and that it is also released from astrocytes and mediates interactions with surrounding neurons and other glial cells, our results further implicate that VNUT may influence the orchestration of cell groups involved in sleep-wake regulation.

PO-2-044

A NOVEL SOX5 SPLICING ISOFORM EXPRESSED IN MOUSE BRAIN DURING SLEEP

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In this study, we elucidated the transcriptional network involved in sleep-wake regulation in the mouse brain by the GeneChip cDNA microarray analysis with mRNAs obtained from cortexes of sleeping (at 10:00) or waking (at 22:00) mice. After discrimination of circadian-rhythm-related genes from the gene pool, GeneChip and quantitative PCR analyses revealed that mRNAs for 55 genes were up-regulated during sleep. The mRNAs of 38 genes including the transcription factor SOX5 increased in a time-dependent manner during the first 4 h of the light period where mice are mostly asleep. Database analysis of cis-element indicated that a SOX5 -binding site can be found with a high frequency in the promoter region of those 38 genes. Among various SOX genes, we found that only SOX5 was up-regulated during sleep and identified a novel splicing isoform of SOX5 with partially truncated exon 2, SOX5-t2. Immunofluorescence staining revealed that SOX5-t2 was highly expressed in the nucleus of neurons of the adult mouse cortex. In gel shift assays, SOX5-t2 bound to the SOX-binding elements in the promoter regions of those up-regulated genes. Over expression of SOX5-t2 induced neurite branching in cultured neuroblastoma. These results suggest that SOX5 is an important regulator of sleep-related function of neurons.

PO-2-045 / AS-7 Presenter

THE ROLE OF PROSTAGLANDIN D2 IN CAUSING POST-ICTAL SLEEP FOLLOWING SEIZURES

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Prostaglandin D2 (PGD2) synthesized by the lipocalin type prostaglandin (PG) D synthase (L-PGDS) is the major prostanoid in the brain. During the last decades, experiments have led to the conclusion that PGD2 is one of the most dominant components of the humoral sleep drive. A femtomolar continuous infusion of PGD2 into the third cerebral ventricle induces rapid eye movement (REM) and non-REM (NREM) sleep in rodents and monkeys and by using knockout (KO) mice for L-PGDS and PGD2 receptor, subtype 1 (DP1R), our group has previously demonstrated that PGD2 is involved in the regulation of physiological sleep. It is well known that sleep follows seizures during epilepsy, but the molecular mechanism by which post-ictal sleep is induced has remained unclear. In recent experiments, we found that pentylenetetrazole (PTZ)-induced seizures significantly increased the PGD2 content of the brain and the amount of NREM sleep in wild-type mice. The PTZ-induced increase of PGD2 was attenuated in the brains of L-PGDS and hematopoietic PGDS (H-PGDS) KO mice and abolished in H-PGDS/L-PGDS double KO mouse brains. We are currently investing the sleep behaviour of L-PGDS, H-PGDS/L-PGDS double KO, DP1R or CRTH2 receptor KO mice to establish a role of PGD2 in seizure-induced sleep.

PO-2-046

CHOLINERGIC SIGNALING REGULATES ARC/ARG3.1 PROTEIN EXPRESSION AND DEGRADATION IN SH-SH5Y CELLS AND CULTURED HIPPOCAMPAL SLICES

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Cholinergic signaling is crucial for learning and memory during wake and sleep. Rapid-eye movement (REM) sleep is associated with high cholinergic tone in the hippocampus. Blockade of muscarinic acetylcholine receptors (mAchR) during REM-sleep results in impairment in long-term memory formation. Arc/Arg3.1 (hereafter Arc) is an immediate early gene involved in consolidation of long-term synaptic plasticity and homeostatic synaptic scaling. Absence of hippocampal Arc expression leads to deficits in long-term potentiation and long-term memory formation. Conversely, low degradation rates of Arc protein also alter synaptic plasticity as observed in the mouse model for Angelman syndrome. Carbachol, a mAchR agonist, induces Arc expression in human SH-SY5Y cells and rat hippocampal neurons. Here we investigated the dynamics of Arc synthesis resulting from stimulation of SH-SY5Y cells and cultured hippocampal slices with carbachol. We show that the duration of mAchR activation temporally and quantitatively modulated Arc transcription and that expression of both Arc mRNA and protein is rapid, but transient. We determined that carbachol-induced Arc protein expression is MEK-dependent. In addition, mAchR-induced intracellular release of calcium from IP3-sensitive stores was found to play an

important role in Arc expression. Finally, we observed that the transient aspect of Arc protein expression originates in its rapid targeting to proteasomal degradation.
In summary, our study provides evidence for tight regulation of Arc expression both in time and magnitude during cholinergic activity. While duration of mAchR activation essentially influences the levels of Arc protein, Arc half-life is controlled by a process which combines translation and degradation. The data support the hypothesis that Arc expression participate in sleep-related consolidation of synaptic plasticity through the occurrence of brief periods of REM sleep-associated cholinergic activity.

PO-2-047 / AS-29 Presenter

SLEEP-DEPENDENT MRNA TRANSLATION CONSOLIDATES CORTICAL PLASTICITY IN VIVO

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Sleep consolidates experience-dependent brain plasticity but the underlying mechanisms are poorly understood. Persistent forms of synaptic plasticity are known to require local production of new synaptic proteins to grow new synaptic structures. Therefore one mechanism promoted by sleep may be translation of mRNAs necessary for synaptic remodeling. We investigated this process in a classic form of cortical plasticity in vivo (ocular dominance plasticity: ODP) known to be consolidated by sleep. Using qPCR and Western blotting, we looked at the influence of sleep on 1) synaptic plasticity-related genes (*ARC*, *BDNF*, *αCamKII*, *GLUR1*) expression at the mRNA and protein level, and 2) translation regulation (initiation and elongation step). In parallel, we inhibit the mTOR pathway (important in local translation regulation) in the sleeping and awake visual cortex and assess ODP using single-unit recordings.We show that decreased transcription of *ARC* and *BDNF* during sleep is an indirect effect of reduced visual input and that their translation at the synapse requires sleep. We found in the same cortical samples a net increase in synaptic translation initiation (4E-BP1 phosphorylation) during sleep. All those molecular events are generally induced during sleep and are further promoted if the brain is triggered to remodel. Finally, we show that local inhibition of mTOR-dependent protein synthesis abolishes sleep-dependent ODP consolidation but has no effect on the induction of ODP during wake. Collectively, these findings suggest that sleep generally promotes cortical mRNA translation, but when the brain is stimulated to remodel, this process is shift toward more translation initiation. Interruption of this process during sleep has functional consequences, as it abolishes the consolidation of experience in the cerebral cortex. To further investigate the role of sleep in synaptic plasticity, we are currently developing a method to image dendritic calcium activity during wake and sleep in freely behaving animals.

PO-2-048

REM SLEEP PLAYS A ROLE IN OCULAR DOMINANCE PLASTICITY CONSOLIDATION

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Introduction: Sleep is thought to consolidate plasticity, but the mechanisms underlying this process are unclear. Ocular dominance plasticity (ODP) in the cat primary visual cortex (V1) is a canonical form of in vivo plasticity induced by monocular deprivation (MD), and is consolidated by sleep. However, the relative contributions of NREM and REM sleep to ODP consolidation are unknown. This study aims to determine whether REM is necessary for ODP consolidation and identify REM-dependent mechanisms that underlie this process.
Methods: Cats were implanted with electrodes for polysomnography recording, and then underwent MD for 6 hours to induce cortical remodeling. MD was followed by normal, REM sleep deprived (RSD), or NREM-fragmented (NF) sleep. NF controlled for the nonspecific effects (e.g. increased wake time, decreased sleep continuity, and decreased delta power) of RSD. A fourth group received intracortical infusions of U0126, an upstream blocker of ERK phosphorylation, or vehicle into V1 during post-MD sleep. Immediately following these manipulations, ODP was assessed using optical imaging of intrinsic cortical signals and single-unit recording in V1. Another set of animals underwent the same sleep-wake manipulations, after which V1 tissue was collected for Western blot analysis of GluR1, ERK and CaMKII, proteins that are phosphorylated during post-MD sleep.
Results: RSD animals had impaired ODP consolidation compared to animals that received normal or NF sleep, indicating that REM is required for ODP consolidation. RSD also reduced ERK, but not GluR1 or CaMKII, phosphorylation in V1 compared to sleeping and NF animals, suggesting that ERK is activated during post-MD REM sleep. Furthermore, blocking ERK activation with U0126 during post-MD sleep impaired ODP consolidation compared to vehicle. Together, these data suggest that ERK phosphorylation during REM is required for ODP consolidation.
Conclusion: These results support a model in which ERK activation during REM may interact with other molecular events during NREM to consolidate ODP.

PO-2-049 / AS-25 Presenter

BASAL FOREBRAIN HISTAMINE: INCREASES DURING WAKEFULNESS, INDUCES WAKEFULNESS AND ACTIVATES THE CORTEX

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Introduction & Objectives: The basal forebrain (BF) participates in the control of vigilance state. The build-up of adenosine in the BF during sleep deprivation (SD) inhibits wake-promoting neurons and thereby promotes sleep. However, the animals are able to stay awake, suggesting increased activity of the ascending arousal systems counteracting sleep pressure. Histamine (HA) excites BF neurons and histamine infusion into the BF induces wake. Therefore we hypothesize that the histaminergic system may be involved in counteracting the effect of sleep pressure in the BF.

Materials & Methods: Male Han-Wistar rats were subjected to a 6 hour SD by 'gentle handling'. In vivo microdialysis was used to sample the BF extracellular space before, during and after SD and samples were analysed using HPLC. The effect of HA on vigilance state and the power spectrum of the electroencephalogram (EEG) was examined by infusing HA or HA antagonists into the BF for 3 hours by means of reversed in vivo microdialyses.
Results: HA levels increased immediately and remained constant throughout the SD period ($n = 8$, ANOVA repeated measures $P < 0.05$), returning to baseline instantly after SD. Infusion of HA into the BF increased wakefulness and altered the EEG power spectrum. Across vigilance states EEG delta power (0.5–4 Hz) was decreased and EEG theta power (4–7 Hz) was increased. Infusion of HA 1 receptor antagonist or HA 3 receptor agonist decreased both wakefulness and EEG theta power.
Conclusions: HA levels do not change due to increased sleep pressure and thus do not appear to be involved in counteracting the effect of enhanced sleep pressure. However, these results do further indicate the BF as a key site for HA to promote cortical activation and wakefulness.

PO-2-050

GLUTAMATE MICROINJECTION IN THE MEDIAL SEPTUM ENHANCES SLOW WAVE SLEEP AND DECREASES PARADOXICAL SLEEP IN RATS

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Medial septum (MS) has connection with various sleep and wake promoting areas. Various studies have shown its involvement in sleep-wakefulness (S-W). Local glutamatergic neuronal network and functional glutamate receptors are present in the MS. Although glutamate microinjections in brain areas regulating S-W have been shown to modulate S-W, the exact role of glutamate in the MS on S-W is not yet known. We studied the effect of L-glutamate microinjection in the MS on S-W in adult male Wistar rats. Under sodium pentobarbital anesthesia, EEG, EMG and EOG electrodes were implanted for recording S-W parameters. For microinjection of glutamate, a guide canula with indwelling stylet was implanted above the MS, as per the atlas of DeGroot. Two baseline polysomnographic recording S-W were taken for 6 hours, after post surgery recovery. L-glutamate (dose 40 ng/200 nl, volume: 200 nl) or equal volume of normal saline (control group) was injected at 12:00 h on the third day following first two hours of pre-injection recordings. Post-injection recording was continued from 12:15–16:15 h. Injection sites in the brain were confirmed histologically. Data were analyzed in 15 seconds epoch by visual scoring. When compared with data from time-matched and vehicle injected controls, significant decrease in the paradoxical sleep during post injection first hour ($p = 0.0317$ and 0.016 respectively) and significant increase in the slow wave sleep during post injection second hour ($p = 0.0159$ for both) were observed. The later resulted in significant increase in total sleep time ($p = 0.0159$ for both) during the same time window. Our study suggests that microinjection of L-glutamate in the MS increases slow wave sleep and decreases paradoxical sleep in rats.

PO-2-051

BASAL FOREBRAIN CHOLINERGIC NEURONS AND NITRIC OXIDE-MEDIATED REGULATION OF SLEEP HOMEOSTASIS

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The levels of adenosine (AD) and inducible nitric oxide (NO) synthase (iNOS)-mediated NO increase during sleep deprivation (SD) in the basal forebrain (BF), and, with prolongation of SD, in the frontal cortex (FC). NO donor infusion increases AD and NREM sleep (NREMS), while iNOS/NO inhibition prevents SD-induced AD increase and recovery NREMS (Kalinchuk et al., 2006). iNOS induction occurs in wake-active neurons in BF and FC (Kalinchuk et al., 2010, 2011), however, the neurotransmitter specificity of these cells is not known. Lesion of BF cholinergic cells attenuates both SD-induced AD increase and recovery NREMS (Kalinchuk et al., 2008). Hence in this study, we tested the role of wake-active-cholinergic neurons in iNOS/NO release in BF and FC as well as in iNOS/NO-mediated homeostatic sleep response.
Methods: Experiment.#1. The effects of SD on iNOS/NO production and the effect of NO donor on sleep were compared in the same animals before and 2 weeks after the lesion of BF cholinergic neurons using immunotoxin 192 IgG-saporin. Experiment #2. Neurotransmitter specificity of cells inducing iNOS during SD was identified using immunohistochemistry and double-labeling with specific markers for iNOS, acetylcholinetransferase (ChAT), vesicular glutamate transporters (VGlut) and glutamatic acid decarboxylase (GAD67).
Results: 1. Before saporin lesioning, SD induced significant increases in NO levels, intensity of waking theta power and in subsequent NREMS/NREMS delta power (by 35/47%). NO donor infusion increased NREMS/NREMS delta power by 39/41%. After saporin lesioning, all these increases were significantly attenuated or totally blocked. 2. The numbers of iNOS+ cells in the BF and FC were significantly increased after SD. In the BF, 96% of ChAT+ cells were iNOS+ after SD, and 85% of iNOS+ cells were ChAT+. Numbers of iNOS+/ChAT+ cells positively correlated with SD-induced increase in theta power.
Conclusion: Data suggest that cholinergic BF cells play an important role in iNOS/NO production during SD that contributes to the generation of homeostatic sleep pressure.

PO-2-052

NOVEL MOUSE MODELS FOR THE INVESTIGATION OF NEURONAL-GLIAL IMMUNE INTERACTIONS

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Immune challenge alters CNS-mediated processes and complex behaviors. These changes in physiology and behavior are collectively referred to as sickness behavior. Sickness behavior is believed to contribute to survival from infection by facilitating fever, thereby upregulating innate immune cell activity and creating a less hospitable environment for pathogens. Pro-inflammatory cytokines such as interleukin-1β (IL-1) and tumor necrosis factor α (TNF) are well characterized

immunomodulators that mediate multiple aspects of the innate immune response. The brain, long thought to be an immune privileged site, contains cytokines and their receptors. IL-1 and TNF respectively bind to IL-1 receptor 1 (IL-1R1) and TNF p55 receptor 1 (TNFR1) present on neurons and glia. Administration of IL-1 or TNF elicits sickness behaviors, such as alterations in sleep, decreased food and water intake, and social withdrawal. It is known that glia and, to a lesser extent, neurons produce these pro-inflammatory cytokines in response to an immune challenge. Collectively, these observations suggest that neuronal-glial interactions involving cytokines are crucial to the manifestation of sickness behavior. Nevertheless, the relative contribution of neurons and glia to the modulation of complex behavior and physiology during immune challenge is not known. To address this knowledge gap, we have engineered four transgenic mouse strains that express IL-1R1 or TNFR1 only in the CNS and selectively on neurons or astrocytes. These transgenic mice express either IL-1R1 or TNFR1 cDNA under the transcriptional control of the neuron-specific enolase (NSE) or the human glial fibrillary acidic protein (gfa2) promoters. These animals provide a novel and unique tool to study CNS responses to systemic immune challenge independent from peripheral actions of IL-1 or TNF. The systematic and selective examination of neuronal-glial cytokine interactions will further our understanding of the central response to immune activation that are relevant to a broad spectrum of pathologies characterized by inflammation.

PO-2-053 / AS-12 Presenter

DEPRESSED MOOD, CHRONIC SHORT SLEEP, AND 5HTTLPR POLYMORPHISM: PRELIMINARY REPORT OF A GENE X ENVIRONMENT INTERACTION

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Introduction: A polymorphism of the serotonin transporter gene (5HTTLPR) is implicated in depressed mood, anxiety, and insomnia. This study examines whether a 5HTTLPR polymorphism is associated with depressed mood in young adults with a chronic pattern of short sleep.
Methods: First-year university students (ages 18–20 y) completed daily online sleep diaries for the first 9 weeks of term (21 to 63 days; median = 58) and Center for Epidemiologic Studies-Depression (CES-D) mood scale at the end of week 9. DNA acquired from buccal cell samples was genotyped for 5HTTLPR and SNP rs25531 A/G polymorphisms. Low-expressing S and LG polymorphisms were designated S'; high-expressing LA was designated L'. Three genotypes were identified (S'S', S'L', L'L'). CES-D was assessed using median split (high >12; low <13). Mean total sleep time (TST) from diaries was short if <7.01 h (n = 49, 20 male; mean TST = 6.5 h, SD = .4) or long if >7.49 h (n = 40, 17 male; mean TST = 7.9, SD = .3 h). CES-D scores did not differ between those with short (mean = 15.6, SD = 9.9) and long (mean = 15.6, SD = 11.5) TST.
Results: Four phenotype groups were compared: 28 participants had a pattern of short TST and high CES-D; 21 had shortTST/lowCES-D; 19 had longTST/highCES-D; 21 had longTST/lowCES-D. Female : male distribution did not vary across phenotype groups (chi-sq = 0.66(3); p = ns). The genotype distribution showed an overrepresentation of S'S' (n = 20) in the short TST/high CES-D group (chi-sq(6) = 20.88; p < .01) compared to other phenotypes. The association was sustained (chi-sq(6) = 16.91; p < .01) after omitting those (n = 19) whose CES-D was high 3 mo before starting university.
Conclusion: These preliminary data indicate a significant vulnerability to high depressed mood in young adults who report short nocturnal sleep and carry a variant of the 5 HT promoter gene associated with low expression of the serotonin transporter. A larger sample size and further analyses are planned to confirm this observation.
Support: National Institute of Mental Health (MH079179); Sleep Research Society Foundation Elliot D. Weitzman, M.D., Research Grant.

PO-2-054

GENOME-WIDE ASSOCIATION STUDY OF SLEEP DURATION OR SELF-PERCEIVED INSUFFICIENT SLEEP IN JAPANESE POPULATIONS

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Background: Duration of self-perceived insufficient sleep may differ among individuals, and the difference may be based on genetic factors. The aim of this study was to identify single nucleotide polymorphisms (SNPs) related to sleep duration or self-perceived insufficient sleep.
Methods: Sleep duration and self-perceived insufficient sleep were evaluated by a self-administered questionnaire. In phase 1, candidate SNPs related to sleep duration or perceived-insufficient sleep were identified by genome-wide association study (GWAS). Subjects were 421 healthy volunteers recruited from Aichi Cancer Hospital in whom suspected cancer had been ruled out by diagnostic tests. Illumina 610 Quad containing >0.5 million SNPs was used for GWAS. The association of SNPs with sleep duration and self-perceived insufficient sleep was screened. Inclusion criteria for candidate SNPs were $p < 10^{-5}$ and minor allele frequency >0.1. Then, to confirm candidate SNPs identified in phase 1 in other populations, confirmation phase 2 was performed. Phase 2 subjects were 4519 individuals participating in the Japan Multi-Institutional Collaborative Cohort (J-MICC) Study from ten study areas. The inclusion criterion for participation in the J-MICC Study was age 35–69 years. The candidate SNPs were genotyped by multiplex polymerase chain reaction (PCR)-based Invader assay. Associations of candidate SNPs with sleep duration or self-perceived insufficient sleep were examined for conformation.
Results and Conclusion: In total, 14 candidate SNPs related to sleep duration or insufficient sleep were identified in phase 1. Among them, five SNPs were located on *NLRP3*, *PTPN5*, *SGCZ*, and *SPOCK1*. Associations between these genes and sleep have not been reported so far. The other identified SNPs were not located on any genes. Genotyping in phase 2 is ongoing; the results of phase 2 will be presented at the conference.

PO-2-055

ASSOCIATION OF SLC6A4 AND 5-HTR2A GENE POLYMORPHISMS WITH DIFFERENT PHENOTYPE OBSTRUCTIVE SLEEP APNEA IN CHINESE HAN POPULATION

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Objective: To investigate the association of SLC6A4 and 5-HTR2A gene polymorphisms with different phenotype obstructive sleep apnea (OSA).
Methods: All the exons and promoter regions of SLC6A4 and 5-HTR2A gene first underwent genetic analysis in 49 OSA and 47 controls in Chinese Han population. According to the primary results, 40705T/G, 40912T/G of SLC6A4 and −1438G/A of 5-HTR2A were chosen for further genetic analysis in 365 OSA and 110 controls. Chin surface electromyography (sEMG) of routine Polysomnograph during normal breath and obstructive apnea were quantified in all the OSA subjects. The sEMG change from normal breath to obstructive apnea was expressed as percent compensated electromyography value (PCEV), PCEV = (normal breath sEMG-apnea sEMG)/ normal breath sEMG. The OSA subjects were divided into three subgroups based on the PCEV. The frequency of genetype and allele was compared between different subgroups.
Results: The PCEV of OSA patients varied from 1% to 92% in this study, which implies the neuromuscular defect is different between OSA subjects and the PCEV can reflect this kind of difference. The genetype and allele frequency of −1438G/A showed statistic difference between OSA patients and controls ($P < 0.001$), but no significant difference was found between different PCEV OSA subgroups. On the contrary, the genetype and allele frequency of 40705T/G and 40912T/G showed statistic difference between different PCEV OSA subgroups ($P < 0.01$, 0.05 respectively), while no statistic difference was found between OSA patients and controls.
Conclusions: The polymorphism of 40705T/G and 40912T/G may be involved in susceptibility to OSA through neuromuscular pathway, while the −1438G/A polymorphism may through other ways affect the incidence of OSA.

PO-2-056

THE RELATIONSHIP BETWEEN CHRONOTYPE AND SLEEP IN CHINESE STUDENTS AT ELEMENTARY AND SENIOR HIGH SCHOOLS

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Entraining factors for biological rhythms (i.e. lighting, activity, meal habits, and so on) have been considered to affect the sleep of humans, and understanding the relationships between these factors and sleep is becoming more important in the present-day environment. In this study, 16students were recruited from Chinese elementary and senior high schools, and the set of students from each school was divided into two groups ("morning" and "evening" types) according to their chronotype (assessed by a morningness-eveningness questionnaire). That is there were four groups (each comprising 4 students): elementary school-morning type, elementary school-evening type, senior high school-morning type and senior high school-evening type. Light exposure, activity, the sleep pattern and meal habits of each subject were measured over the course of four days. Furthermore, the melatonin levels during sleep were measured by urine and awakening levels were measured on the morning of the fifth day. Sleep latency of the senior high school students who were morning types was significantly shorter than that of the evening types from the same school. Exposure to light during the period from 20:00 to 04:00 h was significantly lower in elementary school students than senior high school students, regardless of their chronotype.

PO-2-057

DO D-NEURONS PRODUCE PSYCHOSTIMULANTS?

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When Jaeger et al. originally described D-cells in the rat brains in 1983, these cells were defined as aromatic L-amino acid decarboxylase-containing cells that are not dopaminergic nor serotonergic cells. These cells were regarded as trace amine-synthesizing cells, and the localizations of which were specified from D1 (the spinal cord) to D14 (the bed nucleus of stria terminalis) in the rat central nervous system (Jaeger et al. 1984). Since the cloning of the trace amine receptor in 2001 (Borowski et al. 2001, Bunzow et al. 2001), numerous studies have been performed to elucidate the functions of the trace amine receptor. The trace amine receptors are localized monoamine-related areas, and modulate the functions of monoamines. In the human, D-neurons, presumable trace amine-synthesizing neurons, preferably localized in the forebrain structures rather than the hindbrain, including the midbrain, pons, and medulla oblongata (Kitahama et al. 2009). We also reported the number reduction of D-neurons in the striatum of postmortem brains of schizophrenia (Ikemoto et al. 2003). In the human, the ligands of trace amine-associated receptor, type 1 (TAAR1) are known as phenylethylamine, tryptamine, metamphetamine, 3,4-methylenedioxymethamphetamine (MDMA), or 3-iodothyronamine, a delivative of thyroid hormone, etc., and some of which may act as psychostimulants. D-neurons might be waking-active neurons(Sakai 2011). TAAR1 knockout mice showed schizophrenia-like behaviours (Wolinski et al. 2007), and a selective TAAR1 agonist has been shown to be a promising neuroleptics (Revel et al. 2011). However, due to the paucity of quantity of the trace amines in vivo, in situ visualization of the trace amines has hardly been successful.

PO-2-058

CIRCADIAN CLOCK T3111C POLYMORPHISM ASSOCIATED WITH INDIVIDUAL DIFFERENCES IN EXECUTIVE FUNCTIONING, SLEEPINESS AND MOOD DURING SLEEP RESTRICTION

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The CLOCK T3111C polymorphism is associated with aspects of sleep, sleepiness, and morningness-eveningness in healthy adults, and with insomnia in bipolar disorder and major depressive disorder. We evaluated the CLOCK T3111C polymorphism's role in cognitive, sleepiness, sleep homeostatic and mood responses during baseline and chronic partial sleep deprivation (PSD). 6 *C/C*, 45 *C/T* and 78 T/T healthy adults (29.9 ± 6.9 y;63females) completed 2 baseline (10 h TIB) nights, followed by 5 consecutive PSD nights (4 h TIB) in a laboratory experiment assessing neurobehavioral measures (cognitive and executive function tests, subjective sleepiness, mood and fatigue, MWT) and physiological sleep responses. The *C/C* and *C/T* groups did not differ in outcomes and were combined; comparisons were conducted between C allele carriers (*C/C*+*C/T*;N = 51) and the T/T genotype (N = 78). T/T genotypic and T allelic frequencies were higher in African Americans than Caucasians; results were significant after controlling for ethnicity. During PSD, C allele carriers showed poorer executive functioning performance on the Tower of London (p's < 0.05), which assesses planning and problem solving abilities. This group also showed greater total mood disturbance (TMD) and greater subjective sleepiness and fatigue during PSD (p's < 0.05). At baseline, C allele carriers showed greater TMD and confusion (p's < 0.05), but did not differ in circadian phase typology, physiological sleep characteristics, physiological or subjective sleepiness, or cognitive performance. Both groups demonstrated similar cognitive performance (PVT, Digit Span) decreases, and increases in SWE and subjective and physiological sleepiness (KSS, MWT) in response to PSD. This is the first report of the CLOCK T3111C polymorphism predicting performance on a measure of executive functioning, and sleepiness and mood during chronic PSD. The CLOCK T3111C polymorphism may be a genetic marker for a cognitive-mood diathesis more so than a sleep-circadian diathesis, since it did not predict sleep homeostatic or circadian measures relative to PSD.

PO-2-059 / AS-5 Presenter

ANIMAL MODELS OF HUMAN SLEEP-WAKE CYCLE: NON-SCN CIRCADIAN BEHAVIOR RHYTHMS IN RODENTS

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One of the characteristics of human sleep-wake cycle is a spontaneous desynchronization from the circadian rhythms in core body temperature and plasma melatonin, which are regulated by the circadian pacemaker in the suprachiasmatic nucleus (SCN). In rodents such as rats and mice, it has been known that behavioral rhythms are dissociated from the SCN pacemaker by chronic Methamphetamine (MAP) treatment or restricted daily feeding (RF). The rhythms induced by MAP and RF suggested to be based on the same oscillatory mechanism because of the similarity of these characteristics. These oscillators are called as a MAP-induced oscillator (MAO) and food-entrainable oscillator (FEO). Neither the site nor the mechanism of these oscillators is uncovered. In this study, we analyzed the molecular mechanisms of MAO and FEO in terms of clock gene, *per2* expression. We treated *Period2-luciferase* transgenic rats either to daily MAP injection (2 mg/kg b.w.) or RF (2 hours) starting from ZT4 for 14 days under light-dark cycles of 12 h lights. Wheel-running and spontaneous activities were measured simultaneously. Following the treatment, we made brain slices including the Olfactory bulb (OB), Caudate-Putamen (CPU), Parietal cortex (PC), Substantia Nigra (SN), and SCN for the measurement of *Per2-luc* bioluminescence rhythms in culture. Both groups of rats treated by MAP and RF exhibited the enhancement of activity before the time of treatments and persisted after the termination of treatments. We found that circadian phases of *Per2-luc* rhythms were significantly different between MAP and RF treated groups in the OB, CPU, PC, and SN. The circadian *Per2-luc* rhythm in the SCN was not affected by either treatment. These results strongly suggest that the molecular mechanisms of MAO and FEO are different.

PO-2-060 / AS-22 Presenter

NON-CIRCADIAN DIRECT EFFECTS OF LIGHT ON SLEEP AND ALERTNESS ARE MEDIATED VIA SEVERAL HYPOTHALAMIC PATHWAYS INCLUDING THE SCN AND THE VLPO

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Light is known to influence sleep and alertness indirectly through a well-defined circadian pathway (suprachiasmatic nucleus, SCN), or directly through mechanisms that remain to be further understood. Retinal ganglion cells expressing melanopsin (Opn4, photopigment) convey non-visual light information to the brain. Our recent work looking at c-Fos induction in response to light suggests that the sleep promoting (i.e., galanin-positive) neurons of the ventrolateral preoptic (VLPO) or the SCN may act as possible relays mediating the direct effects of light on vigilance states. To test this hypothesis, we performed SCN lesion and analyzed sleep under various light dark regimen (12 hL : 12 hD, single 1 hL or D-pulses, and 24 hours of 1 h : 1 h LD cycles) in Opn4–/– and WT mice, in arrhythmic (verified with actimetry) lesioned (SCNx) and rhythmic sham mice. The SCN lesion was verified by VIP and AVP staining. Retinohypothalamic fibers to the VLPO and other areas were conserved in lesioned animals (staining of cholera toxin B previously injected into the posterior chamber of the eye). Under LD12 h : 12 h, SCNx mice (WT and –/–) showed an abolished sleep-wake rhythm and slept longer during the 12-hr dark period as compared to sham animals (p < 0.001). Sleep induction in response to a 1 hr light pulse was attenuated in Opn4–/– (p < 0.05) but not in SCNx animals. The wake-promoting effect of a dark pulse was decreased in lesioned and in KO animals (p < 0.05). Under ultradian 1 h : 1 h LD cycle the reactivity to light and dark was reduced in KO sham (–58.7 ± 8.5%, p < 0.05) and WT SCNx mice (–59.3 ± 9.2%, p < 0.05). In the absence of both the SCN and melanopsin the reactivity to light and dark (–87.1 ± 11.2%, p < 0.01) was abolished. These results suggest that, in nocturnal animals, the direct sleep promoting effect of light rely, at least in part, on the VLPO and the wake facilitating effect of darkness on the SCN. These direct effects are mainly, but not only, based on melanopsin photoreception. The SCN, beyond its function as circadian

master clock, play a role to mediate the direct effects of light and darkness on sleep and alertness.

PO-2-061

CHRONIC LIGHT AS A POTENTIAL REGULATOR OF SLEEP: DIRECT PERTURBATION OF SLEEP HOMEOSTASIS IN ARRHYTHMIC MICE

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Mammalian sleep is under control of both circadian clock and sleep homeostasis. The circadian clock is known to be a strong regulator of sleep homeostasis and this makes it difficult to assess the sleep homeostasis system in mammals. To evaluate the dynamics of sleep homeostatic system, removing the circadian clock is necessary. Genetically arrhythmic mice, which have no circadian clock, could solve this problem by enabling direct perturbation of sleep homeostatic system. Generally, analyzing a dynamics of a biological system, quantitative and noninvasive method is ideal. Light is a perfect method that meets these conditions. Using CB57BL/6 J mice (WT) and two arrhythmic strains, *Cry1*$^{-/-}$, *Cry2*$^{-/-}$ mice (CRY) and *Bmal1*$^{-/-}$ mice (BMAL), we first show that daily locomotor can be regulated by chronic light not only in WT but also in arrhythmic strains (CRY and BMAL). Second, we show chronic light can transiently increase sleep time in BMAL. Thus, chronic light is a candidate to perturb sleep in arrhythmic mice. However, the lack of reproducibility of previous locomotor studies while recording electroencephalograms and electromyograms, we are now seeking for a less invasive method to evaluate sleep/wake status in mice.

PO-2-062 / AS-22 Presenter

PROSTAGLANDIN D2 PRODUCED BY LIPOCALIN-TYPE PROSTAGLANDIN D SYNTHASE IN THE LEPTOMENINGES OF THE BRAIN IS INVOLVED IN SLEEP REGULATION

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Prostaglandin D_2(PGD_2) is the most abundant prostaglandin produced in the brain. Injections of nano-molar PGD_2 in rat brains induce sleep in a dose -and time- dependent manner. The PGD_2-induced sleep is indistinguishable from physiological sleep.
PGD_2 is produced by two distinct types of PGD_2 synthase (PGDS), lipocalin-type PGDS (LPGDS) and hematopoietic PGDS (HPGDS), but only LPGDS is related to the sleep regulation. Three potential sites of PGD_2 synthesis have been identified in the brain: LPGDS is localized into oligodendrocytes (OD), epithelial cells of the choroid plexus (CP), and arachnoid trabecular cells of the leptomeninges (LM).
We attempted to identify the site of synthesis of somnogenic PGD_2 and generated a transgenic mouse line with the LPGDS gene amenable to conditional deletion using Cre recombinase.
To identify the tissue or cells responsible for the production of somnogenic PGD_2, we engineered animals lacking LPGDS specifically in:
– OD by cross-breeding flox-LPGDS mice with Nestin-Cre mice to induce a complete KO of LPGDS in the neural but not the leptomeningeal cells (OD-LPGDS KO mice)
– CP by injecting adeno-associated virus (AAV), serotype 5, expressing Cre recombinase (AAV5-Cre) into the lateral third ventricle (CP-LPGDS KO mice)
– LM by injecting AAV, serotype 8, expressing Cre recombinase (AAV8-Cre) into the ventricle of new born mice (LM-LPGDS KO mice)
We recorded electroencephalogram, electromyogram and locomotor activity to measure sleep of 10 weeks old animals without LPGDS in one of the 3 target tissues and demonstrated that selenium tetrachloride, a specific PGDS inhibitor, inhibited sleep in OD-LPGDS and CP-LPGDS KO mice, but not in LM-LPGDS KO mice.
These results indicate that leptomeningeal cells, but not OD or CP, are the source of somnogenic PGD_2.

PO-2-063

MICE LACKING HEAT SHOCK FACTOR 1 SHOW EVENING-TYPE SLEEP/WAKE RHYTHM

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Body temperature is considered to work as a resetting cue for internal circadian synchronization [Buhr et al., Science (2010) 330:379–85]. Block of the function of heat shock factor 1 (HSF1), a transcription factor of heat shock proteins, suppresses the ability of heat pulses to shift the circadian phase and lengthen the free-running period. We hypothesized and tested that mice lacking HSF1 would show the evening-type of sleep/wake pattern because of its longer circadian period. We measured EEG, EMG and body temperature in HSF1 knockout and wild-type mice for 24 hours under 12 h-light and 12 h-dark condition. The acrophase in the rhythm of wake and non-rapid eye movement sleep in HSF1 knockout mice was significantly delayed for about 3 hours in comparison to the wild-type mice, while that in body temperature was not affected. The HSF1 knockout did not change the total sleep/wake durations for 24 hours and averaged body temperature. Present results indicate that HSF1 may be involved in the circadian sleep control.

PO-2-064 / AS-7 Presenter

KINDLING STIMULI DELIVERED AT DISTINCT ZEITGEBER TIME POINTS ALTER HOMEOSTATIC FACTOR AND CIRCADIAN RHYTHM DIFFERENTLY

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Introduction: Sleep is regulated by homeostastic factor and circadian process. Disturbances in the sleep-wake continuum in epilepsy patients are common but often overlooked. We herein employed kindling stimuli delivered at different zeitgeber time (ZT) points to elucidate the effect of epilepsy on the alterations of sleep homeostasis.
Methods: Amygdala kindling protocol was delivered at different ZT points (ZT0, ZT6 and ZT13) to induced temporal lobe epilepsy (TLE) in rats. EEGs and sleep activities were recorded after reaching full-blown epilepsy. ELISA, ribonuclease protection assay and immunocytochemistry were employed to measure corticosterone, interleukin (IL)-1 and Per1 protein expression, respectively.
Results: SWS and REM sleep decreased during ZT0-12 when rats were kindled at ZT0. When ZT13 kindling was given, SWS increased but REM sleep was not altered during ZT13-24. However, the 12:12 h sleep-wake circadian rhythm was not altered. Corticosterone concentrations were increased after ZT0 kindling and the expression of IL-1 was

enhanced after ZT13 kindling. Furthermore, corticotrophin-releasing hormone (CRH) receptor antagonist and IL-1 receptor antagonist (IL-1ra) respectively blocked ZT0- and ZT13-induced sleep alterations. Furthermore, the expression of Per1 protein in the suprachiasmatic nucleus (SCN) was shifted 6 hours in advance and sleep circadian was advanced 2 hours when kindling stimuli was given at ZT6. Microinjection of hypocretin receptor antagonist, SB 334867, directly into the SCN significantly blocked ZT6-kindling induced advance shifting of Per1 expression in SCN and the alteration of sleep circadian.
Conclusion: Amygdala-kindling stimuli delivered at different ZT points may alter the circadian and/or homeostatic factors, indicating the underlying mechanisms for the sleep disturbances in epilepsy patients.

PO-2-065

ULTRADIAN SLEEP-WAKE RHYTHM IN *DROSOPHILA*

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Rhythmic activities are found in a wide range of organisms from unicellular organisms to mammals. Biological rhythms are classified by the length of periods. Rhythms with periodicity shorter than 1 day are referred to as ultradian rhythms. Ultradian rhythms are complicated, as various period lengths are observed. A well-known ultradian rhythm is the neuronal activity of the human brain during sleep. Human sleep consists of two stages, REM and non-REM, which appears alternately with a cycle of about 90 min between sleep phases. Several ultradian rhythms have also been reported in invertebrates. However, nothing is yet known about the biological meaning of ultradian rhythms and that such oscillations can be influenced by external or internal signals. We used *Drosophila melanogaster* to study the behavioral aspect of ultradian rhythms and employed a video-recording system to analyze fly movements and sleep states. Time series data were analyzed by the maximum-entropy method of the MemCalc software package. Ultradian rhythmicity of sleep wake-cycle was detected in circadian rhythm mutant strains. Moreover, ultradian rhythmicity was also detected in a wild-type strain placed under constant dark or light conditions. Notably, robust and precise ultradian rhythmicity was detected in a clock output mutant, *Pigment-dispersing factor* (Pdf^{01}). The ultradian rhythmicity we found in *Drosophila* is not temperature-compensated and has different properties from those of the circadian system.

PO-2-066

NON-REM SLEEP STAGE TRANSITIONS CONTROL ULTRADIAN REM SLEEP RHYTHM

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Study Objectives: The cyclic sequence of non-rapid-eye-movement (non-REM) and REM sleep, the so-called ultradian rhythm, is a highly characteristic feature of sleep. However, the mechanisms responsible for the ultradian REM sleep rhythm, particularly in humans, have not to date been fully elucidated. We hypothesize that a stage transition mechanism is involved in the determination of the ultradian REM sleep rhythm.
Participants: Ten healthy young male volunteers (age: 22 ± 3.7 years, range 19–31 years) spent three nights in a sleep laboratory. The first was the adaptation night, and the second was the baseline night. On the third night, the subjects received risperidone (1 mg tablet), a central serotonergic and dopaminergic antagonist, 30 min before the polysomnography recording.
Measurements and Results: We measured and investigated transition probabilities between Awake, REM and non-REM sleep stages (N1, N2 and N3) within the REM-onset intervals, defined as the intervals between the onset of one REM period and the beginning of the next, altered by risperidone. We also calculated the transition intensity (i.e., instantaneous transition rate) and examined the temporal pattern of transitions within the altered REM-onset intervals. We found that when the REM-onset interval was prolonged by risperidone, the probability of transitions from N2 to N3 was significantly increased within the same prolonged interval, with a significant delay and/or recurrences of the peak intensity of transitions from N2 to N3.
Conclusions: These results suggest that the mechanism governing non-REM sleep stage transitions (from light to deep sleep) plays an important role in determining ultradian REM sleep rhythms.

PO-2-067 / AS-17 Presenter

HUMAN CIRCADIAN RHYTHM POLYMORPHISMS ARE CORRELATED WITH CLIMATE

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Introduction: Numerous studies have reported associations between polymorphisms in human circadian genes and phenotypes describing diurnal preference (DP). However, findings often have not been replicated across populations. There are multiple reasons for lack of replication, including poor linkage disequilibrium (LD) between the reported single nucleotide polymorphisms (SNPs) and the causative allele, and differing LD across populations. An alternate explanation for poor replication could be population-specific effects, given latitudinal clines reported in prior non-human circadian studies. Climate, as opposed to latitude, exacts direct physiological challenges (*e.g.* temperature extremes) that may reflect any ultimate forces responsible for the possible spatial selection of circadian phenotypes.
Methods: Summer and winter climate principal components were constructed using 13 climate variables (New, Clim Res 2002) and NASA insolation data for 45 Human Genome Diversity Project populations (n = 975) (Li, Science 2008). Climate SNPs were defined as Spearman's Rho principal components 1/2 ± 1% outliers relative to 644,192 autosomal SNP allele frequencies. HapMap LD (r^2> 0.8) between climate SNPs and a) SNPs within 35 circadian-associated genes (20 kbp flank) and b) known DP variants was measured for possible correlation.
Results: 13 genes had >10% SNPs tagged by 1% climate SNP outliers, including 4 genes (*BTRC*, *CRY1*, *FBXL3*, and *SIRT1*) with >50% SNPs tagged within a single HapMap population. Near-exact relationships between climate and diurnal preference polymorphisms in multiple populations were found for *PER1* and *PER2* (linking British morningness [Carpen, J Sleep Res 2005] and Japanese eveningness [Matsuo, Sleep Biol Rhythms 2007]), while an extrapolated haplotype relationship affected *PER3*.
Conclusion: These results suggest that human circadian phenotypes may be altered by the environment. This raises the importance of future multiple-population studies, but predicts increased complexity in their interpretation.

PO-2-068

CIRCADIAN DISTRIBUTION OF CSF INOSINE AND HISTAMINE LEVELS IN HUMANS

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Background and Aims: There is evidence for adenosine being an endogenous sleep substance based on results of various experiments. In contrast, histamine is an important wake-mediator. In animals, cerebrospinal fluid (CSF) histamine levels are increased during wakefulness and decreased during sleep. In humans, there is little information on the circadian distribution of adenosine or histamine in CSF. Limited data indicate for lower CSF histamine levels in human narcolepsy. Adenosine is an unstable substance and therefore difficult to measure. Adenosine is converted into the more stable metabolite inosine. We aimed at investigating the circadian course of inosine, hypocretin, beta-trace and histamine in human CSF and to find potential correlations.
Methods: We prospectively studied a series of 184 consecutive patients and healthy controls. 164 patients suffered from different sleep or neurological disorders. There were 110 women (ratio 1.5:1), mean age was 51 years (range 20–85). Lumbar puncture was performed between 6 am and 1am. The study was approved by the institutional ethical committee. The concentrations of hypocretin or beta-trace were measured by specific ELISA for respective protein. The concentration of histamine was measured by using HPLC-fluorometry. The amount of inosine was measured by using HPLC- tandem mass spectrometry.
Results: There was a continuous increase of inosine during the day (8 am to 6 pm, $r = 0.35$, $p < 0.001$). This was also the case for histamine ($r = 0.2$, $p < 0.001$). In addition, there was a positive correlation between inosine and histamine ($r = 0.34$, $p < 0.001$). Subgroup analysis (gender, age, diagnosis, healthy controls) all confirmed positive correlations. Levels of hypocretin and beta-trace during the day varied (n.s.).
Discussion: In our study, the increase of inosine concentrations in the course of day support previous animal data of inosine (adenosine) being an endogenous sleep substance. Histamine increase points to its importance in maintenance of wakefulness and antagonistic role to inosine in human sleep wake regulation.

PO-2-069 / AS-3 Presenter

EFFECT OF SCHEDULED PHYSICAL EXERCISE ON RE-ENTRAINMENT OF HUMAN CIRCADIAN RHYTHMS TO 8 H ADVANCED SLEEP SCHEDULE IN ISOLATION FACILITY

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Bright light is known as a primary zeitgeber for human circadian rhythms. Timed bright light has been reported to produce phase shifts and to accelerate the re-entrainment of circadian melatonin rhythm. Recently, we observed that scheduled physical exercise significantly accelerated re-entrainment of the sleep-wake cycle to 8-h advanced sleep schedule but not the circadian melatonin rhythm under dim light conditions(<10 lx). These results were not consistent with several previous studies which demonstrated timed physical exercise phase shifted the circadian melatonin rhythms. One possible explanation for this discrepancy is the effects of exercise on light perception for rhythm entrainment. To examine this possibility, effects of physical exercise were assessed under bright light condition. Subjects spent for 14 days in an isolation unit without knowing the time of day. For the first three nights, the subjects kept in their habitual sleep time for 8 h. The light intensity in the wake period was fixed to 5000–8000 lx. All illuminations were turned off during the sleep period. The baseline circadian phase of plasma melatonin rhythm was measured on the third night. Afterward, the subjects were not permitted to sleep until the time when the sleep schedule was set at 8 h earlier than the habitual sleep time. They were required to follow the advanced schedule for 4 days. Physical exercise with bicycle ergometer was imposed on the exercise group twice a day during waking period. The 2nd circadian melatonin rhythm was measured on the last day of schedule. Then the subjects were released into free-run condition for 6 days with dim light conditions (<10 lx). On the last day of free-run, the 3rd circadian melatonin rhythm was measured. From the preliminary data of two control subjects, their sleep onsets were fully re-entrained to the shifted schedule by bright lights, whereas the peak phases of plasma melatonin rhythms were still on the way of re-entrainment (transient). We will discuss a possibility whether the timed physical exercise could accelerate the re-entrainment of circadian melatonin rhythm.

PO-2-070 / AS-3 Presenter

EFFECTS OF SINGLE EXPOSURE TO EVENING BLUE LIGHT ON LATENCY TO PERSISTENT SLEEP, SLOW WAVE ACTIVITY, MELATONIN PRODUCTION AND COGNITIVE PERFORMANCE

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Introduction: In former studies it has been shown that light with a wavelength from 446 to 477 nm suppresses melatonin, decreases sleepiness and slow wave activity in the EEG and also shortens Rapid Eye Movement (REM) phase at least for the first cycles after exposure.
Method: 40 healthy subjects have been included in this trial, 17 male and 23 female with a mean age of 25 years. 2 subjects dropped out after night 1. Chronotype was determined by the German Morningness Eveningness Questionaire (D-MEQ). Evening types had been excluded. Participants stayed 2 consecutive nights at the sleep laboratory to undergo polysomnography. Subjects had been randomized to 2 groups. Group 1 went to bed one hour earlier than group 2 and received blue light one hour earlier. In the second night participants received light with a length of 460 nm for one hour. Philips goLite BLU with a lamp colour temperature of 5500 K was used. 23 subjects received light with an intensity of 25%, 7 subjects with 50% and 8 subjects with 75%. To asses subjective sleepiness at different time points Karolinska Sleepiness Scale was used. Cognitive performance was measured by psychomotor vigilance test and Osler test sitting in a dark room for 1 hour in the first night and directly after light exposure in the second night. Melatonin was determined in blood and saliva at different time points.
Results: Analysis of the data is still outstanding. Of special interest are analysis to investigate the effect, on sleep in general, especially on

latency to persistent sleep, slow waves and REM sleep. By increasing light intensity a greater suppression of melatonin production is expected. The correlation between grade of melatonin suppression and sleep EEG activity changes are investigated.
Conclusion: This study has been conducted to clarify if a single exposure to blue light by Philips goLite BLU in the evening can lead to a decrease in sleepiness and enhance cognitive performance compared to no light condition. It has to be clarified if the expected effects provoke changes on sleep parameters in EEG by single exposure.

PO-2-071

DIURNAL VARIATION IN POSITIVE AND NEGATIVE AFFECT SCALE

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Background and Objective: The positive (PA) and negative (NA) affect scale (PANAS) is used in many studies as a facilitative and reliable questionnaire. In PANAS used globally as a questionnaire consisting of each 10-item mood scale (Watson et al. 1998). The Japanese version of PANAS was developed by Sato and Yasuda in 2001, consists of each 8-item. PA has been separated from NA, as independent components in opposite admittedly subjective directions. Each item of both questionnaires is rated on a 5-point scale. Circadian changes in mood by PANAS have been described in a little of studies, but not enough. This study aims to observe the diurnal change of mood in daily life by means of PANAS in Japan and Sweden.
Participants and Method: All of 25 Japanese (18 males and 7 females aged 23–60) and 15 Swedish (3 males and 12 females aged 28–60) participants were daytime office workers, and their working times were almost fixed throughout the year. PANAS was administered to the participants 4 times of day (8:00, 12:00, 15:00 and 20:00) in continuous 4 days every month during the course of a year. The used questionnaires were the Japanese version of PANAS in Japan and the PANAS developed by Watson et al. in Sweden.
Results and Conclusion: The result showed that score of PA and NA were low in evening of all months both countries. It is considered that PA score may relate with photoperiod, because the result on seasonality in this study showed that PA score during summer in Sweden didn't decline at evening, when sun maintains to rise. Consequently, when we used the PANAS in researches, we must consider the timing of the data collection.

PO-2-072

EVALUATION OF HEART RATE VARIABILITY AND RESPIRATORY VARIABILITY DURING SLEEP USING A LORENZ PLOT

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As part of the 24-hour, highly networked information society in Japan, workers have increasingly complained of a lack of sleep or insomnia from working long hours and late at night.

In general, assessing the stage of sleep based on the electrical patterns of the brain, or electroencephalogram (EEG), requires that the subject wear numerous electrodes. This, however, makes sleep measurements in daily life very impractical. Thus, we focused on the Peak-to-Peak intervals (PPIs) of the respiratory waveform (RESP) as an instantaneous and noninvasive method. Sleep is deeply linked to PPIs by the autonomic nervous system, and can change markedly within a few seconds. We had proposed a method using evaluation indexes from the Lorenz plot (LP). To evaluate the changes in these distributions, we projected the LP on a $y = x$ axis, $y = -x$ axis, and analyzed the shifting of the mean (center C) and standard deviation (area S) for each sleep stage. In the present study, the relationship between sleep stage based on EEG and evaluation indexes from the LP during all-night sleep was examined. Sleep stages were found to be related to the stability of evaluation indexes from the LP. We weighed the estimation values from RESP against the measurement values from EEG, and found that the method using LP can estimate the depth of sleep in real time. The mean concordance rate between the measurement and estimation indexes was 73.8% (SD = ±6.5) in all subjects. These results indicate that the sleep level can be evaluated based on RESP using the LP.
In the present study, as a simple method for analyzing the variation in RESP during all-night sleep, the distribution of points on the LP was regarded as an ellipse on the LP. To quantitatively determine the changes in distribution on LP, center M, area S, eccentricity E and flattening F were calculated as evaluation indexes. The characteristic features of fluctuations related to transitions between sleep levels were subsequently obtained. Using these features, the state of sleep can be inferred from the change in shape of the ellipse on the LP. It will be found to help improve people's quality of sleep.

PO-2-073

SEASONAL DIFFERENCES OF SLEEP AND MELATONIN CONCENTRATION IN OBESE SUBJECTS IN JAPAN

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Obesity has become a major health challenge worldwide. In Japan, 28.6% men and 20.6% women is more than BMI 25 kg/m^2. Sleep-wake regulation might be altered with body fatness in different seasons. We investigated seasonal differences of sleep and melatonin concentration in obese subjects in Japan. 5 healthy and 5 obese men participated in this experiment in summer and winter. EEG and ECG were measured continuously during overnight in the climatic chamber at 26°C and 50%RH. Saliva for melatonin was collected at 23:00, 2:00 and 6:00 in each season. Melatonin concentration showed the seasonal changes in obese and control, higher in summer. Obese subjects did not show a lower level of melatonin concentration compared to healthy subjects.

PO-2-074

EFFECTS OF 1-OLEOYL-2-DOCOSAHEXAENOYL PHOSPHATIDYLCHOLINE (PC-DHA) UPON REM SLEEP IN HUMAN STUDY

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We are interested in effects of daily foods, particularly fish oil, on sleep. It is well known that REM sleep was manipulated by the cholinergic

system. 1000 mg/day Salmon roe's oil containing of 5.37% of PC-DHA, which is DHA combined with phosphatidylcholine, was orally administrated every day during three months for nine human healthy male subjects (aged:45 ± 15 years). Their night sleep was recorded by polysomunography (PSG) with the pace of once in a week during the administration session with three consecutive months, and during the wash out session with one week. The relevant local ethical committee approved this study protocol.
It was found that% REM sleep, the relative amount of REM sleep to the total sleep time, was significantly increased to 25%–35% at the 3rd month of the administration session in compared with the base line nights. This increment of% REM sleep disappeared in the wash out session. And the periodicity of REM cycle is higher in the 3rd month of the administration session than the 1st month. REM cycle became gradually regular in proportion to the length of PC-DHA administration period.
These results suggest that PC-DHA increases REM sleep to the optimal amount of REM sleep, and may be contributed to stabilize sleep structure.

PO-2-075

THE RELATIONSHIP BETWEEN CHRONOTYPE AND DIURNAL VARIATION OF TASTE THRESHOLD

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Although many studies have considered nutrition and food intake, few have discussed changes in these variable due to the environment, especially light conditions, and chronotype (timing of biological rhythms). It is possible that these two factors might cause an individual's taste threshold to change, in accord with altered nutritional needs. This study investigated the diurnal variation of taste threshold in subjects of different chronotype in response to living in different lighting conditions. The subjects were 12 female college students and their chronotypes (M-E scores) were estimated by a morningness-eveningness questionnaire. For one week prior to the two experimental days, subjects were instructed to maintain a regular daily lifestyle, getting up at 07:00 h and going to bed at midnight, and not to drink alcohol. On the first experimental day, they entered the experimental room at 10:00 h and stayed under 1200 lux till noon, then remaining sedentary under dim light (50 lux) until retiring and sleeping in the dark. Their taste thresholds (to sweet, salty, sour and bitter stimuli) were examined at 16:00, 20:00 and 24:00 h. On the second experimental day, they got up at 07:00 h and remained in dim light, their taste thresholds being examined at 08:00 and 12:00 h. They were allowed to eat a meal after each examination. The threshold to a salty stimulus tended to be higher at 08:00 h than at the other times in those subjects whose M-E scores were 51–63 (indicating that they were "morning" types). By contrast, those subjects whose M-E scores were 38–47 ("evening" types) showed higher thresholds to a salty stimulus at 20:00 h. However, there were no diurnal variations and no differences between morning and evening types in the taste thresholds to sweetness, sourness, or bitterness.

PO-2-076

DIURNAL VARIATION IN RESPONSES OF MELANOPSIN-EXPRESSING RETINAL GANGLION CELLS TO LIGHT IN THE HUMAN RETINA

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The mechanisms by which melanopsin-expressing retinal ganglion cells (mRGCs) regulate circadian rhythms in humans have not been established. To understand mRGC characteristics and their role, mRGC responses should be induced or measured independent of cone and rod responses. In a prior study (Fukuda et al., 2010), we successfully investigated mRGC responses independent of rods and cones by using our innovative method, which induces responses in only the mRGCs as measured by the electroretinogram (ERG). In the present study, we have attempted to use the ERG to measure changed responses of the mRGCs over the course of the day.
Two healthy female Japanese subjects (22 years old) joined this study. Sleep-wake cycle by using an Actiwatch-L (Mini Mitter Co. Inc., USA) and a sleep diary, salivary melatonin and tympanic temperature were measured as markers of biological rhythms. The subjects undertook test sessions – to investigate changes in mRGC responses to light stimuli as measured by the ERG – at 9 pm on the first day and 9 am and 3 pm on the second. For each test session, the subject's pupil on the left eye was dilated by a mydriatic agent and they wore an ERG electrode while they gazed at the center of circular light stimulus on a diffuser in front of them. The diffuser was at a distance of 300 mm from the subject and the circle subtended an angle 18.9 degrees at the eyes. After 5-min adaptation, in order to saturate rod responses, the light stimuli were given for 250 msec and repeated 30 times at intervals of 5 sec.
The hormone and body temperature rhythms were normal in both subjects. The mRGC and overall amplitudes in the ERG were higher in the evening (9 pm) than in the other time (9 am and 3 pm), indicating the possibility that the sensitivity of the cones as well as of the mRGCs would be heightened in the evening. Therefore, in a modern society, people should take more care with exposure to bright light in the evening, since their light sensitivity might be higher at this time. The results also suggest that light might more easily disrupt human circadian rhythms in the evening.

PO-2-077

WITHDRAWN

PO-2-078

CHRONIC SLEEP RESTRICTION ALTERS SLEEPINESS, SLEEP AMOUNT, NEUROCHEMISTRY, AND SPATIAL MEMORY IN RATS

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The sleep responses to chronic sleep restriction (CSR) are different from those to short-term total sleep deprivation. When CSR continues for

several consecutive days, humans and rats fail to express homeostatic increases in sleep amount, which includes sleep time and sleep intensity (as measured by NREM delta power). Rats exposed to CSR were allowed 6 h of sleep opportunity (SO) per day during the first 6 h of the 12 h light period for at least 5 days, followed by recovery days. Measurements included: 1) sleep latency to assess sleepiness, 2) brain adenosine receptor and adrenergic receptor mRNA, and, 3) spatial reference memory using the water maze. After 18 h sleep deprivation on the first sleep restriction (SR) day, the total sleep time and NREM delta power were significantly increased during the 6 h SO, compared to the corresponding baseline level (BL). However, these compensatory increases in sleep time and intensity were absent from SR days 2 to 5. Sleep onset latencies were significantly reduced from SR1 through SR4 compared to BL day. Adenosine A1 receptor mRNA levels were increased in the basal forebrain throughout the CSR and recovery days, while adenosine A2a receptor was decreased in the frontal cortex throughout the CSR period. Beta-adrenergic receptor mRNA levels were significantly decreased in the anterior cingulate cortex only on SR1. The spatial learning of CSR rats was similar to movement control rats. However, spatial memory recall was impaired compared to the movement control rats. In conclusion, rats exposed to chronic sleep restriction do not sleep longer or deeper even though they continue to experience elevated sleepiness and memory impairments. The data suggest at least two different sleep regulatory systems in the brain: one mediating sleepiness and memory consolidation, and the other mediating sleep amount. Based on the similar time course changes, our findings support the possibility that changes in A1R and the cortical A2aR tone may mediate sleepiness and memory consolidation; whereas the cortical beta-adrenergic receptor tone may mediate sleep time and intensity.

PO-2-079 / AS-29 Presenter

SEX AND MENSTRUAL CYCLE EFFECTS ON SLEEP DEPENDENT MEMORY CONSOLIDATION

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There is growing amount of evidence that memory is consolidated by short midday naps. But until now it remains unclear, which sleep phases or EEG activities are relevant for different tasks and which hormonal influences may play a role in memory consolidation. Effects of short, midday naps on declarative and procedural memory consolidation were investigated in healthy adults, ages 18 to 30 years. A female group was tested during different phases of the menstrual cycle. The subjects were allowed a nap after learning or watched a movie. Memory performance was tested by verbal paired associate task and finger tapping task. In addition the subjects underwent one nap without a previous learning experience. The mens memory benefited significantly from the NREM nap in comparison to wake, and the increase in motor performance correlated with the increase in sleep spindles through learning. The womens performance only increased through a nap during the luteal phase and not during the follicular phase of their menstrual cycle. Only the men and women in their luteal phase experienced an increase in spindle activity after learning matching the learning behavior. Further, in women estrogen correlated with the offline change in declarative learning and progesterone with motor learning. Interestingly the ratio of the 2nd and 4th digit, which has been associated to fetal sex hormones and cognitive sex differences, predicted the average performance of the female subjects in the learning tasks. We are the first to show a gender and menstrual cycle effect on sleep dependent memory consolidation during a nap. Further, we could demonstrate that declarative and procedural memory consolidation cannot be REM sleep dependent as previously assumed, but most likely is connected to sleep spindles.

PO-2-080

NMDA RECEPTOR AGONIST FACILITATES SLEEP-INDEPENDENT SYNAPTIC PLASTICITY ASSOCIATED WITH ENHANCEMENT OF WORKING MEMORY CAPACITY

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Currently, although N-methyl-D-aspartate (NMDA) receptor antagonists suppress sleep-dependent memory processing, it is not well known how sleep and NMDA receptor agonists affect working memory (WM) performance improvement, respectively. In order to investigate the neural basis underlying relationships between WM skill learning and sleep, D-cycloserine (DCS), which is a NMDA receptor partial agonist, and both sleep and DCS together, we evaluated training-retest performance of n-back task in healthy subjects who were given either with wakefulness or sleep. All subjects showed improved WM capacity over successive n-back test trials. Among subjects retested 24 hours after the training session, greater WM capacity improvements occurred when individuals were treated with DCS rather than placebo. Among subjects retested 12 hours after the training session, who received only a placebo, greater improvements in task performance were observed when training session was followed by sleep rather than a period of wakefulness. However, among those who received DCS, greater improvements in task performance were observed only when the training session was followed by a period of wakefulness. These results indicate that WM capacity enhancement is affected by disparity in synaptic plasticity between sleep and wakefulness. Further, these findings suggest potential methods for improvement general fluid intelligence, which is necessary in human for problem-solving activities, and may also influence learning, anti-aging processes, and rehabilitation of higher cognition.

PO-2-081 / AS-32 Presenter

MEG CORTICAL ACTIVITY DURING NREM SLEEP CORRELATED WITH IMPROVEMENT OF A MOTOR SEQUENCE LEARNING

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A growing body of evidence suggests that brain oscillatory activity during sleep plays a key role in facilitatory action of memory and learning. However, the underlying neural mechanisms remain unclear. Here, we used a multimodal neuroimaging technique in combination of MEG and MRI, which allows us to measure brain activation in high spatial and temporal resolution, to test whether such facilitatory effect occurs

in the brain region known to involve with better performance. Healthy participants underwent 4 nightly MEG sessions (2 adaptation nights, pre-training sleep, and post-training sleep) as well as 1 MRI session. Before and after the post-training sleep, a finger-tapping task was conducted, which was previously shown to involve the primary motor area (M1) contralateral to the trained hand, but not other motor-related areas including the supplementary motor area (SMA), for its improvement. MEG data was wavelet-transformed and combined with MRI to constrain the current locations to the cortical mantle individually. Based on the individual MRI, we localized motor related cortical areas including the M1, the SMA and the pre-supplementary motor area (pre-SMA), premotor area, superior parietal gyrus, as well as the primary visual cortex (V1) as a non-motor related area. We found increase in several bands of spontaneous oscillations including the sigma and delta bands during the post-training sleep compared to the pre-training sleep in motor-memory regions such as the supplementary motor area (SMA), and pre-SMA in high correlation with performance improvement after sleep, but not in M1. These results suggest that there is a distinct neural network strongly correlated with the sleep facilitatory effect during post-training NREM sleep, separately from the network involved in the better execution of the task during the subsequent wakefulness.

PO-2-082 / AS-29 Presenter

SLEEP AND MEMORY CONSOLIDATION IN MEMORY CHAMPIONS

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Increasing evidence suggests a supportive role of sleep in memory consolidation. However, the details of the sleep-memory relation are still under debate. While there is a wide consensus on a general beneficial effect of sleep on memory consolidation, in contrast the effects of intense memorizing periods on sleep are much less clear. In addition, little is known about the influence of individual differences (e.g. cognitive capabilities) on the sleep-memory relationship. We are addressing these points in an ongoing study including 15 world-class memory athletes out of the top-50 of the memory championships world ranking list. As a control group served 15 subjects matched for age, gender and intelligence. All subjects underwent three nights of polysomnography and a battery of declarative learning tasks. In a crossover-designed manner, subjects spent a night in the sleep lab either after an intense learning session of four consecutive hours, memorizing 1000+ information chunks, or after a day without active memorizing activity. Sleep data of the test and control nights are presented and their relation to memory consolidation discussed.

PO-2-083

SLEEP EXTINGUISHES FALSE PERCEPTION ACQUIRED BY LEARNING OF VISUAL-TACTILE INTEGRATION

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It is well known that delayed learning of various perceptual skills is facilitated by sleep following repetitive skill training (Stickgold & Walker, 2005). Although cross-modal integration (e.g. visual and tactile sensations) plays is important for adaptation to different environmental conditions (Stein, 1998), it remains unclear whether or how sleep affects learning of cross-modal integration. To explore this issue we compared delayed learning properties of visual-tactile integration during sleep and wakefulness. All subjects initially acquired the newly formed visual-tactile integration by using the rubber hand illusion paradigm (Botvinick & Cohen, 1998) to provide false visuospatial perception. Twelve hours later, following continuous normal daytime waking (Wake group: N = 20) or an equal interval containing a normal night's sleep (Sleep group: N = 20), we measured visuospatial false perception and habituation as represented by the skin conductance response. The false perception rate in the delayed test decreased in both groups. A greater decrement in the visuospatial false perception rate was observed in the sleep group than in the wake group. In contrast, a greater decrement in the skin conductance response was observed in the wake group than in the sleep group. Here we show that sleep reduces the learning of visuo-tactile integration. Sleep may discriminate inappropriate learning from beneficial learning, facilitating beneficial learning while extinguishing inappropriate learning based on successful adaptation.

PO-2-084

IMPLICIT LEARNING IS PERSISTENT EVEN IN A DROWSY CONDITION

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The aim of the study was to investigate whether implicit learning would be improved by a short afternoon nap or bright light exposure. Seventeen partial sleep deprived participants (8 women; 30.4 ± 7.69 years old; 20% reduction from normal nocturnal sleep time) carried out the implicit learning task and subjective sleepiness rating twice a day (1145–1300h, 1415–1530h) before and after an afternoon short nap (20 min) or rest. During the second task, bright light treatment (2000 lux) was applied, so that the participants took part in a total of four experimental conditions (control, short nap, bright light, and short nap + bright light conditions). In the implicit learning task, participants searched a 90 degrees rotated character "T" (target) among randomly rotated and deployed characters "L" (distracter) on a computer display. In the task, participants were required to indicate the direction of "T" (either right or left) by pressing a button as quickly as possible. Twelve blocks (24 pictures for each block) were performed in total. In the first block, all the pictures were new (NEW) for the participants, but in the subsequent blocks, half of them (12 pictures) were the same pictures as they responded in the first block (OLD). The experiment was designed so that participants did not notice that OLD pictures were shown amongst NEW pictures in the subsequent blocks. In the result, the search time was significantly shorter against OLD than NEW pictures ($p < .05$), which means that implicit learning was occurred during the task. This factor interacted with neither nap nor light treatments. The search time was significantly shorter in the nap condition compared to the control condition ($p < .05$). Subjective sleepiness was significantly reduced in the short nap, bright light, and short nap + bright light conditions compared to the control condition ($p < .05$). In conclusion, implicit learning per se occurred regardless of a short nap and bright light exposure. A short nap improves cognitive performance to search a target from distractive stimuli, though it has no significant effect on implicit learning amount.

PO-2-085

ALTERATION OF EEG SPECTRAL POWER DURING SLEEP AFTER MOTOR LEARNING

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The beneficial role of sleep in motor memory consolidation is now well documented. However, there has been only insufficient evidence to document neurophysiological mechanism of sleep on memory consolidation.
PURPOSE: We examined the effects of 2h daytime nap on three-ball cascade juggling. In addition, in order to elucidate neurophysiological mechanism of sleep related to the memory consolidation, sleep EEG spectral analysis was performed in addition to sleep stage scoring.
METHODS: Subjects were 18 female college students. They were divided into nap group and control group. All subject practiced juggling for 15min, and juggling technique was evaluated at 10:30. Subsequently, nap group took a 2h nap from 14:00 while control group stayed awake. Both groups retested juggling at 17:30. One week before these experiments, nap group had taken 2h nap in the same environment as a baseline nap condition. These EEG were recorded at 7 scalp sites. EEG was subjected to fast Fourier transform analysis (FFT).
RESULT: Nap group improve the juggling performance after 2h nap ($p < .001$). Control group did not show the improvement. Compared to the baseline nap, increasing time of slow wave sleep (SWS) was marginally significant ($p = .09$). FFT revealed that slow oscillation (0.3~1.0Hz) power and delta EEG (1.0~4.0Hz) power showed increasing trends (slow oscillation: $p = .08$, delta: $p = .06$), theta EEG (4.0~8.0Hz) and sigma EEG (12.0~16.0Hz) power was significantly increased (theta: $p < .05$, sigma: $p < .05$) during NREM sleep in after learning nap. During REM sleep, only 23–25Hz showed an increasing trend ($p = .07$).
CONCLUSION: Sleep facilitate memory consolidation in three-ball cascade juggling. Slow and delta showed increasing trend, and theta and sigma showed significant increment during NREM. These results may indicate that SWS related the motor memory consolidation process. Increasing sigma EEG power may suggest that sleep spindle activities are involved in procedural memory consolidation process during sleep. Increasing trend of 23–25Hz during REM may suggest that REM sleep is also involved.

PO-2-086

CONTRIBUTION OF A NAP TO THE CONSOLIDATION OF DECLARATIVE AND PROCEDURAL MEMORIES

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A number of studies have demonstrated that declarative and procedural memories improve across nocturnal sleep. The relationship between memory consolidation and sleep stages has been under discussion. Nocturnal sleep contains all of the sleep stages so that it is difficult to eliminate the influences of each sleep stage. Then we focused on **a daytime nap** to examine the influence of **sleep stage 2** and **slow wave sleep** for memory consolidation. At 2 pm., 22 participants took a nap including sleep stage 2 ($n = 10$) or slow wave sleep ($n = 12$), while the other participants remained awake ($n = 11$). All participants trained paired association and finger tapping sequence task at noon and were tested at 5 pm. The participants who took a nap containing **slow wave sleep** tended to improve the performance of paired association task than those who stayed awake. In addition, improvement of this task positively correlated with the amount of sleep stage 2 for the participants who took a nap including slow wave sleep ($r = 87$, $p < .05$). These results suggest that a certain amount of sleep stage 2 is necessary to consolidate the memory trace of declarative memory.

PO-2-087

THE RELATIONSHIP BETWEEN SCHOOL ACHIEVEMENT AND SLEEP AMONG ELEMENTARY AND JUNIOR HIGH SCHOOL STUDENTS IN OKINAWA

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To clarify the relationship between school achievement and sleep and life-style among 6 th. grade elementary school students (ESS) and 3 rd. grade junior high school students (JHSS) in Okinawa, the authors conducted a survey. The questionnaire consisted of self-rated school achievement for Japanese language, mathematics, science, social studies, English and physical education, sleep indexes such as total sleep time, sleep quality, regular sleep, attitude and value of sleep and sleep satisfaction, life-style indexes such as physical activity, regular breakfast, reading time, studying time and television viewing time, and mental health indexes such as self-esteem and depression. Subjects were 981 ESS and 1,051 JHSS. We received 948 (97%) and 962 (92%) valid responses, respectively. Results showed that 13% of ESS and 33% of JHSS suffered from insomnia. Moreover, 5% of ESS and 20% of JHSS were "short sleepers who slept less than 6 hours" and 5% of ESS and 6% of JHSS were "poor quality sleepers". Furthermore, 2% of ESS and 3% of JHSS were "not satisfied sleepers" and "irregular sleepers" numbered 5% for ESS and 8% for JHSS. Short sleepers had a lower achievement for mathematics, social studies, humanities and natural science. Poor quality sleepers had a lower achievement for Japanese language, science, humanities and natural science. Concerning life-style, students who had regular physical activities, ate breakfast regularly, who did not have depress moods, and studied longer, had a higher school achievement. This study suggested that students' sleep quality and quantity may effect school achievement.

PO-2-088

EFFECTS OF NAPS, AND HEAD MASSAGES ON IMPROVING MEMORY AND REDUCING FALSE MEMORY IN YOUNG ADULTS

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Research has shown that naps and head massages can improve memory. However, their effects on false memory, often found among young people, are a matter yet to be soundly addressed.

The present study focuses specifically on young adults, comparing the relative efficiency of naps and head massages on improving memory, and on reducing false memory. Thirty undergraduate university students have volunteered to participate in the study. They are all right-handed, with demonstrated regular word memory, and having no history of neurological disease or mental illness.
A pre-post with control group quasi experimental design will be used. The Deese-Roediger-McDermott paradigm (DRM) test will serve as the pre-test. One experimental group will nap for 60 to 90 minutes; another will receive a traditional Thai head massage for 30 minutes. The DRM will be administered again as a post-test.
Other research instruments to be used include the Thai General Health Questionnaire (for screening), the Wechsler Adult Intelligence Scale-Third edition (WAIS-III) verbal comprehension (as a covariate), with electroencephalograms (EEG) used in the nap group to measure and record electrical activity in the left anterior temporal lobe (LATL), known to be vital for semantic processing.
Hypotheses to be tested: naps and head massages will both improve memory; head massages will be more effective than naps in reducing false memory.

PO-2-089

IMPAIRED SLEEP-DEPENDENT PROCEDURAL MEMORY CONSOLIDATION WAS ASSOCIATED WITH FAST SPINDLE ACTIVITY IN MEDICATED DEPRESSIVE PATIENTS

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Introduction: A growing corpus of evidence demonstrates that sleep enhances consolidation process of memory, ranging from declarative memory to other kinds of memory system. Although procedural memory was consolidated in normal human subjects, whether the sleep-dependent procedural memory consolidation occurs in medicated depressive patients is still unclear, with pharmacological and physiological mechanism in neural network.
Methods: Healthy comparison subjects (n = 19) and medicated depressive patients (n = 9) were recruited. We used motor sequential tapping test (MST test) paradigm, comparing the archived score between pre and post-learning sleep. In MST test subjects were offered to use their left non-dominant hand. Subjects were recorded during all night with 16 channels EEG between MST test. Sleep scoring and frequency analysis were performed in recorded EEG. In addition, we detected sleep spindle by using automatic algorithm, dividing into fast spindle (12.5–16Hz) and slow spindle (10.5–12.5Hz).
Results: Motor memory consolidation was significantly impaired in patients compared with normal controls. In normal controls, the amount of stage 2 NREM sleep was correlated with the magnitude of motor memory consolidation. In patients, the ratio of fast spindle for slow spindle in left centro-parietal region, which was opposite side of the left hand, was correlated with improvement.
Conclusions: These data suggest that spindle activity has the potential of regulate offline procedural memory consolidation. In medicated depressive patients, the activity of fast spindle within the right motor cortex showed decreased correlation with motor memory improvement. Benzodiazepines may inhibit underlying brain plasticity of the area where offline consolidation take place, modulating the propensities of fast and slow spindle activities. Further studies are needed regarding cerebral connectivity of physiological biomarker, linked with cognitive process.

PO-2-090

WHICH CEREBRAL ACTIVITY DIFFERENTIATES DREAMERS FROM NON-DREAMERS?

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Dreaming is still a mystery of human cognition. In the fifties, dreaming has been associated with rapid eye movement sleep (Dement & Kleitman 1957; Sastre & Jouvet 1979) but this hypothesis which cannot explain all the characteristics of dream reports has been challenged (Solms 1997; Nir & Tononi 2010). The neurophysiological correlates of dreaming remain thus unclear. We used event-related potentials during wakefulness and sleep to measure brain activity in subjects who report dreams frequently (Dreamers) versus rarely (Non-Dreamers). During data acquisition participants passively listened to sounds while they were (1) watching a silent movie (2) sleeping. Here we show that the primary steps of auditory processing (N1, Naatanen et al. 1978, 1987) match in Dreamers and Non-Dreamers. However, latter brain responses, reflecting higher cognitive processing, dramatically differ in the two groups both during pre-sleep wakefulness and during sleep. Our results support the idea that the ability to recall dream is associated with a particular cerebral functional organisation independent of the state of vigilance.

PO-2-092

ASSOCIATION BETWEEN FREQUENCY OF BAD DREAMS AND DEPRESSIVE SYMPTOM AMONG MIDDLE-AGED AND ELDERLY ADULTS IN THE COMMUNITY

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AIMS: Frequency of bad dreams has been related to depression in adolescent, this association among middle-aged and elder remains unknown. This study aims to examine the association between frequency of bad dreams and depressive symptom among middle-aged and elderly adults in the community.
METHODS: A cross-sectional analyses were performed using residents who participated in a prospective cohort study which is Locomotive Syndrome and Health outcome in Aizu Cohort Study (LOHAS), in Tadami and Minami Aizu, Fukushima Prefecture, Japan. We administrated a questionnaire consisting of dreams, sleep variables and sleep quality (Pittsburgh Sleep Quality Index), depressive symptoms (The five-item Mental Health Index), physical activity (International Physical Activity Questionnaire), and demographic factors. Presence of bad dreams was defined as experiencing a bad dream at least once a week. Logistic regression models were used to examine the association between bad dreams and depressive symptom.
RESULTS: 3400 subjects were included in the analyses (39.4% male, mean age = 66.3 years). The prevalence of bad dreams was 2.9%. Sleep characteristics differentiating subjects with bad dreams from those

without were significantly longer sleep latency, decreased sleep efficacy, and poorer sleep quality. Bad dreams were significantly associated with depressive symptoms ($p < 0.001$).
CONCLUSIONS: Depression symptoms and sleep quality are independently associated with bad dreams. Interventions for improving bad dreams and sleep quality may therefore decrease depressive symptoms. The further studies need to determine directions of causality for those correlations.

PO-2-093

RECURRENT DREAMS AND BAD DREAMS IN CHILDREN: A LONGITUDINAL INVESTIGATION

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Bad dreams and recurrent dreams are two types of oneiric experiences that have long interested researchers and clinicians alike. In adults, the presence of recurrent dreams is associated with lowered psychological well-being and bad dream frequency with increased scores on measures of anxiety and depression. However, little is known about the concurrent and longitudinal psychological correlates of bad dreams and recurrent dreams in children. We present findings from an ongoing longitudinal study focusing on the social, psychological, and cognitive development of children in the province of Quebec, Canada.
Participants were 172 children (50% of each gender) studied yearly between the ages 11 and 13 years. As part of their assessment, children provided information about their dreams and various aspects of their psychosocial adjustment. The incidence of bad dreams as well as of recurrent dreams was found to decrease between the ages 11 and 13 (from 82.7% to 63.8% for bad dreams; from 35.3% to 12.2% for recurrent dreams). At age 11, presence of bad dreams or recurrent dreams was associated with greater emotional difficulties. Emotional problems as well as anxiety at age 11 did not predict subsequent occurrence of bad dreams or recurrent dreams at age 12 or 13. However, the presence of bad dreams or recurrent dreams at age 11 predicted the occurrence of bad dreams and recurrent dreams at ages 12 and 13. These results suggests that the presence of recurrent or bad dreams at age 11 is associated with concurrent emotional difficulties but that the presence of negative oneiric experiences in older children is better predicted by past negative oneiric experiences than by previous emotional problems. How relations between repetitive or negative dream content and waking adjustment jointly evolve over time from childhood through adolescence remains to be determined.

PO-2-094

SEXUAL CONTENT OF MEN AND WOMEN'S DREAMS

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Introduction: Given the longstanding interest in dreams with sexual content, it is surprising to note the paucity of empirical literature on this topic. The aim of the present study was to investigate the content of sexual dreams across a large sample of everyday dream reports collected prospectively from both student and non-student men and women.
Methods: Participants were 220 women (30.3 ± 14 years) and 60 men (29.9 ± 14.4 years), who recorded their dreams in a daily sleep log for 2 to 4 weeks. Since the evaluation of sexual experiences in dreams was not the focus of the original investigation, they were not asked to take special note of these elements. Dream reports were scored on a variety of scales including type of sexual content, characters, and setting.
Results: Participants reported a total of 5521 dreams, including 323 sexual dreams representing 6.7% of men's (M) and 5.6% of women's (W) dreams. Sexual propositions were the most common type of sexual dream content (M = 35%; W = 26%), followed by intercourse (M = 26%, W = 27%), kissing (M = 21%, W = 27%) and fantasies (M = 21%, F = 24%). Irrespective of gender, sex dreams were more likely to take place in an unknown setting rather than in a familiar one. Men more often described themselves as having initiated sexual contact (M = 39%, W = 28%) but women were more likely to describe at least part of the sexual activity as being unwanted (17% versus 11%). Current or past partners were identified in 30% of women's sex dreams compared to 11% for men. Older adults were more likely than students to have sexual dreams containing one's current partner (24% vs 14%) and older males were almost 2.5 times more likely than student males to describe themselves as the initiators of erotic activities.
Discussion: To our knowledge, this is the first study to have investigated sex-related dream content variables in a large sample of log-based dreams. The findings reveal multiple gender and age based differences. In line with the continuity hypothesis of dreaming, these variations may be indicative of different waking needs, experiences, desires and attitudes with respect to sexuality.

PO-2-095

SLEEP ARCHITECTURE IN SYNOMOLOGUS MACAQUE ACROSS A 24-H LIGHT AND DARK PERIOD

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Basic sleep research typically involves the use of animal models such as mouse, rat, rabbit, cat and dog. The non-human primate synomologus macaque (Macaca fascicularis) is widely used for research on human diseases, including neurological disorders; however, little is known about this animal's sleep architecture. Thus, we investigated the sleep-wake patterns of synomologus macaque in 24-h polysomnographic recordings using telemetry.
Five male synomologus macaques, weighing 3–5 kg each, were chronically implanted with cortical EEG, orbit EOG and neck EMG electrodes. All electrodes were connected to wires that passed subcutaneously and terminated at the telemeter transmitter in the abdomen. EEG, EOG, and EMG were continuously recorded by the telemetry system across circadian dark (19:00–07:00) and light (07:00–19:00) periods. Polysomnographic data were visually scored using criteria based on the standards for staging human sleep.
In synomologus macaque, non-REM sleep accounts for 90.5 ± 2.5% (n = 5) of total sleep time while REM sleep accounts for 11.1 ± 1.9% (n = 5) of total sleep time during the dark period. Most of the slow wave sleep states appeared during the first few hours of the dark period. These results clearly demonstrate that synomologus macaques are diurnal animals with mono-phasic sleep-wake circadian patterns. Furthermore, the sleep architecture of synomologus macaques is closely related to that of humans.
In conclusion, our results suggest that synomologus macaque, a diurnal non-human primate, may be a promising experimental animal model for studying sleep disorders and newly developed drugs.

PO-2-096

NONINVASIVE DETECTION OF SLEEP/WAKE CHANGES IN OREXIN/ATAXIN-3 TRANSGENIC MICE ACROSS THE DISEASE ONSET

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Introduction: Narcolepsy is characterized by excessive daytime sleepiness, a fragmented sleep/wake pattern, cataplexy and other dissociated manifestations of REM sleep. The hypocretin/ataxin-3 transgenic (TG) mice exhibit a phenotype similar to human narcolepsy. Hypocretin-containing neurons in TG mice are selectively ablated postnatally and lost over 99% by 84 days postnatal age. No sleep recordings were, however, conducted at the disease onset. This is partially due to the methodological limitation; implantations of an EEG headstage in growing young mice and a long term monitoring are difficult. In this study, we evaluated the sleep/wake changes of narcoleptic mice from 2 weeks old and across the disease onset using the piezoelectric (PZT) system as a noninvasive sleep monitoring system.
Method: Sleep recordings of 6 TG mice and 6 respective wild type (WT) littermates were performed. PZT sensor can detect the movements and the heart rate and respiratory variation. Mice were simply placed on the PZT-sensor for 3 hours during the light period, and the recordings were repeated on 14, 28, 56, 84, and 98 days after the birth. The amount of sleep and the sleep/wake bouts of TG and WT mice were analyzed using our original software.
Result: The sleep amounts in TG mice over 28 days old become larger than those of WT mice, but the differences did not reach to the significant levels. There were no changes in wake bout length nor any differences between the genotypes during the study period. In WT mice, there was also no change in sleep bout length. In contrast, sleep bout length in TG mice decreased over the age. As a result, significant differences in sleep bout length between the genotypes were observed over 56 days old.
Conclusion: The sleep fragmentation in narcoleptic mice progresses during the period of progressive loss of hypocretin neurons. Our results confirm that the piezoelectric sensor is useful as a noninvasive sleep and behavior monitoring system, especially in the developmental period. Analysis of other sleep behavioral changes using the piezo signals obtained is also in progress.

PO-2-097

CATECHOLAMINERGIC DRUGS MODIFY THE NARCOLEPSY-CATAPLEXY EPISODES IN MUTANT TAIEP RAT

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In 1989 Holmgren et al. described a new mutant rat which develops a progressive motor syndrome during its lifespan. The syndrome is characterized by a tremor in the hindlimbs followed by ataxia, immobility episodes (IEs), epilepsy, and paralysis. The acronym of these symptoms named this autosomic recessive mutant trait as taiep. In this study, we analyzed the effects of systemic administration of several catecholaminergic drugs in the expression of gripping-induced IEs in 8-month-old male taiep rats. The animals were housed under a 12:12 light-dark cycle (lights on at 0700) with controlled conditions around 21 Celsius degrees and 30%-45% relative humidity all the time. The administration of drugs was done by i.p. route with an increasing dose scheme every 48 h. We recorded the frequency, total duration of each IEs and the latency of the first IEs. The drugs used were: yohimbine, clonidine, prazosin, D-amphetamine and modafinil. All experimental procedures were approved by the IACUC and the experiments start at 0800 and lasted 90 min. Systemic administration of clonidine or prazosin produced an increase in the frequency and mean duration of gripping-induced IEs, while D-amphetamine modafinil, two dopamine reuptake blockers, are very effective to decrease a diminution in the frequency and duration of IEs. On the other hand, yohimbine, an alpha 2 antagonist, is capable to abolished IEs with the higher dose tested (1 mg/Kg). These findings correlate with the pharmacological observations made in narcoleptic dogs and humans, in which chatecholaminergic including dopaminergic and adrenergic mechanisms are involved in the modulation of cataplexy. So, taiep, a myelin mutant rat with a severe demyelination is an adequate model to study cataplexies and then an adequate option to study the new therapeutic options available to treat cataplexy.

PO-2-098

SEX-SPECIFIC ASSOCIATIONS BETWEEN SLEEP PROBLEMS AND HYPOTHALAMIC-PITUITARY-ADRENOCORTICAL AXIS ACTIVITY IN CHILDREN

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Study objectives: Sleep problems are associated with reduced physical and mental health. Altered function of the hypothalamic-pituitary-adrenocortical axis (HPAA) may be one underlying mechanism. We studied the associations between sleep problems and HPAA activity in children.
Design: A cross-sectional epidemiological cohort study.
Setting: Salivary cortisol was sampled throughout one day at home and during the Trier Social Stress Test for Children (TSST-C) in clinic. Sleep disorders were measured with a parent-rated Sleep Disturbance Scale for Children, and sleep duration measured by actigraphy for one week.
Participants: 284 (51 percent girls) 8-year-old children.
Results: Boys with sleep problems (85th percentile in any of the sleep-wake transition, arousal, excessive daytime somnolence or sleep hyperhydrosis subscales) had lower diurnal salivary cortisol levels and salivary cortisol responses to TSST-C stress in comparison to boys without sleep problems. Girls with sleep problems (85th percentile in disorders of initiating and maintaining sleep) displayed a higher overall level of salivary cortisol during the TSST-C. Salivary cortisol responses

to stress were lower in boys and higher in girls with more than one sleep problem.
Conclusions: Sleep problems in children are associated with altered HPAA function, after controlling for actual sleep quantity measured by actigraphy. Boys with sleep problems had lower HPAA activity and girls with sleep problems had higher HPAA activity, compared to children without sleep problems.

PO-2-099

CLINICAL SIGNIFICANCE OF LONG-TERM HOME MONITORING OF FETAL MOVEMENT DURING SLEEP IN TWO HIGH-RISK PREGNANT WOMEN

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Fetal movement is an index of fetal well-being. We have developed a record-analysis system for fetal movement during maternal sleep at home using a new sensor (FMAM: Fetal Movement Acceleration Measurement).* Pregnant women who previously experienced stillbirth or neonatal death have high anxiety when facing another pregnancy. This study looked at the use of long-term home monitoring of fetal movement in high-risk pregnant women in order to reduce their anxiety.
Methods: Subjects were ten normal pregnant women (range: 29 yr–39 yr) and two high-risk pregnant women (33 yr and 38 yr) who previously experienced stillbirth or neonatal death. All subjects gave written informed consent to the study. We provided FMAM recorders to the subjects. In addition, midwives visited the homes of the two women at risk to check their health. All subjects used the FMAM recorder once every four weeks. One sensor was placed on the abdomen to record fetal movement, and the other was placed on the thigh to record their own movement. All women recorded fetal movement during sleep by themselves.
Results: Median (and range) numbers for fetal movement per hour during sleep for the normal pregnant women were 116 (56–206), 110 (42–173), 108 (68–152), and 99 (31–146) at 24, 28, 32, and 36 gestation weeks respectively. There were large individual differences in fetal movement. The numbers for fetal movement for the woman who previously experienced stillbirth were 53 and 47 at 34 and 36 weeks respectively. The numbers for fetal movement for the woman who previously experienced neonatal death were 52, 81, 94, and 93 at 24, 29, 34, and 37 weeks respectively.
Conclusion: The number of fetal movements per hour during sleep for the two women who experienced stillbirth or neonatal death was similar to those for the normal pregnant women. Knowing weekly variation of fetal movement at night contributed to reducing anxiety in the pregnant women at risk. Interviews were also useful for reducing their anxiety.
*K. Nishihara, S. Horiuchi, H. Eto, M. Honda.Early Human Dev. 84:595–603, 2008

PO-2-100

THE DISCREPANCY BETWEEN ACTIGRAPHIC AND SLEEP DIARY MEASURES OF SLEEP IN ADOLESCENTS

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STUDY AIMS: To explore the discrepancy between sleep diary and actigraphic measures of sleep in adolescents and to ascertain whether these discrepancies may vary according to characteristics of the participant.
PARTICIPANTS: 385 adolescents aged 13–18 years (X = 15.6, SD = 0.95; 60% male) from eight high schools in South Australia.
MEASUREMENTS & METHODS: Adolescents completed the School Sleep Habits Survey and Paediatric Daytime Sleepiness Scale during class time, followed by an 8-day Sleep Diary and wrist actigraphy. The Flinders Fatigue Scale was completed on the final day of the study. Parents completed a Sleep, Medical, Education and Family History survey.
RESULTS: Actigraphic estimates of wake after sleep onset (WASO) were substantially greater than sleep diary estimates (74m actigraphy vs. 7m sleep diary) and conversely actigraphic estimates of sleep were substantially less than both sleep diary and parent-report (6h51m actigraphy vs. 8h16m sleep diary vs. 8h51m parent-report). Sleep diary estimates, but not actigraphy, displayed significant relationships with daytime functioning. Actigraphy showed weak relationships with concomitantly recorded sleep diary variables. Sex and puberty-related differences were found in actigraphic scoring. Actigraphy scored more WASO and less sleep in boys compared to girls, and more WASO amongst pubertally-mature boys than boys of less advanced pubertal development.
CONCLUSIONS: There may be differences in the sleep of adolescents that result in less actigraphic total sleep scored than perceived, particularly in boys, possibly because of increased sleep motor activity in adolescents that actigraphic algorithms score as wake. This is a significant concern that requires further examination with PSG.

PO-2-101

SLEEP LATENCY ON MSLT IN HEALTHY YOUNG ADULT-COMPARISON BETWEEN 7-HOUR SLEEP AND 3-HOUR SLEEP

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Purpose: Japanese young adults have insufficient sleep. We studied the influence of subacute partial sleep deprivation on their sleep latencies (SL) and frequency of sleep onset REM periods (SOREMPs) on multiple sleep latency test (MSLT).
Methods: Subjects were healthy seven females and three males (mean age: 21.4 ± 0.7 years). We obtained written informed consents from all of them. The study schedule was as follows: in the control (C) condition, the subjects were allowed seven-hour sleep for the baseline week (BW) and the following experimental week (EW); in the partial sleep deprivation (SD) condition, they were allowed seven-hour sleep for BW and three-hour sleep for EW. The wakeup time was the same

clock time. C and SD conditions were done in crossover design for each subject. The subjects' wrist activity was measured by using Actiwatch (Mini-Mitter Co., Inc., Bend, Ore) for both two weeks and actigraphic sleep-wake state was calculated by the recommended method. On both final days on EWs, polysomnography (PSG) and MSLT were performed.

Results: Nighttime actigraphic sleep was approximately five hours on both BWs, and those of C and SD conditions on EWs were about 5.5 and 3.5 hours, respectively. Total sleep time on PSG was about six hours in C condition and about three hours in SD condition, respectively. The mean SL (mSL) on MSLT was 6.3 minutes in C condition and 3.9 minutes in SD condition. The frequency of SOREMPs was higher in SD condition than C condition.

Conclusion: Even in C condition, mSL of the subjects was less than eight minutes. In SD condition, mSL was shorter and the frequency of SOREMPs was higher than in C condition. When we examine young adults, we should exclude insufficient sleep syndrome carefully from other hypersomnias as narcolepsy.

PO-2-102

VIGILANT ATTENTION IN SLEEP WAKE DISORDERS: NORM VALUES ON THE PSYCHOMOTOR VIGILANCE TASK (PVT)

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The Psychomotor Vigilance Test (PVT) is one of the leading assays of vigilant attention in sleep research and highly sensitive to the effects of sleep loss. Rather little is known about PVT performance in patients suffering from sleep-wake disorders. With the present study, we aimed at evaluating the use of PVT in clinical routine in a sleep laboratory. The objective was to examine the patterns of PVT outcomes in patients with different sleep-wake disorders and in healthy control subjects, and interpret these patterns in relation to other tests of sleep and wakefulness.

We compared PVT data of 356 patients and 67 healthy control subjects. Patients were diagnosed with one of the following sleep-wake disorders: narcolepsy with cataplexy, behaviorally induced insufficient sleep syndrome (BIISS), hypersomnia, fatigue, sleep related movement disorder (SRMD), central and obstructive sleep apnea, REM-sleep parasomnia and insomnia. The following PVT outcomes were analysed: median reaction time, lapses (>500 ms), false starts (<100 ms) and variability (interpercentile range between 10th and 90th percentile). PVT performance was significantly better in healthy controls than in patients with sleep-wake disorders. Furthermore, we found additional differences between specific sleep-wake disorders. Based on the comparison between patients and healthy controls we suggest cut-offs of 270 ms for median reaction time, 1 for lapses and 120 ms for variability. There was a correlation between PVT and Steer Clear, but correlations between PVT and MSLT/MWT were weak to absent. As there were influences of age, sex, major depression and Parkinson disease on PVT results, they must be interpreted in combination with other clinical findings and sleepiness tests.

In conclusion, our study quantified the differences in vigilance performance between patients with sleep-wake disorders and healthy controls. It is the first to publish cut-offs for the distinction between normal and impaired vigilant attention measured with PVT.

PO-2-103

DETECTING DETERIORATED PERFORMANCE USING PERCENTAGE OF EYELID CLOSURE TIME DURING OXFORD SLEEP RESISTANCE TESTS

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Several researchers have investigated the relation between vigilance and ocular variables such as saccade, slow eye movement, pupil, blink, or eyelid closure. This study was undertaken to find the most effective indicator among these ocular variables for evaluating short-term (1 min) fluctuation of vigilance, and to investigate the ability of the most effective ocular variable for predicting deteriorated vigilance during behavioral maintenance of the wakefulness test (Oxford sleep resistance test: OSLER test). Nine healthy volunteers (two women, 19–30 years old, 23.4 ± 3.9 years old) participated in this study. Ocular variables were recorded during the OSLER test at 10 A.M. and 2 P.M. before and after partial sleep deprivation (4 hr sleep). The periods during the OSLER test were divided into 1 min epochs. Each epoch was classified according to the number of consecutive missed responses. Decreased blink frequency and pupil diameter as well as increased PERCLOS (percentage of eyelid closure time) and slow eye movement were observed as the consecutive missed responses increased. Among these variables, PERCLOS showed the highest ability to detect occurrences of any missed responses and three or more consecutive missed responses. Our study also found that a missed response seldom occurred (0.2 ± 0.2 / 20 trial / min) when the PERCLOS was lower than 11.5% per 1 min. Our research has added a new finding: PERCLOS is the most effective indicator for detecting deteriorated vigilance among the ocular variables. Maintaining PERCLOS below 11.5% might be effective for preventing deteriorated vigilance.

PO-2-104

ELECTROCARDIOGRAM-BASED MEASURE OF SLEEP STATE INSTABILITY PREDICTS SLOWER REACTION TIME IN PSYCHOMOTOR VIGILANCE TASK: A PRELIMINARY STUDY

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Introduction: Numerous clinical and experimental data have demonstrated that disrupted or diminished sleep leads to the impairment in cognition and psychomotor vigilance. Therefore, good quality and adequate amount of sleep is essential to the waking cognitive performance. Early attempts to understand the effect of sleep quality on cognition were based on subjective scales such as Pittsburgh Sleep Quality index or insomnia symptoms. In this study, we adopted the electrocardiogram (ECG)-based cardiopulmonary coupling (CPC) analysis as

an objective index of sleep quality, and its effect on the psychomotor vigilance were investigated.
Methods: We performed CPC analysis on ECG signal derived from home portable sleep study of 401 participants (aged 56.3 ± 7.1, 69% male) of ongoing Korean Genome and Epidemiology Study (KoGES). Sleep state stability was determined in terms of high-, low-, and very low frequency coupling between the heart rate and the respiration (frequency, Hz.), and namely, spectrographic measure of very frequency coupling (VLFC) was used as an index of wakeful/REM sleep slate. Psychomotor vigilant task (PVT) was administered in the morning (8:00 AM to noon) as a measure of daytime cognitive function, and the effect of CPC parameters and conventional sleep structures on psychomotor vigilance was investigated.
Results: Reversed PVT mean reaction time (1/mean reaction time, msec-1), was negatively associated with VLFC ($p = 0.005$). With age, sex, body mass index, education, apnea-hypopnea index, sleep duration, Becks Depression Index, and Epworth Sleepiness Scale (ESS) adjusted, VLFC remained an independent predictor of slower mean reaction time ($p = 0.003$) in a step-wise multiple linear regression analysis ($R2 = 0.18$, $p =< .0001$).
Conclusion: CPC parameters as the objective metrics of sleep quality were closely related to the psychomotor vigilance. In particular, VLFC (REM/wakeful state) has a prominent impact on vigilant attention.

PO-2-105

THE PATTERN OF BREAST BREATH DURING SLEEP ONSET PERIOD

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Respiratory movements during wakefulness is predominant abdominal, however that changes to a pattern of breast dominance in sleep. The purpose of the present study was to investigate the pattern of breast breath in sleep onset period with a sheet sleep sensor.
Sleep was recorded in 8 healthy college students (mean age = 21.0 yr., SD = 0.76) who slept for 4 consecutive nights in their home. Subjects were given a thorough explanation of the protocol and provided written informed consent prior to participation in the study. Sleep latency was calculated using a sheet sleep sensor (SANYO Electric Co., Ltd.) and Actigraph (A. M. I). Both measuring devices are nonconstraining and noninvasive. A short sleep latency day (mean = 20.9 minutes) and long sleep latency day (mean = 63.0 minutes) were compared with the quality of sleep, subjective sleep and number of breast respiration.
Result of the present study demonstrated that a short sleep latency day led to a significantly increased total sleep time. On a short sleep latency day, subjects experienced easily with falling asleep and displayed maintaining sleep, according to the Oguri – Shirakawa – Azumi (OSA) sleep feeling questionnaire. The number of breast breath during sleep onset in the short sleep latency day was many than that of long sleep latency day. An increased number of breast breath was also shown 30 minutes after sleep onset. These results suggest that measuring the number of breast breaths may constitute a new way to assess sleep quality.

PO-2-106

NORMALIZATION AND CASE-SPECIFIC DEFINITION OF EEG BANDS IN SPECTROGRAMS FOR IMPROVING VISUALIZATION AND AUTOMATED SCORING OF SLEEP STUDIES

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EEG spectrograms display a grid where columns represent time epochs and rows represent frequency bins. The intensity of each cell in the grid denotes the FFT amplitude of the EEG signal at given time and frequency. These graphs are useful for all-night recording visualization and are remarkably helpful as a first step for automating state and stage assignments. We propose here a mathematical treatment based on spectrogram normalization to improve visualization and on subject-specific frequency band definition to improve automated scoring. A single EEG channel, typically C3M1, undergoes FFT processing according to Welch method using 4 s Hanning tapered windows with 50% overlapping. Frequencies over 30 Hz are discarded. The resulting spectrogram is log scaled, aggregated in 30-second epoch averages and normalized for zero mean and unitary variance in each frequency bin. Spectrogram normalization emphasizes the relative distribution of bands throughout sleep time and enhances particularly the descriptive value of higher frequency bands. From the normalized spectrograms, a frequency covariance matrix is computed and displayed. Four bands corresponding to delta, alpha, sigma and beta become evident. The highly contrasted limits between these bands are obtained by locating the extremes of a standard central-difference-derivative estimation method. Theta band is operationally defined in rapport to the lower alpha band. Band activities are calculated by averaging the normalized spectrogram over each band range for each epoch, and then normalizing the results in turn. Activities are used, by themselves or in combinations such as the theta-alpha difference, as the key features that optimize clustering for state segregation (Vivaldi EA et al., Conf Proc IEEE Eng Med Biol Soc 2010:280–3, 2010). Spectrogram normalization provides a compactly informative all-encompassing view of sleep states and their transitions, employing one-channel EEG data. The frequency covariance matrix allows tailoring the band limits to each case.

PO-2-107

THE DETECTION OF EEG FEATURE OF SLEEP STAGE 2 BY A NEW SCORING SYSTEM

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We have reported that the recuperative power of a daytime short nap depends on the length of sleep stage 2 (Hayashi et al., 2005). However, it is not clear what the quality of the nap has recuperative power. Then, we tried to make a new scoring system to classify the quality of sleep stage 2, referred to the 5s-EEG stages of hypnagogic state (Hori et al., 1994) and REM sleep (Takahara et al., 2006). Eleven healthy university students (9 female and 3male; 21 to 24 yr.) participated in the study. They took a nap for 1 hour from 14:00 in a bed (n = 3) or in a reclining seat (n = 9). Sleep stages were scored every 20s by the standard procedure, and then C3-EEG during sleep stage 2 was divided into 5s and was rescored. EEG stages of sleep stage 2 could be scored as the 5s-epochs composed of more than 50% of the following EEG wave forms. 1) Flattening: suppressed waves with the amplitudes of less than

20μV. 2) Theta: theta waves with the frequencies of 4 to 7Hz and amplitudes of more than 20μV. 3) Spindle: spindles with duration of more than 0.5s or with composed of more than 6 consecutive waves. 4) K-complex: the appearance of delta waves with frequency of less than 4Hz followed by positive peak of which amplitude of negative and positive peak is more than 200μV. 5) Small delta: delta waves of 2 to 4 Hz with the amplitudes of more than 20μV or those of 0.5 to 2 Hz with the amplitudes of less than 75μV. 6) Large delta: delta waves of 0.5 to 2Hz with the amplitudes of more than 75μV. And 7) Mixed: the epoch with no more than 50% of any EEG waves listed above.

PO-2-108

AN ATTEMPT OF SLEEP MONITORING USING A NON-INVASIVE AND AMBULATORY CARDIAC MEASUREMENT ON A BEAT-BY-BEAT BASIS

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Sleep monitoring has been drastically advanced in these two or three decades. Especially, importance of screening and evaluation of sleep apnea syndrome (SAS) has enhanced polysomnography. Besides of them, we have been developed a non-invasive cardiovascular measurement. In this abstract, we would like to report our newly developed a wearable cardiovascular monitoring monitor and its application to physiological measurement during sleep.

The developed non-invasive wearable cardiovascular monitor includes beat-by-beat continuous and non-invasive blood pressure (BP) and cardiac output (CO) simultaneous measurement whose measurement methodologies are based on volume-compensation method and transthoracic admittance plethysmograph method. And ambulatory monitoring during daily life using the monitor has been reported [1]. In this time, continuous monitoring during sleep was attempted. Continuous cardiovascular measurements were done on seven healthy male subjects (yrs. 22–24). In the measurement, the subject was attached the cardiovascular monitor and asked to work at his desk and sleep after the work. The five of seven subjects were slept during the experiment. The study was approved by a local ethical committee.

As results, BP and CO were able to be measured during the measurement (including their sleep period) and total peripheral resistance was derived from BP and CO then found that BP was clearly decreased in sleep period but fluctuated as wakefulness period.Moreover, hemodynamics parameters HP (hemodynamic profile) and CO (compensation deficit) proposed by Gregg [2] were obtained and information of relative myocardial-and-vascular balance during sleep was evaluated. After this, we'll try to analyze baroreflex sensitivity during sleep using measured data.

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PO-2-109

INVESTIGATION OF SLEEP STAGE IDENTIFYING ALGORITHM FOR SLEEP MONITORING SYSTEM BY DETECTING HUMAN ORIGINATED LOW-FREQUENCY SIGNAL IN UNRESTRAINT WAY

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We are developing sleep state monitoring system detecting human originated low-frequency signals in unrestraint way. We have been aiming to establish quantitative sleep evaluation by means of the signal processing of human originated low-frequency vibration signals including heartbeat, breathing and body movement which are detected by using a sheet-like vibratory sensor, however the improvement of the accuracy to identify the sleep stages is one of the challenges of the system. In this study, we used the signals which were recorded by Polysomnography (PSG) and attempted linear discriminant analysis using several pre-calculated characteristics derived from time and spectrum analysis of heartbeat fluctuations, variability of abdominal breathing and frequency of body movement. Then we evaluated concordance rate between our results and clinical diagnostic solutions by R&K method. Furthermore, we tried SVM which is one of nonlinear discriminant analyses, and compared the result with that of linear analysis. As the result, under a giving condition and in the case of stage recongnition in four stages, we obtained the concordance rate of around 50% by linear method. In contrast, by nonlinear method, we obtained above 70%. It suggested that the derived algorithm is useful for improvement of accuracy.

PO-2-110

RELATIONS BETWEEN SLEEP ACTIVITY INDICES AND VERRAN AND SNYDER-HALPERN (VSH) SLEEP SCALE USING STATISTICAL ANALYSIS

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Sleep activity indices derived from wearable activity sensors such as actigraphy are regarded as reliable indicators to represent objective sleep quality, whereas the Verran and Snyder-Halpern (VSH) sleep scale are regarded as a reliable tool to represent subjective sleep quality. The relations between the sleep activity indices and the VSH sleep scale score using statistical analysis are investigated in this study. The participants are instructed to wear an actigraphy for measuring the acceleration signals produced by body activities during their sleep. The sleep activity indices derived from the acceleration signals include: 1) the amount of activity during all night sleep, 2) the average amount of activity of each hour during sleep, 3) the amount of activity in the first ninety minutes after lying on the bed, and 4) the amount of activity whose counts are larger than 50. The VSH sleep scale employed in our study includes three subscales: 1) disturbance, 2) effectiveness, and 3) supplementation of sleep. Several items are included in each subscale and the score of each item ranges from 0 to 100. The Spearman rank-order correlation is utilized in the relationship analysis between the

sleep activity indices and the VSH sleep scale. The statistical analysis results show that three of the sleep activity indices have negative correlation to that of the disturbance and effectiveness of sleep ($p < 0.05$). These three sleep activity indices are: 1) the amount of activity during all night sleep, 2) the average amount of activity of each hour during sleep, and 3) the amount of activity whose counts are larger than 50.

PO-2-111

USING A WEARABLE PHYSICAL ACTIVITY SENSOR SYSTEM FOR SLEEP/WAKE STATES DETECTION

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Low activity levels and prolonged motionlessness are two main features of sleep. In clinical practice, polysomnographic (PSG) recordings are a gold standard for sleep assessment. However, the PSG is expansive and not suitable for use in home environment. This paper introduces a wearable physical activity sensor system for monitoring physical activity during sleep. The portable watch-type sensor modules are placed on wrist and ankle simultaneously and the epoch-by-epoch comparison of sleep/wake states to PSG is made. In our validation test, a total of seventeen normal subjects (13 males and 4 females) aged between 19 and 30 years are included. The subjects are asked to sleep in our sleep laboratory for two consecutive nights and the first night is for environment adaptation to avoid the first night effect caused by the laboratory environment. The all-night PSG recordings are scored visually according to the AASM rule by experienced sleep scorers. The experiment results show that the overall sensitivity and specificity for sleep detection are 90.9% and 64.4%, and the overall accuracy is 88.9% when we only use the wrist data for analysis. However, when we use both the data from the wrist and ankle sensors, the overall sensitivity and specificity to for sleep detection are 89.4% and 69.7%, and the overall accuracy is 88.0%. The specificity can be improved for more than 5.3% if the data from both wrist and ankle are used for detecting sleep/wakefulness. We conclude that the wearable physical activity sensor system provides a good accurate detection of sleep/ wakefulness on an epoch-by-epoch basis.

PO-2-112

CAN HANDHELD DEVICE ACCURATELY MEASURE SLEEP PARAMETERS? COMPARISON OF ACTIGRAPH, SLEEP DIARY AND ELECTRONIC SLEEP DIARY APPLICATION

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Introduction: Development and validation of user-friendly portable sleep recording devices have important implications in sleep research and education. The aim of the study was to report rates of agreement between actigraphy (ACT), manuscript sleep diary (SD) and an electronic sleep diary (ESD) application for handheld device.
Method: 38 healthy adults (29 ± 9 yrs; 45% women) recorded sleep data for 6 to 7 days. Participants wore wrist actigraph and used an application for handheld device (Scextan) set on one-minute intervals. For each one-minute epoch, Sadeh's algorithm was used to score actigraph recordings as wake or sleep. Nineteen participants also recorded data from a manuscript sleep diary at 15-minute intervals. Total sleep time (TST), wake after sleep onset (WASO), and sleep efficiency (SE) were derived from the three methods. Sleep onset latency (SOL) was determined from ESD bedtime information to ACT and ESD sleep onset.
Results: Inter-group deviation analysis between ACT and ESD did not show statistical differences (*t* test). TST analysis revealed better correlation (Spearman) and agreement rate (using the Bland and Altman method) for ACT *vs* ESD (bias = −6.2 min; SD = 10.9; rho = 0.93; $p < 0.0001$), than for ACT *vs* SD (bias = −5.1 min; SD = 30.1; rho = 0,70; $p < 0.0001$). SOL analysis showed high correlation and good agreement between ACT and ESD (bias = 3.7 min; SD = 10.1; rho = 0.80; $p < 0.0001$). WASO correlation coefficient was low for ACT *vs* ESD (rho = 0.14) as for ACT *vs* SD (rho = 0,32). SE analysis also revealed poor correlation for ACT *vs* ESD (rho = 0,18) and for ACT *vs* SD (rho = 0,25).
Conclusion: Electronic sleep diary is a valid method to measure TST in healthy subjects and is more accurate than a manuscript sleep diary. SOL measurement appears to be the most efficient for short latencies. We agree that subjective assessments need to be supplemented by the use of an accelerometer to detect awakenings during sleep. Nevertheless, electronic sleep diary application on handheld device could offer more educational facilities than manuscript sleep diary and remains cheaper than the actigraph.

PO-2-113

A LONG-TERM SLEEP MONITORING OF THE ELDERLY WITH DEMENTIA USING A NONWEAR ACTIGRAPHY DEVICE (NEMURI SCAN)

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OBJECTIVE: Considering day-to-day and week-to-week variability, it is reported that a valuable improvement in the reliability of actigraphic sleep evaluation can be obtained by increasing the number of recording nights. However, few studies record sleep of persons with dementia using wrist acitgarphy (WA) devices over several weeks. Nonwear devices are better suited for a long-term sleep monitoring of the elderly with dementia (ED) than wear-type devices such as WA. A nonwear actigraphy (NWA: NEMURI SCAN, Kogure et al., J Physiol Anthropol 2011) device placed under a mattress that can score sleep/wake and in-bed/out-of-bed from body motion in bed was recently developed. We conducted a long-term sleep monitoring of ED using the NWA device.
METHODS: NWA recordings for 12–14 days were made for 62 ED participants (18 men, 44 women), aged 70–95 years (average 84.2 ± 5.6). We calculated sleep parameters by NWA and investigated the in-bed/out-of-bed regularities. Ethical approval was obtained prior to the study.
RESULTS: The data containing unidentified into-bed-time or arise-time (5 participants) were excluded. As a result, we analyzed data of 57 ED participants (17 men, 40 women), aged 70–95 years (84.3 ± 5.7). Mean values of total sleep time, sleep latency, sleep efficiency, and wake time after sleep onset were 488 min (range, 305–692), 20.9 min (8.1–133), 77.5% (51.9–94.4), 114 min (20–270). Mean values of time in bed, into-bed-time, and arise-time were 630 min (472–742), 20:14 (19:10–22:08), and 6:42 (5:02–8:10). Mean values of total out-of-bed time and number of out-of-bed were 15.4 min (0–76.8) and 2.9 (0–17.1). Each participant's range of total sleep time was 69–541 min (219 ± 110). The

in-bed/out-of-bed regularities were observed in 41.7% of participants who go out of bed at least once a sleep time.
CONCLUSION: Sleep of ED differed greatly in individuals and sleep parameters of ED varied greatly from day to day. It is expected that the NWA device, a non-wear device for scoring sleep/wake and in-bed/out-of-bed, enables the convenient sleep-related evaluation over several months or years.

PO-2-114

DEVELOPMENT OF A NETWORK SYSTEM FOR LONG-TERM SLEEP MONITORING AT HOME AND ITS APPLICATION TO MEDICAL CARE FOR CARDIOVASCULAR DISEASE

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The demand for less-burdensome daily sleep monitoring at home has been increasingly raised as an effective scheme for early diagnosis and treatment of sleep apnea syndrome: SAS. Moreover, there is a need to monitor such sleep status of patients having chronic cardiovascular disease requiring acute life support or chronic therapies. Commercially available devices for sleep monitoring at hospital are cumbersome in terms of attachments of biological sensors and operations of the devices. From these view points, we developed the under-pillow type and the sheet-type sleep monitoring systems without any attachment of biological sensors and operations of devices, showing its usefulness for simple screening of SAS. Furthermore in this study, we have newly developed a fully automated network system for long-term sleep monitoring at home combined with the under-pillow type and the sheet-type pressure sensors. The system can monitor the pulse and the respiration in bed during daily living, using the pillow-type sensor. Moreover, the contact pressure distribution can be also detected to evaluate not only sleep condition such as the body position, but also the risk of the bedsore, using the sheet-type multipoint pressure sensor. These data are fully automatically transferred to the server located at hospital and the medical staff can check the daily sleep status of the patients using a web application in real time. In six patients with chronic cardiovascular disease, the daily sleep statuses such as the pulse rate, respiration rate and the body position were successfully measured in the home of patients using the system. The results demonstrated that the system appears useful for less-burdensome monitor of daily sleep condition in the patient with chronic cardiovascular disease.

PO-2-115

HIGH RECALL ACTIGRAPHIC SLEEP/WAKE DETECTION BASED ON STATISTICAL CLASSIFICATION

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Introduction: Many existing algorithms for actigraphic sleep/wake detection are based on single feature regression, yet various research (de Souza, 2003) find that such methods successfully identify only 34% of all wake epoches. We propose using a statistical classifier to combine a larger set of features to improve sleep/wake detection, and evaluate this using PSG-generated labels.
Methods: 15 healthy adults underwent a night of full PSG while wearing a triaxial accelerometer ("Life Microscope" life recorder, Hitachi Ltd.) on their left wrist. The PSG data was scored in 30 second epoches according to the R&K sleep stage scale. Our proposed method has two stages:
(1) Training: periods of body movement during sleep are identified by an acceleration threshold. A feature vector is calculated for each period from a set of 115 features, such as zero-crossing count and maximum scalar power. The period is associated with a target class "Wake" or "Sleep" depending on its cooccurrence with a wake stage, to which a Random Forest classifier is trained on.
(2) Prediction: the classifier is applied against all movement periods, and any 1 minute epoche that clips a "Wake" period is predicted as a "Wake" epoche.

Results and Discussion: Per-epoche sensitivity and specificity of sleep detection was evaluated by cross validation. The proposed method maintained similar sensitivity to Cole (Cole: 99%, Proposed: 96%), but with higher specificity (Cole: 34%, Proposed: 59%). We thus conclude that usage of a larger feature set is effective in sleep/wake detection.
We observe that the most important feature was the average power, in contrast to the zero-crossing count usually used as per Cole. This suggests that single feature regression can also benefit from a more informed choice of features.

PO-2-116

AGREEMENT OF ACTIGRAPHIC SLEEP/WAKE STATES BETWEEN ACTIWATCH AND ACTIGRAPH

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Purpose: The activity monitoring is used to help sleep study. However, the methods of measurements and algorisms used to evaluate sleep/wake state are various. Those are different from polysomnography (PSG). Then, in this study, agreement of actigraphic sleep/wake states between Actiwatch (AW, Mini-Mitter Co., Inc., Bend, Ore) and Actigraph (AG, Ambulatory Monitoring Inc., Ardsley, NY), and agreement between each equipment and PSG were examined.
Methods: Subjects were healthy four females and three males (mean age: 21.7 years). Their wrist-activity was monitored by AW and AG simultaneously for 48 hours in two conditions that were control (seven-hour sleep) and partial sleep deprivation (three-hour sleep). And PSG were conducted on each second night. For each minute, actigraphic sleep/wake state was calculated by each recommended method and polysomnographic sleep stage was scored by the standard method. In each method, sleep/wake state was assumed as 0/1. Then for each minute, AW-PSG, AG-PSG and AW-AG were calculated ("0" means the judgement was agreed).
Results:
(1) The agreement rate between AW and AG sleep/wake states was low when their activity was moderate range.
(2) In the partial sleep deprivation, the agreement rate between AW and PSG was significantly lower than that between AG and PSG. As compared with AG, AW more overestimated sleep during sleep deprivation and wake during sleep after the deprivation.

Conclusion:
(1) The agreement rate between the two devices' sleep/wake states was low when activity is moderate. There is no help for it because actigraphic sleep/wake state is based on the amount of activity.
(2) Misjudgments by AW were more than that by AG. To solve this problem, improvements of sensitivity and algorism for sleep/wake state should be done for AW.

PO-2-117

ESTIMATING SLEEP CYCLE USING OCCURRENCE RATE OF BODY MOVEMENTS

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Polysomnography (PSG) is an objective means of evaluating sleep and waking states that uses brain waves, eye movements, and electromyograms. However, because this method requires the subject to wear a large number of electrodes, at-home measurements of sleep and waking states remain difficult. Several studies have shown that the occurrence rate of body movement closely relates to sleep stage, and that this occurrence rate decreases as the sleep stage deepens. Thus, we devised a new method for estimating the sleep cycle that uses the occurrence rate of body movement. To make measurements less cumbersome for subjects, body movement was measured using an infrared motion sensor. In the present study, sleep stage determined by PSG as the main physiology index was compared to the values estimated by measuring body movement. The stages of sleep follow the international standards of Rechtschaffen & Kales for sleep stage. Sixteen healthy, non-medicated subjects (13 males, 3 females; 20–23 years old) participated in the present study. All subjects provided written informed consent prior to participation in the study.
The occurrence rate of body movement is an important element in the estimation of sleep stages. Thus, in the present study, body movement density (BMD) is defined as the number of body movements that occur in 30-min intervals and is used as a value for evaluating body movement. Results show that BMD did not directly correlate with sleep stages. However, transitions between sleep stages within the sleep cycle and BMD were synchronous. Therefore, estimating the changes in sleep stage is possible using BMD. Moreover, using BMD in this manner, the sleep cycle can be estimated without any additional information.
The quality of sleep is related to the sleep cycle, and the present results shows that the sleep cycle can be estimated using BMD. While there is a trade-off between accuracy and convenience using this method, the long-term goal of this study is to develop a method to easily measure sleep stage at home. From this perspective, measurements of BMD are both convenient and sufficiently accurate.

PO-2-118

PREDICTION MODEL OF LIGHT-INDUCED MELATONIN SUPPRESSION

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The prediction method of melatonin suppression values was based on previous studies related to melatonin suppression and pupil constriction. Estimated values that considered pupil constriction were larger than the actual suppression values. We focused on the pupil constriction and its correction factor to interpret the action spectrum for the properties of the melatonin suppression model. When the correction factor was used to modify the model, actual suppression values were almost completely predictable. These factors suggest that it might be possible to explain the indescribable results.

PO-2-119

SLEEP EDUCATION BY USING SELF-HELP TREATMENT FOR JUNIOR HIGH SCHOOL STUDENTS IN JAPAN.

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INTRODUCTION: knowledge of sleep related to modification of lifestyle (Gallasch et al., 2007). Brief cognitive-behavioral method (self-checking and sleep diary for 2 week) is effective on sleep in high school students (Tanaka, 2008). The purpose of this study was to examine the effects of sleep education by using brief cognitive-behavioral method (knowledge, self help treatment) for Junior high school students. Additionally, examine effective behaviors for ensuring of sleep, preventing night type lifestyle.
METHODS: Sleep education by using self-help treatment carried out for 10 days for 318 (age 13, 14, 15) students who gave informed consent. Sleep instructors lecture them about sleep hygiene using text, 10 questions relation to sleep carried out pre and post lecture. In this program the self-checking for daily life-habits, goal setting for behavioral changes and self-monitoring were used by sleep diary. Instructor asked student to check their own life-habits and to select one target behavior from it. The questionnaire involving lifestyle was used to assess the effects of program.
RESULTS& DISCUSSION: After ten days of the sleep education by using self-help treatment bed time changed to earlier. The difference of bed time between weekday and holiday changed to shorten, significantly ($p < 0.05$). Sleep latency, sleepiness of day significantly improved. These show that treatment is effective to prevent night type lifestyle and to reduce irregular sleep-wake patterns. Lifestyle, regular sleep-wake patterns, such as reduce the difference of wake up time of weekday and holiday below 2hour, exposing sunlight in the morning, having every morning breakfast, not taking the nap after evening, relaxation before bed times occupy important position to improvement of ensuring of sleep times, preventing night type lifestyle. Especially, not taking the nap after evening effected on initiating sleep, preventing night type lifestyle, feelings of wakening. Present results suggest sleep education by using self-help treatment improve sleep, arousal levels of daytime for students.

PO-2-120

THERAPEUTIC OUTCOME BY TWO-MONTHS INTENSIVE CIRCADIAN RHYTHM TREATMENTS IN JAPANESE CHILDREN AND ADOLESCENTS WITH CHRONIC FATIGUE

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Objectives: We have started to treat patients with chronic fatigue at new pediatric medical research center for sleep and developmental disorder since April 2009. Here we show the therapeutic outcome of our first year trial.
Methods: 30 patients (15 boys and 15 girls, age 11 to 25) with chronic fatigue induced by sleep deprivation were admitted in the first year of our center. All patients were treated for 8 weeks with bright light therapy, thermal therapy, medication, cognitive behavioral therapy and lifestyle teaching. Self-sleep-logs (S-log) have been recorded during hospitalization. 48 hr core body temperature (CBT) monitoring was performed at the beginning and the end of therapy. Delay of circadian rhythm (D-CBT; >= 60 min.), poor daily variation (CBT amplitude <1.0 degree centigrade) and totally high CBT (1.0 degree centigrade higher than control) were detected in CBT recordings. Long total sleep time (L-TST; >= 10 hr), delayed sleep phase (D-SP; sleep onset later than 24:00), irregularity of sleep onset and offset (I-SOs; larger variation than 90 min.) and sleep segmentation (segmented more than 7 days per 2 weeks) were also detected in S-log recordings. With or without these factors were compared between the beginning and the end of therapy using fisher's exact test.
Results: D-CBT ($p < 0.01$), L-TST ($p < 0.0001$), D-SP ($p < 0.05$) and I-SOs ($p < 0.0001$) were significantly improved at the end of therapy.
Conclusion: Our intensive treatments were effective to improve circadian rhythm. However, recoveries of other chronic fatigue related symptoms and poor performances were insufficient at the time of discharge. Recovery from sleep disturbance is not the goal but the first stage of improvement for the patients with chronic fatigue. From this point of view, more clinical trials will be needed.

PO-2-121

ASSOCIATION BETWEEN MORNINGNESS-EVENINGNESS CHRONOTYPE, SLEEP DISTURBANCES AND MENTAL HEALTH IN THE UNIVERSITY FRESHMEN IN HONG KONG

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Objective: There has been a close link between circadian disruption and a vulnerability to psychopathology. The aim of the current study was to explore the relationships among morningness-eveningness, nocturnal sleep disturbances and mental health in first-year university students in Hong Kong.
Methods: A battery of questionnaires was distributed to all the first-year university students. Study inventories included a sleep questionnaire, Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), Morningness and Eveningness Questionnaire (r-MEQ) and General Health Questionnaires (GHQ-12).
Results: In total, 1207 students (response rate: 58.5%, mean age: 18.9 ± 1.1 years; male 57.9%) completed the questionnaires. The prevalence of morning-, intermediate-, and evening-type was 8.5%, 63.7% and 27.8%, respectively. As compared to the subjects of intermediate-type, those evening-type had shorter sleep duration during weekdays (7.2 ± 1.2 vs. 6.5 ± 1.5 hours, $p < 0.001$), and scored significantly higher on PSQI (5.5 ± 2.1 vs. 6.3 ± 2.1, $p < 0.001$) and ESS (8.4 ± 3.6 vs. 9.4 ± 3.9, $p < 0.001$). More subjects of evening-type reported insomnia disturbances (15.4% vs. 14.9% vs. 9.5%, $p < 0.01$) and alcohol drinking (27.2% vs. 18.6% vs. 13.9%, $p < 0.01$) than their peers of intermediate- and morning-type. Eveningness was associated with minor psychiatric disturbances after adjusting for age, gender, frequent insomnia and nightmares [Odds ratio = 1.5 (95% C.I. 1.1–2.1)].
Conclusion: Eveningness was associated with insomnia, mental disturbances and alcohol use in university students. Interventional program should address circadian disruption in relation to psychiatric disturbances in university students. Future prospective studies should be conducted to investigate the stability of chronotypes and its association with future development of sleep disturbances and psychopathology.

PO-2-122

COMPARATIVE STUDY ON SLEEP SATISFACTION AND QUALITY OF LIFE IN HEALTHY STUDENTS BETWEEN JAPAN AND THAILAND

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Study objective: The 24 hours-commercialization is accelerated in the Japanese modern society. Some reports have shown that the quality of life (QOL) is positively correlated with the quality of sleep. QOL is influenced from whether the quality of sleep is enough. There have been several reports on the relationship between QOL and sleep quality for hospitalized patients. There are few reports in healthy population. This study aims to compare the QOL and sleep quality between Japan and Thailand in healthy students.
Participants and Method: The integrated questionnaire was administered to 424 students (Japan 198, Thailand 226) and included 10-items Pittsburgh sleep quality index (PSQI) and 26-items WHOQOL-BREF (WHOQOL). A cross sectional statistical analysis was performed.
Result: The average sleep hours were 6.35 h in Japan and 6.55 h in Thailand. The average PSQI score was significantly higher in Thailand than in Japan ($p < 0.001$). Several scores as follows were significantly worse in Thailand than in Japan: longer sleep latency, worse habitual sleep efficiency, more frequent sleep-onset and -offset disturbance and more frequent daytime dysfunction (respectively $p < 0.05$). Additionally, participants in Thailand tended to use sleeping pills more frequently than Japanese ones ($p = 0.05$). On the other hand, the average score of QOL was higher in Thailand than in Japan ($p < 0.001$). In all domains including physical health, psychological, social relationship, environment and global, scores were higher in Thailand than in Japan ($p < 0.001$). It meant that QOL in Thailand was better than in Japan.
Discussion and Conclusion: PSQI was better in Japan, whereas QOL was worse in Japan than in Thailand. This suggests that Japanese sleep quality is better than Thailand participants, although Japanese students are little satisfied in their life. This replicates the difference between Japan and Thailand in the relationship between sleep quality and QOL. Furthermore, some difference in life style might be related the relationship.

PO-2-123

SLEEP BEHAVIOR AND RISK FACTORS FOR DETERIORATION OF SLEEP PATTERNS AMONG JAPANESE MIDDLE-SCHOOL STUDENTS

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Background: Many studies have shown that sleep deprivation of may promote both lifestyle-related diseases and mental illness. To a large extent sleep behavior is affected by the environment in childhood and adolescence.
Purpose: To determine the current sleep behavior of teenagers and to clarify risk factors, we investigated sleep patterns and patterns of spending time in various activities among middle-school students in Kyoto city.
Subjects and methods: Subjects were 1545 students at 13 public middle-schools in Kyoto city. The questionnaire included sleep pattern, smoking experience, drinking experience, diet pattern, study habits, watching TV, Internet usage and frequency of visiting convenience stores (CS). We analyzed how these behaviors were related to sleep patterns.
Results: Valid responses were obtained from 818 boys and 721 girls. Mean lights-off time, wake-up time and sleep duration were 7:30 AM, 11:13 PM, 6.9 hr. 4.2% of subjects slept less than 6 hours. Boys slept significantly longer than girls ($p < 0.01$): 6.9 hr versus 6.8 hr, because boys turned off the lights earlier than girls (11:06 PM versus 23:19 PM) and woke up later (7:39 AM versus 7:21 AM). Subjects who skipped breakfast, ate late at night, spent long hours to use the Internet, did not study, had experience with drinking and visited convenience stores frequently, slept for shorter periods ($p < 0.01$). Watching TV for longer periods, reading books, experience with smoking and belonging to school clubs did not show any association with sleep patterns.
Discussion: Sleep deprivation among middle-school students in Kyoto city was extremely serious. The situation is likely to influence not only current health problems but also promote health problems in future. Skipping breakfast might be due to sleep deprivation because eating at midnight or short sleep contribute to reducing hunger in the morning. Unlike skipping breakfast, visiting CSs and long periods of Internet use have the potential to deteriorate sleep patterns because these activities are accessible 24 hr a day and are attractive to adolescents.

PO-2-124

SLEEP EDUCATION BY USING COGNITIVE BEHAVIORAL METHOD FOR TEACHERS OF JUNIOR HIGH SCHOOL IN JAPAN

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INTRODUCTION: Recently, the deterioration of teacher's health, volition is serious relation with the aggravation of an educational problem. Brief cognitive-behavioral method (self-checking for target-behavior and sleep diary for 2 week) is effective in improving sleep quality for local residents or high school students (Tanaka, 2007). The purpose of this study was to examine the effects of sleep education by using Brief Cognitive-behavioral method (knowledge of sleep, self-checking for target-behavior and sleep diary for two weeks), self-help treatment.
METOD: Sleep education or sleep education by using self-help treatment carried out for the 22 teachers in junior high schools who gave informed consent. In this program the self-checking for daily life-habits, goal setting for behavioral changes and self-monitoring were used as behavioral modification techniques, it ran for each 2 week in 4 week. Each teacher practiced two conditions (only sleep education condition, sleep education with self-help treatment condition) with crossover design. They were lectured about sleep hygiene. And then, asked participants to check their own life-habits and to select three target behaviors from it. The questionnaire involving lifestyle and sleep health was used to assess the effects of program. Furthermore, compliance of targets behavioral habits was assessed.
RESULTS & DISCUSSION: After the sleep management for two weeks, sleep and fatigue significantly improved. Furthermore, feelings of wakening, volition improved ($p < 0.05$). Sleep education with self-help treatment condition was effective compared to only sleep education condition, significantly. Sleep and volition are related to the life habits such as 1) Getting up in the every morning approximately decided time, 2) Don't take a nap after go home, 3) Going to bed by 0:00 a.m., 4) Having a regular sleeping time, 5) Relaxing before bed time, 6) Getting to bed after becoming sleepy, 7) Don't worry in bed. Present results suggest sleep education by using brief cognitive-behavioral method improve sleep, fatigue, volition for teachers.

PO-2-127

A NOVEL CHILD SLEEP SCREENING QUESTIONNAIRE: CHILD AND ADOLESCENT SLEEP CHECKLIST (CASC)

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Background: As characteristics of sleep changes dramatically both in quality and in quantity during childhood, assessment of sleep using a single questionnaire for wide range of ages requires special considerations.
Objectives: The aim of this study was to develop and validate a sleep questionnaire for the screening of sleep problems among children and adolescents.
Methods: Child and Adolescent Sleep Checklist (CASC) is consisted of 36 questions commonly used from infants up to high-school students. CASC has three versions; for caregivers (common for all age groups), for elementary school children (6–12 years of age), and for high-school students (12–18 years of age). 53 children (29 community sample and 24 clinical sample) were recruited for the validation study. CASC sleep problem scores were compared with other sleep questionnaires; parental reports (preschoolers and elementary school children, $n = 26$) were compared with Childrens' Sleep Habits Questionnaire (CSHQ) and the self reports (high school students, $n = 19$) were compared with Pittsburgh Sleep Quality Index (PSQI). Subjects were also asked to answer CASC twice with 2 weeks interval, and the responses were compared.
Results: CASC sleep problem scores of the parental reports showed good correlation with CSHQ total scores ($r = 0.770$, $p < 0.001$). CASC sleep problem scores of the self reports showed good correlation with PSQI scores ($r = 0.599$, $p = 0.007$). CASC sleep problem score showed good correlation between the first and second responses ($r = 0.787$, $p < 0.001$).
Conclusion: CASC has its advantage in making cross sectional screening of sleep problems in wide range of ages by using both parental and

self report. In addition, CASC is especially useful in interventional or cohort study as this questionnaire allows to use same questionnaire throughout the study period.

PO-2-128 / AS-13 Presenter

SLEEP HABITS AND SLEEP PROBLEMS IN SCHOOL-AGED CHILDREN IN JAPAN: A CROSS-SECTIONAL STUDY

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INTRODUCTION: Although it is known that low sleep qualities or sleep disturbances are common in children and are associated with excessive daytime sleepiness, impaired daytime neurocognitive performance, obesity, incidence of psychiatric disorders or development disorders, there is an insufficient data of large sample of school-aged children. In this study, we conducted a population survey to characterize sleep habits and sleep problems among school-aged children in Japan.
METHODS: The participants were parents who raised children aged 6 to 15 belong to 148 elementary schools and 71 junior high schools in 10 areas across the country. They were requested to answer a newly prepared questionnaire based on A Brief Screening Questionnaire for Infant Sleep Problems (Sadeh et al.) and Children's Sleep Habits Questionnaire (Owens et al.). This questionnaire consisted of thirty-one items to evaluate sleep habits and sleep problems of their children for the past one month.
RESULTS: Of the 25,211 children, mean bedtime and rise time were 21.9 h and 6.6 h, respectively. Approximately half of children (12,700/25,211) went to bed after 22 p.m. or later and 20.4% (5,144/25,211) went to bed after 23 p.m. or later. As grade shifted higher, bed time was significantly delayed, while rise time minimally changed across all grades. Consequently, a significant shortening in total sleep time for the higher grades relative to the lower grades was observed. The highest grade children slept an average of 126.5 min less than the lowest grades. Similarly, the prevalence of daytime sleepiness and sleep problems related to awakening behaviors were greater in higher grades. On the other hand, sleep problems related to initiating sleep and behaviors during sleep showed higher prevalence in lower grades compared to higher grades.
CONCLUSION: The present study has clearly shown that delayed bed time, short sleep duration, excessive daytime sleepiness and various difficulties in initiating, maintaining and terminating sleep were highly prevalent in school-aged children in Japan.

PO-2-129

RISK FACTORS OF SLEEP DISTURBANCE AMONG SCHOOL CHILDREN IN JAPAN: THE 2-YEAR FOLLOW-UP STUDY

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Objective: To examine the association between life-style habit including school life and newonset of sleep disturbance among school children in Japan.
Methods: A follow-up survey was conducted in December 2006 (T1) and 2008 (T2) among 844 school children from 4 elementary and 4 junior high schools in Japan. Multivariate logistic regression analyses were performed to examine the associated factors with sleep disturbance assessed by self-reported questionnaire. The study protocol was approved by the Ethical Committee of Osaka City University Graduate School of Medicine.
Results: The prevalence of morning fatigue, difficulty initiating sleep, arousal during sleep, and excessive daytime sleepiness at T2 was 9.4%, 9.5%, 7.1%, and 27.2%, respectively. Sleep disturbance was found to be significantly associated with eating regularly, frequency of exercise, computer time, relationships with family and friends.
Conclusions: The risk factors for sleep disturbance were having an unhealthy life-style and poor interpersonal relationship at school and home. Insufficient sleep has been reported to cause poor mental health and decreased motivation for learning among school children. Confirmation of the correlates of sleep disturbance has implications for screening susceptible students and may help prevent the occurrence of such disturbance at an early stage.
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PO-2-130 / AS-30 Presenter

CULTURE AND SLEEP: HOW DO SLEEP HABITS COMPARE BETWEEN HIGH AND LOW ALTITUDE DWELLING BOLIVIAN CHILDREN AND A LOW LAND NORTHERN EUROPEAN POPULATION?

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Background: Sleep is important for child development and should be conserved across populations. However, sleep habits are culturally determined both within and between countries. Bolivia has distinct urban populations in low altitude (LA) and high altitude (HA) locations. We studied the sleep habits of LA and HA dwelling children and compared them to a UK population.
Method: Healthy Bolivian children aged 4–10 yrs were recruited, 39 (23 male) from Santa Cruz (altitude 500 m), and 52 (22 male) from La

Paz (3700 m). Parents completed the Child Sleep Habits questionnaire (CSHQ); questions about infant swaddling and siesta practices and estimated their child's total 24 hour sleep time. Children aged 6–12 yrs in Hampshire, UK, recruited to a sleep and behavioural study completed a CSHQ.
Results: There were no age differences between HA and LA children (6.7 yrs SD 1.9; 7.0 SD 1.9). As infants, 86% slept in the parents' bedroom, (35% in parents' bed). Before 6 months, 62% slept supine and 33% prone, 13% were swaddled. Most 4 yr olds had siestas as did 25% of 5–6 yr olds and 19% of 7–10 yr olds. There were no altitude differences in these practices. HA children had more sleep/24 hrs than LA children (9 hrs 56 mins v. 9 hrs 05 mins) and had earlier bedtimes. Bedtimes across altitudes were late: weekdays 21.07 for 4–6 yr olds and 21.25 for 7–10 yr olds (range 20:00 to 23:00 hrs). LA children had more bedtime resistance and sleep anxiety than those at HA. Comparing 45 Bolivian children, 7–10 yrs, (8.6 SD 1.0 yrs, 25 male), age-matched, with 55 (8.6 SD 1.0, 25 male) from the UK, adjusting for multiple comparisons ($p < .002$), sig. differences in specific sleep habits emerged. Bolivian children were more likely to need a parent in the room to fall asleep; be afraid to sleep alone; have irregular bedtimes, take >20 minutes to fall asleep and have difficulty waking spontaneously in the morning.
Conclusion: Bolivian children, particularly those in the hot lowlands, had more sleep problems than British children. Multiple factors may contribute including later bedtimes driven by warm evenings and the loss of regular siestas.

PO-2-131

SLEEP HABIT, CIRCADIAN TYPOLOGY, MENTAL HEALTH, AND TV GAME PLAYING OF CZECH AND JAPANESE INFANTS AGED 5–6 YRS

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Objective: This study attempts to compare sleep habit, circadian typology, mental health, and TV game playing between "winter" Czech and "summer" Japanese infants aged 5~6 yrs (both severe seasons) from an epidemiological point of view.
Participants and Methods: 79 Czech (Ceske Budejovice at 49 degree north) and 269 Japanese (Kochi at 33 degree north) infants (70~80% response rate) answered an integrated questionnaire in January 2011 and in July 2010, respectively. The questionnaire included MEQ of Torsvall and Akerstedt (1980), questions on sleep habits (such as wake-up and bed times and sleep quality and quantity), meal habits, mental health (such as anger and depression) and TV game use.
Results: Japanese infants were significantly more evening-typed ($p < 0.001$), showed later bedtime ($p < 0.001$), were depressed less frequently ($p < 0.001$), showed anger more frequently ($p = 0.004$), took sweet drink ($p = 0.018$) and sweet stuff ($p = 0.032$) less frequently, took well balanced breakfast less frequently ($p < 0.001$), played TV game more frequently ($p < 0.001$) and were exposed to morning sunlight for longer minutes ($p < 0.001$) than Czech infants. Only 13% of Japanese infants woke up once or twice during the night sleep and lower than 33% of Czech ones ($p < 0.001$).
Discussion and Conclusion: Frequent depression and lower sleep quality shown by "winter" Czech infants might be related to the shortage of morning sunlight. Evening typology shown by Japanese infants even in summer is hypothesized to be partially related to TV game playing after the sunset.

PO-2-132

EFFECT OF PSYCHOLOGICAL STRESS ON NIGHTTIME SLEEP AND CORTISOL RESPONSE DURING MORNING IN CHILDREN

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To investigate the effect of some stressful activities just before bedtime on the following sleep in children, we conducted psychological tasks and examined the sleep quality by means of PSG and HRV. In addition, we investigated salivary cortisol levels before and after the experimental night sleep. The participants were 8 children (6–8 years old). In the Task night, they had to engage in two tasks with a computer about an hour before their own bedtimes. One was the Stroop Task, and the other was a continuous detection task. Each task lasted 10 minutes. On the No-task night, they spent an equal amount of time reading a book of their choice and seeing a video of their choice. All the children experienced the Task night and the No-task night (the order was counterbalanced). A polysomnogram, including electroencephalogram, electrooculogram, electromyogram was recorded each night. The heart-rate variability, as determined by the MemCalc method, was also obtained each night. Furthermore, saliva samplings were obtained before and after the both experimental manipulations, and after the night sleep. All recordings of all children were made at their own houses. We quantitatively analyzed sleep parameters and measures of heart-rate variability, including heart rate (HR),%LF and HF. Amount of cortisol in each saliva were measured by ELISA method. Sympathetic nerve activities which evaluated with HRV were higher for the Task night than for the No-task night during both the waking state and the sleeping state. There was less amount of REM sleep especially in the first and fourth 2-hour periods on the Task night than on the No-task night. Amounts of slow wave sleep, wake time after sleep onset and movement time were not different between the two conditions. This might be related with small arousals which were so brief that they did not affect on the sleep architecture. Amount of change in saliva cortisol before and after the experimental night sleep was smaller for the Task night. The present study revealed that all-night sleep quality in children can be affected by some exciting activities 1 hour before bedtime.

PO-2-133

IMPACT OF OBLIGATORY DAYTIME NAP IN JAPANESE NURSERY SCHOOLS ON CHILDREN'S NIGHTTIME SLEEP AND MORNING MOODINESS

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Newborn infants show scarce evidence of circadian rhythmicity of sleep and wakefulness. Around the 7th week after the birth, the first evidence of sleep circadian rhythm is found in full-term infants (Fukuda & Ishihara, 1997). Recently preterm infants are found to show the

emergence of sleep circadian rhythm exactly at the same timing as the full-term infants, if the timing is counted from their conception, not from their birth. In the both groups, the sleep circadian rhythm emerged at the 46th week from the conception (Takaya *et al.*, 2009). During 2 to 5 years of age, percentage of the children who take an afternoon nap gradually decreases. At the age of 3, about 60% of children take naps, then the percentage decreased to about 30% at the age of 4, about 15% at the age of 5, then almost none at the age of 6. However, In many Japanese nursery schools, obligatory lengthy daytime nap was taken by children of all ages, i.e., before the entrance to primary schools. The obligatory daytime nap for about 90 min was found to cause the delay of nocturnal sleep onset, morning moodiness, and reluctance to go to preschools. The authors conducted surveys on children attend preschools. Informed consent was given by the parents of the children. In Japan, the obligatory nap was taken only in nursery schools, not in kindergartens, because these two preschools are regulated under different laws, and supervised by the different ministries, i.e., ministry of health and labor, and ministry of education and science, respectively. Nursery school children showed significantly later bedtime, severer morning moodiness, and more frequent reluctance to go to preschools than kindergartners. Children's bedtime was not associated with parents' bedtime. The authors recorded children's activity with an actographic monitoring device to estimate their sleep wake patterns. Preschool children with long obligatory naps showed significantly delayed onset of nocturnal sleep (over one hour) than the children without naps. The impact of unnecessary lengthy daytime naps on nighttime sleep was confirmed also by the objective measurements.

PO-2-134 / AS-16 Presenter

THE EFFECT OF INCREASING ARTIFICIAL LIGHT LEVELS ON REST-ACTIVITY RHYTHMS OF OLDER PEOPLE LIVING IN CARE HOMES

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Introduction: As people age ocular changes occur reducing the amount of light, in particular short wavelength blue light, reaching the retina. This, coupled with age-related changes to the circadian and homeostatic regulation of the sleep-wake cycle, may contribute to sleep problems and reduced circadian amplitude in older people. Lighting in care homes is of poor quality and low intensity. The aim of this study was to investigate the effect of blue-enriched white light compared to control white light on actigraphic rest-activity rhythms.
Methods: The study was conducted over 12-week periods (autumn/winter 2008–2010) in a randomised, crossover design in communal rooms of 7 care homes in south-east England. After a baseline week (original care home lighting), each light intervention period (4000 K, 200 lux or 17 000 K, 1000 lux) lasted for 4 weeks with a 3-week washout period (original care home lighting, <100 lux) in between. Rest-activity data were collected continuously using Actiwatch-L monitors. Cosinor analysis and non-parametric circadian rhythm analysis (NPCRA) were used to quantify each participant's 24-hour rest-activity rhythm for each week and for light condition (5 males, 43 females, MMSE range 6–24, age 85 ± 8 years). RMANOVA fixed effect model (SAS 9.1), adjusted for medication, sex, age, MMSE score, mobility,% time spent in light rooms .
Results: No significant differences were found in the rest-activity rhythms between light conditions. Higher cosinor mesor, IS (interdaily stability) and M10 (average activity for 10 most active hours) was associated with increasing% time spent in the rooms with lights ($p < 0.05$). Medication use (hypnotics, anti-depressants, anti-psychotics) was associated with a delay in the timing of the activity rhythm (acrophase, L5 onset, M10 onset) and a reduction in amplitude.
Discussion: The light intervention did not affect the amplitude or timing of rest-activity rhythm. Time spent in the rooms with lights and medication were shown to influence the strength and timing of the activity rhythm.

PO-2-135

CORRELATION BETWEEN SLEEP AND LIFESTYLE PATTERNS AND STRESS HORMONE DYNAMICS IN THE ELDERLY

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The dynamics of stress hormones are said to exhibit elevated values when waking up, and these values are said to be elevated before going to bed in elderly persons with dementia disturbed sleep patterns. The purpose of this study is to identify the correlation between sleep and lifestyle patterns and stress hormone levels in saliva in normal elderly persons before bed and when waking up in the morning. The subjects consisted of 25 elderly persons participating in classes for preventing the need for long-term care and the like (average age: 75.8 years), and the subjects were surveyed using a questionnaire relating to sleep and lifestyle patterns, and tested for stress hormone: human chromogranin A, levels before going to bed and when waking up in the morning. The data was analyzed using the t-test and the Mann-Whitney U-test after dividing the subjects into 14 members of a bedtime elevated hormone and 11 members of a wakeup hormone group. Ethical considerations consisted of acquiring approval of the ethics committee of the participating health care institution and obtaining the consent of the subjects. The subjects were generally healthy, demonstrated an average sleep time of 6.6 hours, spent a total of 7.0 hours in bed, and exhibited sleep efficiency of 89.2%. Among subjects in the bedtime elevated hormone group, time spent in bed was significantly longer ($p < .05$) and sleep efficiency was poor ($p < .05$). Values were low when these subjects woke up, thereby confirming the effects of this hormone on sleep even in normal elderly persons, and indicating that alleviation of psychological stress prior to going to bed is an important key in support of promoting sleep. There were no correlations observed between stress levels and lifestyle patterns.

PO-2-136

ASSOCIATION OF LEISURE-TIME, HOUSEHOLD AND WORK-RELATED PHYSICAL ACTIVITY WITH SLEEP CONDITION IN OLDER ADULTS

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BACKGROUND: Although many investigators have been reported that daily exercise is related to good sleep condition, little information is known on relationships of each physical activity excepting for exercise (e.g. household, working) with sleep condition in older adults.

PURPOSE: This study was conducted to reveal which type of physical activity would be strongly relevant to sleep condition in older Japanese adults.
METHODS: Three hundreds and fifty-five community-dwelling older Japanese adults, aged 65 to 85 years (average 73.4 ± 5.3 years), were randomly drawn from Basic Resident Register as subjects. Pittsburgh Sleep Quality Index was used to evaluate mean sleep duration, sleep latency and daytime nap time. Physical activity was assessed by Physical Activity Scale for the Elderly, consisted of five kinds of leisure-time activity (e.g. walking, low intensity exercise), six kinds of household activity (e.g. light housework, lawn work), and a work-related activity. We evaluated the association of the leisure-time, household and work related physical activity with sleep condition using logistic regression analysis with an adjustment for age, sex, and Geriatric Depression Scale score. Each sleep condition was used as a dependent variable (good = 0, poor = 1) and each physical activity score was used as an independent one (high = 0, low = 1).
RESULTS: Logistic regression analysis showed that inappropriate sleep duration was associated with lower scores of light housework (OR = 2.15, 95%CI = 1.02–4.50) and heavy housework (OR = 1.85, 95%CI = 1.03–3.33). Those who had long sleep latency were less likely to practice light recreational activity (OR = 1.56, 95%CI = 1.01–2.41) and muscle strength exercise (OR = 2.74, 95%CI = 1.41–5.29). Long daytime napping was associated with low score of heavy house housework (OR = 1.95, 95%CI = 1.05–3.45).
CONCLUSIONS: These findings suggest that increasing leisure-time activity is associated with shorter sleep latency. To obtain good quality of sleep may be necessary for older Japanese adults to practice not only exercise but also household activity.

PO-2-137 / AS-13 Presenter

THE SLEEP AND TECHNOLOGY USE OF AMERICANS: RESULTS FROM THE 2011 NATIONAL SLEEP FOUNDATION'S *SLEEP IN AMERICA POLL*

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Introduction: Advances in the accessibility and portability of technology has led to claims that technology use is impacting Americans' sleep. However, nationally representative surveys have been lacking. The primary aim of the present work was to measure the presence and use of technology on sleep and compare them across age groups.
Methods: 1,508 respondents, representative of the USA population between 13–64 yrs of age, completed the survey either via telephone interview (N = 750) or the web (N = 758). The survey contained questions about sleep, technology use, daytime functioning and coping with sleeplessness. The sample was categorized into different age groups: Gen Z'ers (13–18 yrs), Gen Y'ers (19–29 yrs), Gen X'ers (30–45 yrs), Baby Boomers (46–64 yrs) to contrast the diverse use of technology by different age cohorts. Each age group was weighted to 2009 USA Census data. The maximum sampling error was±2.5% at the 95% confidence level.
Results: 95% of the total sample used technology in the hour before bed. Several distinctions were found between the under 30 s (Gen Z and Y'ers) and over 30 s (Gen X'ers and Baby Boomers). Younger groups were higher users of cell phones (67–72%), laptops/computer (60%), music devices (34–64)%, and video game consoles (18–23%) in the *bedroom* in the *hour* before bed than the over 30 s. Further, respondents under 30, had later bedtimes, were more likely to report difficulty falling asleep, and took longer to fall asleep than those respondents over 30. Once asleep, under 30 s were more likely to be awakened by their cell phone at least a few nights a week (18–20% vs 3–11%). When awakened, under 30 s were more likely to text, listen to music, talk on the phone, and surf the internet than over 30 s. Despite under 30 s getting more sleep, they were nonetheless more likely to report daytime sleepiness and napping.
Conclusions: Technology use prior to bed and during the night is prevalent in the USA, especially in adolescents and emerging adults. The pervasive use of this technology demands we learn causal links between technology use and sleep.

PO-2-138

ASSOCIATION BETWEEN SLEEP DURATION AND LIFESTYLE-RELATED DISEASES IN NAGAHAMA 0-DEGREE COHORT STUDY

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Introduction: Nagahama city (Shiga prefecture, Japan) and Kyoto University made a contract to perform a genome-cohort study and biobanking (Nagahama 0-degree cohort study).
Method: The first cross-sectional survey with questionnaire and physical examination was conducted between 2008 and 2010. 9853 residents (30–74 years, 32.8% male) participated in the study. Sleep duration and current medical condition were asked in the questionnaire. Arterial stiffness was measured by CAVI (Cardio-ankle vascular index). Logistic regression models were constructed to examine the independent associations of important covariates (age, gender and BMI) with lifestyle-related diseases (hypertension, diabetes mellitus, lipidemia, depression, insomnia and arterial stiffness).
Results: Mode of sleep duration was 6 hrs (6–7 hrs). Compared to 7–8 hrs of sleep, shorter sleep (–5, 5–6, 6–7 hrs) was related to a significantly increased risk for insomnia. Sleep shorter than 5 hrs and longer than 8 hrs were both significantly associated with depression. Hypertension and arterial stiffness were both significantly associated only with sleep longer than 8 hrs. We could not find any association between sleep duration and lipidemia. Diabetes mellitus showed a U-shape, but not reached a statistical significance with sleep duration. Unlike the previous reports in US, our population did not showed U-shape with sleep duration in hypertension.
Conclusion: Sleep duration is associated with insomnia, depression, hypertension and arterial stiffness. Sleep duration might affect differently on Japanese and Caucasians.

PO-2-139

DIFFICULTY MAINTAINING SLEEP AND EARLY WAKE-UP TIMES ARE ASSOCIATED WITH VASCULAR DYSFUNCTION IN JAPANESE HEALTHY INDIVIDUALS

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Introduction: Previous investigations have shown that sleep loss causes hypertension and atherosclerosis. Sleep fragmentation and earlier wake-up times characterize sleep patterns of older adults in relation to age-related circadian phase advance. These findings raise the question of whether vascular dysfunction with aging is associated with the age-related changes of circadian phase and sleep-wake patterns. In the present study, wehave cross-sectionally investigated whether self- reported difficulty sleep maintaining, habitual wake-uptimes, and sleep timing are associated with higher blood pressure and vascular dysfunction.
Methods: The study included 3066 apparently healthy individuals (mean aged 57.2 ± 10.1,1634 male) who underwent a human doc program in a general hospital. Habitual patterns concerning sleep ((bed times, wake-up times (WT), and symptoms of difficulty initiating or maintaining sleep (DMS)) were recorded from answers on the questionnaire. Vascular condition was assessed by blood pressure andbrachial-ankle pulse-wave velocity (PWV) value. Hypertension (HT) was defined as blood pressure ≥130/85 mmHg, and Atherosclerosis (AT) was determined as the highest tertile of baPWV values. Logistic regression model, adjusted for variables including gender, age, sex, body mass index, blood pressure, sleep duration were applied.
Results: DMS was associated with increased prevalence of HT with adjusted ORs of 1.23 (1.01–1.50). WT 5:00 a.m or before were associated with increased prevalence of HT and AT with an adjusted ORs of 1.48 (1.06–2.07) and 1.83 (1.12–2.99), respectively, compared to WT after 5:00 a.m. Sleep timing (ST) (midpoint of BT and WT) advanced by 1 hour was associated with higher prevalence of AT, with adjusted ORs of 1.18 (1.05–1.33). Sleep duration did not contribute to the association between the sleep parameters and vascular condition.
Conclusion: DMS , early WT, and advanced ST were strongly associated with vascular dysfunction. Age- associated changes of circadian timing and sleep forms might influence vascular condition.

PO-2-140

COMPARISON OF SLEEP ON PUBLIC BATHING AND BATHING AT HOME

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OBJECTIVE: The purpose of this study is to evaluate core temperature difference between taking Public Bathing (with hot spring ingredients) (PB) and Bathing At Home (BAH) and analy1zed its effect on sleep.
METHODS:
Settings and Subjects: Subjects are 22 to 25 years old 6 male and 1 female who has no record of psychiatric disease including sleep disorder. All subjects marked high score by Morningness-eveningness questionnaire (mean score 36.3 ± 8.2) and regular time in bed tended to be late.
Condition: Subjects chose two certain days out of 6 consecutive days and they took BAH on the first day and took PB on the second day. On both two days subjects took bath two hours prior to their regular in bed time. Bathing time was 10 minutes and water temperature at home was approximately 41 degrees (38–42), at public bathing was 38–42 degrees. Subjects spent regular school days in day time and went to bed on regular time.
MEASUREMENTS: Wireless core temperature sensor (Mini-Mitter Co.), was used to measure core temperature. The consecutive core temperature data was taken from 12:00 pm on the first day to the second day 12:00 pm. Sleep diary was recorded on Time In Bed, Get Up Time and bathing time.
ANALYSIS: We compared sleep latency and total sleep time of two groups. Core temperature was picked up at 5 points of "Before Bathing", "After Bathing", "Time in Bed", "The lowest temperature ", and "At wake up" and analyzed difference by one-way ANOVA. We set combination of "Before and After Bathing", "After Bathing-Time In Bed", "Time In Bed-The Lowest Temperature", "The Lowest Temperature-At Wake Up" for both PB and BAH and compared data by two-way ANOVA.
RESULTS: Mean time of TST was 1.97 ± 0.67 for BAH and 1.88 ± 0.55 for HSB and there was not significant difference. Core temperature of PB at After bathing temperature was higher than BAH but rest three points showed the same temperature. PB showed significant decreasing of core temperature before sleep. PB showed higher rate of decreasing with core temperature and might help to fall asleep promptly.

PO-2-141

SLEEP FACILITATION BY JAPANESE HOT SPRING; EEG, CORE, PROXIMAL, AND DISTAL TEMPERATURE EVALUATIONS

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Background: Bathing, especially with hot spring with various mineral compositions, is known to facilitate/improve sleep by warming the body. It is postulated that the heat dissipation decreases the elevated core body temperature, facilitates sleep. It was also reported that sleep is more easily induced when the DPG (Distal-proximal temperature gradient) exhibit the most positive values (Krauchi1999). In this study, we thus evaluated the effects of usual (plain hot water; PH) and hot spring bathing (HS) on sleep using clinical thermometers and EEG.
Methods: Eight healthy men (average age 20.1 years) were divided into 3 groups and each group received the HS (Akita-Onsen Satomi), PH bath and no bathing (NB) a week interval. The temperature of the bathwater was set to be 40 C degrees. Subjects soaked in the bath deep enough their chests touched the water at 22:00 for 15 min. From the time they finished bathing to the next morning, we measured their core body temperature (CT: rectum), distal skin temperature (DT: top side of the foot), proximal skin temperature (PT: lower part of the clavicle) and EEG using a single channel portable device (Moomin-kei, SleepWell). Subjects were told to sleep from 24:00–7:00.
Results: The amount of delta power per min in the first sleep cycle significantly increased in the bath groups ($p < 0.04$, ANOVA), and the

highest power was observed in HS group. Sleep latency also decreased in the same order but the difference did not reach to the significant level. Total sleep time increased in the order of PH, HS, and NB groups ($p < 0.05$). Bathing significantly increased CT and the subsequent declines during initial 40 minutes ($p < 0.05$). Changes in the DPG were associated with significant decrease in PT, and the larger decline in PT was seen in the HS group.
Conclusion: These sleep changes are associated with large decline in the elevated CT, increased heat dissipation and positive DPG values. Hot spring bathing had the larger effects on these parameters. It is proposed that some mineral compositions of hot spring likely produced larger temperature changes and subsequent sleep facilitations.

PO-2-143 / AS-8 Presenter

PROMOTING SLEEP QUALITY THROUGH MEDITATION

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Meditation techniques are claimed to enhance the quality of sleep. Very few studies are available on the objective assessment of sleep following various yogic practices. Changes in theta rhythm during slow wave sleep along with significant alteration in EMG and enhanced REM duration were observed following TM. The purpose of this study was to seek evidence of EEG and EMG alteration to determine whether Preksha Meditation (PM) practice causes any positive impact on the quality and quantity of sleep. The study was carried out on randomly selected 16 experimental subjects (8 long term and 8 short term PM practitioners) and a group of 16 matched control subjects. EEG and EMG recordings of all 32 subjects conducted in a sound proof room, dimly lit and in lie-down position consecutively at different occasions as per availability of the subjects. EEG records was taken from surface electrodes by using 32 channel digital EEG machine with brain mapping and EMG was recorded from a surface electrode applied at wrist by using RMS Aleron 401 (4 channel). Recordings were analyzed for the alpha rhythm, total sleep duration, sleep efficiency index, spindle amplitude, spindle duration, intra-spindle frequency, S1, S2 and REM percentage. The findings indicate prominent appearance of theta rhythms during slow wave sleep along with low EMG and also enhanced REM duration in long term practitioners of PM. Spindle amplitude, spindle duration, intra spindle frequency were found to be insignificantly increased in short term practitioners where as they increase significantly in long term practitioners and alpha rhythm dominance was significant in both groups. Out of the results obtained it may be inferred that PM helps in improving the quality of sleep and bringing in the state of relaxation. The detailed pathway of possible mechanism involved in the process will be discussed.

PO-2-144 / AS-4 Presenter

MEDIA USAGE AS A PREDICTOR OF IRREGULAR SLEEPING PATTERNS

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Introduction: Regularity in sleep schedules is important part of good sleep hygiene, enabling good sleep quality and sufficient amount of sleep. The aim of this study was to examine do frequent media consumption and media presence in the bedroom at baseline predict irregular sleeping patterns 1,5 years later.
Methods: The baseline sample, from 2006, consisted of 10- to 11-year-old children from 27 Swedish-speaking schools in Helsinki region in southern Finland. A follow-up was made in 2008. Only subjects ($n = 677$, response rates 74% and 93%, 2006 and 2008 respectively) who answered in both years are included in the analyses. Media consumption was assessed as watching television, using computer and total screen time (h/day). Irregular sleeping patterns were defined as later bedtimes at weekends than school nights and as difference in sleep duration between school and weekend nights. Linear regression analyses were used. Model 1 was adjusted for gender, grade, living with mother and father and model 2 further by baseline sleep irregularity.
Results: More frequent computer use, screen time and media presence in bedrooms at baseline predicted later bedtimes at weekends than school nights. Adjusting for baseline irregularity in sleep patterns, computer use and computer in bedroom predicted later bedtimes. Computer use and screen time predicted sleeping more at weekends than school nights. Adjusting for baseline sleep irregularity, screen time and watching television predicted sleeping more at weekends.
Conclusion: Media consumption at baseline predicted irregular sleeping patterns. Media presence in bedrooms predicted later bedtimes at weekends.

PO-2-145

BETTER SLEEP PROPOSAL FOR THE FUTURE: LEARNING THE HUMAN ASPECTS FROM SLEEPING POSTURES DEPICTED ON PICTURE SCROLLS DURING THE MEDIEVAL TIMES

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People sleep. There is no exception to it at any time any place. Since the ancient glory times of Japan we have a lexis, Oki-fushi, which describes our daily lives as cycles of getting up and going to sleep. Production of picture rolls was flourished during 12th to 14th centuries in Japan and they were exactly presenting the world of Oki-Fushi. Scenes in picture scrolls are marvelously color-painted and intriguing storylines are inserted next. Themes vary in scrolls to scrolls – they could be dynasty themes, Buddhist narratives, or they could be scandalous incidents happened in the Capitol City. The movement of people inside of residences in picture scrolls was introduced as knees, crawls, and lies down instead of walk and sit. Eshi, the scroll painters, depicted fear of the people for the night. Night was the time when people believed vengeance and apparition surrender their world. Frightening the dark, yet all they could do was to sleep with complexity of weirdness and confusion. Nowadays science and technology are what we believe which have contributed and transformed the sleeping customs and habits revolutionary. At the same time it has led people to lose the sense of having night and day. People find themselves mislay the rhythm of sleep and some of us struggle to sleep at night with the stress produced from the day time. Evaluating both depiction of sleeping habits and episodes from Medieval Times and sleep problems in nowadays, what can we propose for the better sleep in the future?

PO-2-146

EFFECTS OF VIEWING NEGATIVE AFFECTIVE PICTURES ON NIGHTTIME SLEEP: LATENCY TO SLEEP STAGES, THE TOTAL AMOUNT OF SLEEP STAGES, AND RAPID EYE MOVEMENT DENSITY

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This study investigated the effects of a certain kind of emotion elicitation on the latency to rapid eye movement (REM) and non-REM sleep stages, on the total amount of these stages, and on REM density in healthy participants, by using polysomnographic recordings. The study included 5 women and 4 men. Sixty different pictures drawn from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 2005) were used to elicit emotions, and included 20 pleasant, 20 neutral, and 20 unpleasant pictures. The participants underwent full-night polysomnography on 4 nights in a sleep laboratory. After the measurements were obtained on the first night, i.e., the adaptation night, 1 of the 3 picture-viewing tasks–i.e., viewing and rating pleasant (task 1), neutral (task 2), or unpleasant (task 3) pictures–was randomly assigned for the second, third, or fourth night. The participants engaged in 1 of the 3 tasks before bedtime on these 3 nights. The 8-hour polysomnographic recordings commenced at 2400, at which time all the lights, except for an emergency fluorescent light bulb, were switched off. REM density was calculated as a percentage ratio of the number of 30-s epochs in which one or more REMs were observed and the total number of epochs evaluated as REM stages. In this report, the author presents the results of the effects of the unpleasant picture-viewing tasks, compared to the neutral. The polysomnographic measurements obtained after the unpleasant picture- and neutral picture-viewing tasks were compared by one-way repeated measures analysis of variance. These analyses showed that the latency from the time when the lights were switched off to sleep stage 3 after the unpleasant picture-viewing task was significantly longer than that after the neutral picture-viewing task ($p < 0.05$). No significant differences were found between the total amount of any of the sleep stages or in the REM density after these 2 types of tasks were performed on the measurement nights. These data indicate that using unpleasant affective stimuli before bedtime extends latency to deep sleep stages.

PO-2-147 / AS-3 Presenter

MULTI-COLORED EFFECTS OF LED LIGHT ON COGNITIVE FUNCTION AND PSYCHOLOGICAL PARAMETER IN THE EVENING

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Objective: This study aimed to examine the multi-colored effects of LED light on cognitive and psychological parameters in evening.
Participants and Method: All of 20 participants were male student (age: 18–19). They conducted GO/NOGO task, Kwansei-gakuin Sleepiness Scale (KSS) and Positive and Negative Scale (PANAS) at every 30 minutes from 18:30 to 23:30 under three light conditions. From 18:30 to 21:00, participants were in dim light condition in all settings. From 21:00 to 23:00, the light conditions were in Dim (a), the Blue LED light (7000K, 30lx) (b) and the Red LED light (3000K, 20lx) (c). From 23:00 to 23:30, the light was again in dim condition.
Results: In GO/NOGO task, on error rate compared to the average rate of before lighting, the average rate of after lighting decreased in setting (b) and (c) (b $p = 0.018$, c $p = 0.062$). On reaction time the score at 21:30 was significantly faster than the average score before lighting in setting (c) ($p = 0.005$). In KSS, the score at 21:30 and 22:00 were significantly lower than the average score of before lighting in setting (c) (21:30 $p = 0.09$, 22:00 $p = 0.02$). At the same time in setting (b) and (c) the PA score (PANAS) at 21:30 and at 22:00 were significantly higher than the average score of before lighting (b: 21:30 $p = 0.000$, 22:00 $p = 0.006$, c: 21:30 $p = 0.009$, 22:00 $p = 0.026$, respectively). There was a significant decrease on PA score at 22:00 compared to that at 21:30 in setting (b) ($p = 0.045$). However in setting (c), between the score at 21:30 and at 22:00 there was no significant difference ($p = 0.901$).
Conclusion: Our data suggest that we should consider how to use the LED light for depending on a purpose by its multi-coloristic in the evening.

PO-2-148

CHANGE IN SLEEP QUALITY BY OUTDOOR AIR TEMPERATURE RISE

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Background: Air temperature rise worsens sleep quality. Okano et al (2008) conducted the survey on a total of 838 subjects living in Tokyo in summers of 2006 and 2007. They found that about 2% more subjects become "poor" sleepers for each 1 degree C increase in outdoor air temperature at 0000 LST over 25.3 degree C. However, there was a problem that the rate of "poor" sleepers under 25.3 degree C in the survey was 48.8% and it was significantly higher than 26.4% for male and 31.1% for female by Doi et al (2001) surveyed on Japanese residents in October. Both of the surveys used the Japanese version of the Pittsburgh Sleep Quality Index (PSQI-J) and the cutoff value, 5.5. In order to apply Okano et al to Japanese residents, influence by some factors which are different among these two surveys should be evaluated. This study focuses on difference of season.
Subjects & Methods: We conducted a survey via the Internet on a total of 2,421 adults living in Tokyo during four seasons from 2009 to 2010. The survey days were 20 April, 8 September, 17 November, and 22 January. Questionnaire for each day was consisted of four sections; personal attributes, housing and bedroom environments, subjective sleep quality using PSQI-J, and bedclothing.
Results: A total of 1,263 male and 1,163 female are included in the responders. The response rate was 100% because of the Internet survey. The PSQI-J global scores among the four seasons are 4.2 ± 2.7, 4.8 ± 2.9, 4.3 ± 2.9 and 3.9 ± 2.4 for male and 4.4 ± 2.6, 5.2 ± 2.8, 4.5 ± 2.6 and 4.4 ± 2.6 for female. There is a significant difference among the seasons for both sexes ($p < 0.005$). Using the cutoff value, the rates of "poor" sleepers are 28.3%, 31.8%, 23.1% and 18.4% for male and 28.7%, 38.6%, 29.3% and 25.4% for female.
Conclusion: The rate of "poor" sleepers is changed in season. It can explain a part of the difference between Okano et al (2008) and Doi et

al (2001). Additionally, there is a correlation between monthly air temperature at 0000 LST of the survey day and the PSQI-J global score. Seasonal change in sleep quality can include air temperature change.

PO-2-149

EFFECT OF USING AIR CONDITIONER ON FATIGUE AND SLEEP QUALITY

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Background: It is common senses that there is a relationship between poor sleep quality and fatigue status. However their relationship was neither well studied nor characterized. We examined the follow-up studies by questionnaire for about 200 healthy subjects in Osaka every one month for three terms to estimate impact of air conditioner use on hot days and/or nights.
Subjects & Methods: We administered about a total of 662 subjects for the study. The subjects answered the questionnaire for 6 days at every term (from July to October in 2010; T1-T3). Questionnaire was consisted of four sections; demographic variables, lifestyle, fatigue, and sleep quality. We used Chalder's fatigue scale for assessment of fatigue and Pittsburgh sleep quality index for assessment of sleep quality.
Results: The response rate is 95.6%. Increase of fatigue score are shown in the subjects who are at over 30 degree of the outside air temperature Taking deep sleep induces low fatigue score. However even if taking deep sleep, subjects who use air conditioner at night shows high fatigue score. Even in the hot days, some subjects show low fatigue score. Therefore we divided subjects into two groups , high group (CS = > 17) and low group (CS < 17), and examined the effect of living environment on fatigue score between the two groups. There are significant differences on air conditioner use daytime and/or during sleep between two groups.
Conclusions: Good sleep quality may contribute low fatigue score. Using air conditioner is recommended as a good method for keeping good sleep quality, but our data suggested it might induce fatigue on the next day.
Acknowledgment: This study was conducted by research project for creation of housing that promotes health and well-being.

PO-2-150

EFFECTS OF BED MATTRESS MATERIAL ON SLEEP ONSET UNDER MILD HUMID HEAT EXPOSURE

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The purpose of this study was to investigate the effects of bed mattress material on sleep onset during naps taken under mild humid heat exposure that simulated Japanese summers. The study included 11 healthy male subjects who wore short-sleeved pajamas and shorts and slept from 1330 to 1530 wearing a cotton blanket on a bed covered with a sheet. Two types of bed mattresses containing different materials were compared: polyurethane foam mattress (U) and camel mattress (C). Ambient climate conditions were maintained, with the temperature at 29°C and relative humidity at 70%. Electroencephalogram (EEG), electrooculogram (EOG), and mental electromyogram (EMG) recordings; and the skin temperature (Tsk), microclimate temperature, and humidity measurement for the waist and chest areas of the subjects were continuously obtained. The subjective sensation was asked before and after sleep. The protocols for this study were approved by the ethics committee of Tohoku Fukushi University. No significant differences were observed in the amount of sleep stages and in sleep onset latency. However, the rapid eye movement (REM) sleep in the first hour for the U was significantly increased than that for the C. The leg, arm, and mean Tsks for the U were significantly increased than those for the C at the sleep onset. The microclimate temperature and humidity of the chest area for the U were significantly increased than those for the C at 40 min after the lights were switched off. The subjective sensation of humidity for the bed mattresses was significantly high, and the requirement for decreasing the mattress temperature in for the U was significantly higher than that for the C. These results suggest that bed mattress properties can affect an increase in the subjective sensation of humidity and the requirement for decreasing mattress temperature during sleep by (1) increasing the mean Tsk at the onset of sleep and microclimate temperature and humidity of the chest area in the later segment of sleep and (2) changing the REM sleep distribution pattern.

PO-2-151

CONSUMPTION EFFECT OF TYROSINE AND PHENYLALANINE AS PRECURSORS OF CATECHOLAMINE ON MENTAL HEALTH EXISTS NOT AT SUPPER BUT AT BREAKFAST IN JAPANESE INFANTS

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Objective: This study challenges to examine the effects of tyrosine and phenylalanine intake at breakfast and supper as precursors of dopamine on Morningness-Eveningness (M-E) scores and mental health in Japanese young children aged 2–6 yrs from epidemiological point of view.
Participants and Methods: An integrated questionnaire was administered to 1367 infants attending 10 nursery schools governed by Kochi City and affiliated kindergarten of Faculty of Education in June-July 2008. The questionnaire included M-E questionnaire, questions on sleep habits (wake-up and bed times, sleep quality and quantity and so on), meal habits (regularity of timing and contents), mental health (anger and depression). Intake amount of tyrosine and phenylalanine were calculated based on contents questionnaire, and tables on the components of amino acids in foods (Gomyo and Hasegawa, 1993).
Results: Infants who took more than 800 mg (per meal) of tyrosine or phenylalanine at breakfast were more morning-typed than those taking less than 800 mg (One-Way ANOVA: df = 1, F-value = 7.997, p = 0.005). However, this effect disappeared in the Two-Way ANOVA (deleting effect of covariance as tryptophan intake: df = 1, F-value =

0.018, p = 0.894). Infants who took more than 800 mg of the two amino-acids at breakfast showed significantly higher scores of mental health (lower frequency of depression and anger) than those taking less than 800 mg (One-Way ANOVA: df = 1, F-value = 8.302, p = 0.004), and this effect remained significant even after deleting covariance = tryptophan effect (Two-Way ANOVA: df = 1, F-value = 5.773, p = 0.017). However, infants who took more than 1600 mg of tyrosine or phenylalanine at supper showed similar scores of M-E and also mental health (One-Way ANOVA, M-E: df = 1, F-value = 0.018, p = 0.894; Mental health: df = 1, F-value = 0.058, p = 0.810).
Discussion and Conclusion: Activity of dopamine synthesis in infant brain might be hypothesized to be higher in the morning than in the evening. Tyrosine and phenylalanine taken not at supper but at breakfast could affect mental health in infants.

PO-2-152

EFFECT OF AROMA OIL ON AUTONOMIC NERVOUS SYSTEM IN THE MORNING UNDER DIFFERENT LIGHT CONDITIONS

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Aromatherapy is popular in modern life in the world; it has been particularly accepted as nursing care recently. However, the efficacy data are scant, and potential mechanisms are disputable. As the experiment environment, the light condition is important, because the bright lights in daytime is effective in promoting the sympathetic nervous system. The purpose of this study is to investigate the effect of aroma oil on human physiological parameters in bright and dim conditions.
Seventeen healthy male volunteers aged between 18 and 31 years (mean age: 22.4 years) participated in this experiment. The experiments were carried out in October 2010. Participants were experienced in sitting position with essential oil (Boswelliacarterii; sedative aroma) on bright (500lux) or dark (50lux) condition in the morning. Four essential oils were previously tested by these participants and this oil was selected for this experiment, because the number of persons preferring this oil equal to un-preferring number. Autonomic nervous function was evaluated based on heart rate variability using Lorenz plot method (Map1060). Heart rate variability was analyzed by paired t-test in this study. In bright condition, CSI index, the activity of sympathetic nervous system, shown by preferred group tended to be higher in comparison with that by un-preferred group during aroma inhalation (p = 0.10). Furthermore, also after the aroma application, CSI index by the preferred group was higher than that by un-preferred group (p = 0.01). However, in the preferred group, the aroma oil effect on the CSI index tended to be reduced under the bright condition than under the dim condition (p = 0.065).
In conclusion, brightness and the preference are possible to affect the activity of sympathetic nervous system when exposed to this aroma. Further studies are also required to clarify the significant effect of aroma under light condition and preferred level.

PO-2-153

EFFECTS OF ONE MONTH INTERVENTION PROGRAM ON MEAL HABIT, SLEEP-WAKE CYCLE AND MENTAL HEALTH OF JAPANESE UNIVERSITY SPORT CLUB MEMBERS

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Objective: This study aims to estimate effects of intervention which is asking Japanese university students to take breakfast including protein and Vitamin B6, followed by the exposure to sun-light and to be exposed to incandescent lights ("low temperature" light) at night (Oct–Nov, 2010) on meal habit, sleep-wake cycle and mental health.
Participants and Methods: 94 male attendants of university football club were divided to 3 groups (G1: no intervention; G2: asking them to have protein resources like as fermented soybeans and VB6 resources like as banana at breakfast and to be exposed to sun-light after breakfast; G3: asking them to do as G2 plus to use incandescent lamp at night). To estimate the effects of the 1 month intervention, an integrated questionnaire was administered to all participants three times, first just before the intervention and second just after that and third one month later. The questionnaire included MEQ and questions on sleep habit, GHQ and SOC. Just after the intervention, questions on "implementation rate" and the satisfaction on their implementation were administered to G2 and G3. Salivary melatonin was measured around 23:00 at mid-point and just after 1 month period.
Results: Just after the intervention, participants satisfied with their implementation of breakfast took their breakfast more frequently and regularly (p = 0.069, p = 0.038) and showed more morning-typed (p = 0.006) than those with lower satisfaction. Participants who took their breakfast more frequently have less mid-night snacks (p = 0.003) than those with less frequency. Participants who implemented the contents of both morning and night intervention in more days showed higher conc. of salivary melatonin at the midday of the intervention than those with lower implementation rate (p = 0.025). The frequency of irritation was lower just after intervention than that before intervention in G3 (p < 0.001).
Discussion and conclusion: These may indicate that the one month intervention program is effective to promote the morning-typed sleep-wake cycle and to improve mental health, and meal habits.

PO-2-154

THE EFFECTS OF DIFFERENT TIMING OF THE EVENING MEAL ON SLEEP EEG AND SUBJECTIVE SLEEP AMONG YOUNG ATHLETES

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Subjects: Subjects were 5 college students aged 19 to 20 years old who exercise regularly.

Methods: The experiments took place from November to January in the sleep laboratory. This study compared four conditions: [C1] undernourishment after exercise, [C2] a meal just after exercise (within an hour after exercise), [C3] a meal just before sleep and after exercise (within an hour before sleep), [C4] only a meal (meal time was same as [C2] condition. The experiments were conducted once a week. The subjects exercised by bicycle ergometer for an hour between 17:00 and 19:00, after that they executed each condition, then slept between 23:00 to 24:00. Sleep was evaluated with the OSA questionnaire and by polysomnography.
Results: According to the OSA questionnaire, Condition [C2] had a significantly higher score for sleep maintenance ($p = 0.005$) and for sleep initiation ($p = 0.021$) than [C1]. Condition [C2] also had a significantly higher score ($p = 0.029$) for sleep maintenance than that of [C3]. Condition [C2] also had a significantly higher ($p = 0.028$) score of sleep initiation than that of [C4]. According to the results of the polysomnography, Condition [C1] had a significantly higher score of sleep efficiency ($p = 0.005$) and significantly lower number of awakenings ($p = 0.037$) than that of [C3]. In this study subjective indicators were inconsistent with objective indicators, therefore deeper investigation is necessary.
Conclusions: This study suggests that exercise may improve sleep initiation and a meal just after exercise may improve subjective sleep when compared to conditions of undernourishment after exercise, and a meal after exercise just before sleep.

PO-2-155

INFLUENCE OF ACUTE MODERATE AEROBIC INTENSITY EXERCISE ON QUALITY OF SLEEP ESTIMATED BY MAT-BASED SLEEP MONITOR

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This study was to examine the influence of moderate intensity of aerobic exercise during early evening and late night on sleep. Twenty young adults aged 26–35 participated. From 8 days before the experiment day, usual sleep time was obtained by standardized questionnaire for 7 days. In addition, we measured total durations of sedentary, light-intensity activity, and moderate- to vigorous-intensity activity during the 7 days by accelerometer. The participants were randomly allocated, matched age, sex, objectively measured daily total physical activity and daily total sleep time, to early evening exercise group (exercise I, $n = 9$), late night exercise group (exercise I, $n = 9$) and control group ($n = 9$). Subjects in the exercise I group attended an exercise program of 120-min duration (1500–1700) which started with warming up stretching for 15 min, followed by 60 min of aerobic exercise at intensity between 60–70% of the heart rate reserve. Subjects in the exercise II group attended the same exercise program at late night (2100–2300), while the control group performed book reading at the same time (1500–1700). On the experiment night, we estimated total sleep time and total duration of each sleep stage during sleep at home by using mat-based sleep monitor with body movement sensor. Sleep stages were estimated by using pulse wave, respiration, and body movement measured by the sensor. Analysis of covariance showed that total duration (or ratio) of the estimated sleep stages 3 or 4 and the estimated rapid eye movement sleep were significantly longer (or higher) and shorter (or lower), respectively, for both exercise groups (I and II) than the control group. In addition, the total duration (or ratio) of stages 3 or 4 was significantly longer (or higher) for exercise I group than exercise II group ($p = 0.04$). As expected, our results indicate that acute moderate intensity exercise during early evening or late night might improve quality of sleep at home estimated by mat-based sleep monitor with body movement sensor. Mat-based sleep monitor might be useful for self-monitoring of quality of daily sleep at home.

PO-2-156

MODERATE INTENSITY EXERCISE PERFORMED IN THE EARLY EVENING ELICITS A POSITIVE EFFECT ON SLEEP FOR YOUNG PEOPLE WHO DO NOT SLEEP WELL

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Many studies pointed out a methodological limitation that good sleepers have little room to achieve improvements in sleep by exercise. So in this study, we examined the effects of early evening exercise on sleep for people who do not sleep well. 19 male college students completed a sleep-monitoring by actigraph on more than three non-exercise days, and seven subjects (mean (SD) age of 20.6 (1.1) years) were selected, who showed less than 90% of sleep efficiency (SE; total sleep time / time in bed). After an adaptation day, the subjects completed three experimental treatments, consisting of baseline non-exercise (NE) and 2 exercise timing conditions, in which subjects completed 60% of heart rate reserve at 3 h (3HE) or 5 h (5HE) before bedtime. The subjects maintained a sedentary condition except for the exercise period, going to bed at 23:30 and getting up at 07:30. Total sleep time, sleep onset latency, wake time after sleep onset, and SE were assessed by actigraph. In addition, subjective physical fatigue and sleepiness were assessed by a set of visual analog 100 mm scale administered before retiring on each experimental night. Results did not show any significant difference among the three experimental treatments. However, significantly higher value of SE was observed for the exercise day (mean of 3HE and 5HE) than NE (88.5% > 81.2%). Also, higher scores of physical fatigue and sleepiness were observed for the exercise day compared with NE (52 > 24, 66 > 53, respectively). These results indicate that early evening exercise, without difference in specific exercise timing, might enhance subjective sleepiness to improve sleep for young people who do not sleep well. This work was supported by KAKENHI (20700542).

PO-2-157

SLEEP IN MIDDLE-AGED AND ELDERLY WOMEN AND ITS RELATED FACTORS

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Aim of the study: To analyze factors that impact on sleep in middle-aged and elderly women for health consultation.
Subjects: Two-hundred and twenty-one middle-aged and elderly women who belong to the JA Women's Group of A Peninsula in Japan;

34.9% were middle-aged, 48.4% early elderly, and 16.7% late elderly.
Survey method: An anonymous self-administered questionnaire was administered and body height was measured. We investigated the sleep status in terms of achievement of sufficient sleep, difficulty in falling asleep, use of hypnotics, early morning awakening, and daytime sleepiness.
Contents: Basic attributes, physical factors, psychological factors, and life environment factors.
Analysis: Statistical analysis were performed using PASW statistics17.0, descriptive statistics, and Spearman's rank correlation coefficient. A level of 5% was considered statistically significant.
Ethical consideration: This study was approved by the Institutional Review Board of Sugiyama Jogakuen University School of Nursing (no.11). The nature of the study and the privacy protection were explained to the subjects, they were asked to participate in the study, and informed consent was obtained.
Conflicts of interest: Not applicable.
Conclusion: Women living with family fell asleep more easily ($p < 0.01$); those living alone had more difficulty in falling asleep ($p < 0.01$) and felt a lack of sleep ($p < 0.01$). Those with lower weight ($p < 0.01$) and a stronger tendency to feeling depressed had more sleep disturbances ($p < 0.01$), and those who consumed more meat ($p < 0.01$) and reported higher subjective well-being experienced better sleep ($p < 0.01$). This study identified several factors related to sleep status in middle-aged and elderly women.

PO-2-158

CORRELATION BETWEEN SLEEP AND MINOR SYMPTOMS DURING PREGNANCY

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Sleep is involved in apprehension and depression, and has both physical and psychologocal effects. Thus, sleep is thought to be useful in improving minor symptoms during pregnancy. This study was therefore conducted for the purpose of identifying the correlation between sleep and minor symptoms during pregnancy.
Methods: Aquestionnaire survey was conducted on 239 complication-free pregnant women. The contents of the survey consisted of the frequency at which the time of going to bed or waking up varying by more than 2 hours during pregnancy and the occurrence of minor symptoms (including constipation, stiff shoulders, drowsiness, lower back pain, lazy, easily, fatigued, irritability, light sleep, depression and stomach discomfort). These minor symptoms were scored by determining the product of the frequency and degree of each symptom. The total of these scores was defined as overall minor symptom score. The subjects were analyzed by categorizing into a regular bedtime/wakeup group, in which changes in bedtime/wakeup time did not vary or only varied 1 or 2 times a month, and an irregular bedtime/wakeup group, in which changes varied daily or 1 to 2 times a week, and the two groups were compared for the occurrence of minor symptoms during pregnancy.
Results: As a result of comparing the two groups, with respect to bedtime, the regular group demonstrated significantly lower overall minor symptom scores as well as scores for stiff shoulders, lazy, easily fatigued, irritability, light sleep and depression ($p < .05$). With respect to wakeup time, the regular group demonstrated significantly lower overall minor symptom scores as well as scores for easily fatigued and depression ($p < .05$).
Conclusion: A definite correlation was observed between sleep regularity and the occurrence of minor symptoms during pregnancy.

PO-2-159 / AS-16 Presenter

SLEEP RELATED OCCUPATIONAL IMPAIRMENT DECREASES WITH AGE IN MALE WORKERS IN THE UK

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While 'sleep-related occupational impairment' is widely utilized as a diagnostic criterion in sleep medicine, the construct itself has been poorly operationalized and under-researched. Using the 'Loughborough Occupational Impact of Sleep Scale (LOISS)', these analyses explore sleep-related aspects of occupational performance within the UK workforce. 1054 workers (54% male) aged 18–65, from a range of occupational settings, completed a questionnaire including the 19-item LOISS which captures sleep related occupational impairment over the previous 4 weeks. The mean LOISS score was 12.2(range 0–61, SD 10.9). 20% of all respondents scored in the range 21–61, indicative of moderate to severe occupational impairment.
While reported sleep durations for work days showed no significant age effects, sleep durations for non-work days showed a significant age gradient, declining by 62 minutes from the age group 18–24 (mean estimated TST = 516.3 minutes; SD = 69.4) to the age group 54–65 (mean estimated TST = 453.68 minutes; SD = 56.7; main effect $F(1,4) = 17.93$, $p < 0.001$). Despite the evidence of an age related decline in sleep quantity, LOISS scores showed a reduction in sleep-related occupational impairment with increasing age. This trend was mainly due to the male respondents (LOISS scores as age increased: ($r_p = -.156$, $r_2 = 0.02$, $p < 0.01$) while scores remained stable, below the mean for females. The relationship between increased age and decreased occupational impairment in males remained significant after controlling for sleep duration, perceived workability, health indicators and work hours. Two different hypotheses, alone or in combination, could explain these findings. First, age related increases in attention to detail, risk management, accident avoidance and role autonomy may account for the ageing-related decrease in sleep-related occupational impairment among men. Second, poorer sleep management among younger workers may result in sleep-related workplace underperformance, which declines with age and experience. Both hypotheses will be addressed in future research.

PO-2-160

SLEEP QUANTITY AND QUALITY OF WORKERS LIVING IN BIG CITIES IN JAPAN

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An accurate tool for the objective collection of sleep data over many nights in a wide population could have important implications in sleep research and clinical practice. The ability to discriminate between sleep stages beyond subjective sleep/wake measures by a questionnaire may be especially useful in the objective assessment of sleep quantity and quality. We investigated actual sleep situation of over 300 working Japanese living in big cities from 2009 to 2011 using a simple, small and easy-to-use portable electroencephalogram (EEG) acquisition device and analyzed sleep stages based on the Rechtschaffen and Kales1

method. Participants were healthy 318 adult volunteers living in the Tokyo metropolitan or Kansai area. Average age was 37.8 years old (10.7, SD) and no sleep complaints. They measured EEG by themselves with the portable EEG at home. Average of total sleep time: 6 h 06 min (all, 1.4 h, SD), 6 h 20 min (male, 1.4 h, SD), 5 h 40 min (female, 10 min, SD). Sleep latency: 10.5 min (all, 9.6 min, SD), 11.3 min (male, 8.2 min, SD), 8.8 min (female, 3.2 min, SD). Total time in bed for male was increased age dependently, but not for female. Total wake time during sleep: 16.4 min (all, 12 min, SD), 19.4 min (male, 18 min, SD), 14.5 min (female, 10.2 min, SD). Our results of sleep quantity was over 1 h shorter than the results by questionnaire recently conducted by NHK (Japan Broadcasting Corporation, 2010) or OECD (Organization for Economic Cooperation and Development, 2009), were reported that total sleep time was 7 h 14 min and 7 h 50 min, respectively. EEG based home monitoring could reflect the present precise sleep situation of workers living in Japan.

PO-2-161

THE EFFECT OF NAP IN AN ENVIRONMENTALLY-CONTROLLED VEHICLE ON PSYCHOLOGICAL CONDITION, AND WORK ABILITY

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Purpose: We operated in-house and outside experiments to verify that the nap during which the environment is appropriately controlled does not cause the sleep inertia easily even immediately after the nap, and the work result improves too.
Method:
[laboratory experiment]
The car room sized space was made in the soundproof room, and the environment control equipment was arranged in that space. We experimented by "System nap condition" and "Control nap condition" in consideration of the counterbalance. In "System nap condition", participants took a 20 minute nap in an environment where massage, intense illumination lighting, angle of the seat, sound, and image, etc. were controlled. In "Control nap condition", the massage and the intense illumination lighting were deleted.
On the experiment day, we evaluated the effect and the sleep inertia before/immediately after/30 minutes after the nap by the subjective measures (VAS) and performance test.
[Field experiment]
We made the same environment as the laboratory experiment in the car and experimented in "System nap condition" and "Free break condition" in consideration of the counterbalance.
Operation similar to the laboratory experiment was done in "System nap condition", and TV whose volume was controlled was appreciated in "Free break condition".
Conclusion: A similar tendency to both experiments was seen, and "System nap condition" was able to confirmed in 30 minutes after it takes a nap and to confirm awake the level and concentration rise significantly compared with "Free break condition". In addition, the experiments showed that the work result increased significantly by making it to "System nap condition" immediately/30 minutes after the nap. Moreover, it demonstrated that the illuminance of the lighting had greatly influenced subjective awake actually feeling.
Therefore, by the present study we suggest that "System nap," even for the massage and the intense illumination lighting to control the environment, suppresses the sleep inertia and it has effect on taking an effective nap while running.

PO-2-162

RESEARCH ON SLEEP PATTERN OF INFORMATION TECHNOLOGY ENGINEERS

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Purpose: Recent years, Information Technology infrastructures such as the Internet become important. IT (Information Technology/Computer) engineers work hard to keep IT infrastructures as 24 hours 7 days. Working style of IT engineers would be different from others. We study sleep patterns of IT engineers to know life style of them.
Method and Subject: We selected six males IT engineers.
Six IT engineers: Male/24.4 years old (Average)
Six healthy adults (Control): Male/22 years old (Average)
All of subjects ware actigraph on their wrist during two weeks. Actigraph records activity in every minute. Engineers also keep a sleep diary in same two weeks.
Result: We found two typical sleep patterns. One is irregular sleep-wake rhythm. In this pattern, subject works very irregular working style. Someday, he works normally. But, he wake up midnight then works until morning. Another pattern is "night owl" style. This pattern shows that subject wakes up in the evening or night. He works until early morning via midnight. He basically works as same pattern in everyday.
We compare average total sleep time per day between subjects and controls. Following is result.
Total sleep time (min.): 539.61 (subject) / 644.20 (control)
According to t test of average total sleep time per day, result is $P < 0.018484$. This means that a significant difference between subject and control is exist.
Conclusion: Average sleep time for Japanese adult male of 20–24 years old is 7.54 hours. Subject and control show enough sleep time. According to sleep diary, subjects are doing basketball or tennis. But, they complain headache, eyestrain fatigue of the eyes and neck stiffness. This means that IT engineers working style cause several stress to subjects. Currently, all of subjects don't show significant problems in their life. But, there is a possibility of causing significant problems after a long term experience.
IT engineers are new jobs in current new age. We should track them to keep health, since IT infrastructure is important social infrastructure.

PO-2-163

SLEEP DURATION AND SLEEP SURROUNDINGS IN OFFICE WORKERS-COMPARATIVE ANALYSIS IN TOKYO, NEW YORK, SHANGHAI, PARIS AND STOCKHOLM

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The importance of sleep has recently been emphasized, and many epidemiologic investigations about the relationship between sleep and life-style diseases have been performed. Based on the results of the investigations, several countries have made guidelines for beneficial sleep. However, most questionnaire surveys of sleep were done in a single country, while comparisons among different countries have been investigated less thoroughly. The objective of this study was to compare the sleep and sleep surroundings in five large cities through a questionnaire survey. The subjects were chosen from office workers living in Tokyo, New York, Shanghai, Paris and Stockholm by internet screening; 90 males and 90 females were included in each area. Sixty subjects were included in their 30's, 40's and 50's, respectively. The questionnaire contained 10 main questions about sleep duration and surroundings. The effects of gender and age on sleep duration were not significantly different among the cities. Average sleep duration on weekdays in Tokyo (5.99 h) was the shortest (6.58–7.47, for the other 4 cities) and the differences between actual and ideal sleep duration in Tokyo was the largest (1.36 h, 0.77–1.32 for other 4 cities). The National Sleep Foundation suggests that healthy adults need 7–9 h sleep per day, the percentage of the people within the range was the lowest in Tokyo (22.8). Sleep surroundings also differed among the countries; subjects in Tokyo and Paris gave sleep the highest priority over other activities, such as meals and work, but they were willing to cover the least cost for improving their sleep. It is important to perform further studies on how the differences in sleep and sleep surroundings among different cities affect their health and diseases.

PO-2-164

THE NUMBER OF CONCURRENT NON-COMMUNICABLE DISEASES AND POOR SLEEP QUALITY: THE JAPANESE CIVIL SERVANTS STUDY

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Introduction: The elderly often suffer from several non-communicable diseases simultaneously. Non-communicable diseases cause poor sleep quality, and the reverse is also true. This study aims to evaluate whether individual and combined non-communicable diseases is independently associated with poor sleep quality.
Methods: The subjects were 2799 public sector employees (1818 men and 981 women) aged 20–65. Questionnaire survey was conducted in 2003. The subjects answered whether they had doctor-diagnosed heart disease, stroke, hypertension, dyslipidemia, diabetes, obesity, bronchial asthma, gastroduodenal ulcer, and back pain. Sleep quality was evaluated using the Pittsburgh Sleep Quality Index.
Results: Although subjects who had any non-communicable disease tended to have poor sleep quality, the associations were not necessarily statistically significant. The larger the number of concurrent non-communicable diseases, the poorer the sleep. In men, the prevalence of poor sleep quality was 19.7% for those without any non-communicable disease, 19.7% for those with 1 disease, 21.9% for those with 2 diseases, 22.1% for those with 3 disease, and 29.4% for those with 4 diseases or more. In women, the prevalence of poor sleep quality was 26.9% for those without any non-communicable disease, 38.1% for those with 1 disease, 32.9% for those with 2 diseases, 36.7% for those with 3 disease, and 66.7% for those with 4 diseases or more. The associations of the number of concurrent non-communicable disease with poor sleep quality remain significant after adjustment for age and mental disorders.
Conclusions: A dose-response relationship between the number of concurrent non-communicable diseases and poor sleep quality was observed. Reducing the number of concurrent non-communicable diseases may have beneficial effects on sleep.

PO-2-165

POOR SLEEP STATUS INCREASES THE RISK OF FATIGUE

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Background: It is a common sense that there is a relationship between poor sleep quality and fatigue status. However their relationship was neither well studied nor characterized. Therefore we examined the follow-up studies by questionnaire for about 200 healthy subjects in Osaka every one month.
Subjects & Methods: We administered about a total of 662 subjects for the study. The subjects answered the questionnaire for 6 days at every term (from July to October in 2010; T1–T3). Questionnaire was consisted of four sections; demographic variables, lifestyle, fatigue, and sleep quality. We used Chalder's fatigue scale for assessment of fatigue and Pittsburgh sleep quality index for assessment of sleep quality.
Results: The response rate is 95.6%. A total of 267 males and 366 females are included in the responders. There is a significantly positive relationship between fatigue score and sleep score ($r = 0.51$). The mean sleep score is higher in females than that in males. ($p < 0.001$). The 166 subjects out of those completed all questionnaire through the three terms. We divided them into two groups with a sleep score by the stated cutoff value, 5.5, and are re-categorized into poor (over 6) and good (under 5) sleep status. Those who show poor sleep status at T1 significantly increasing fatigue status at T3 as compared with those who show good sleep status at T1.
Conclusions: Poor sleep status might be one of the risk factors for increasing fatigue even in the short term.
Acknowledgment: This study was conducted by research project for creation of housing that promotes health and well-being.

PO-2-166

A COMPARATIVE STUDY OF THE SLEEP-WAKE SCHEDULE AND THE LIGHT ENVIRONMENT BEFORE ONE THOUSAND YEARS WITH THE MODERN SOCIETY; FOR THE NEXT GENERATION LIGHTING

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In modern Japanese society, sleep time shortening caused by a phase delay becomes social problems. Changes of light environment are supposed to affect the sleep-wake schedule. It is necessary to evaluate the historical changes of sleep-wake schedules and artificial lighting. In this study, we inferred the sleep customs and the artificial light in the Heian era, before approximately one thousand years in Japan, and try to consider how the sleep-wake cycle had been entrained by light environment.
In order to infer the sleep-wake schedules in the Heian era, we analyzed the expressions about the timing of awakening and social life in "the Tale of Genji" and "the Diary of Lady Murasaki". As a characteristic of the sleep custom, we found the many descriptions in which the people wake up and start activity on the astronomical twilight, several hours earlier than modern society. However, bedtime is indistinct and the people may not always go to sleep immediately after sunset, and especially in the court service, shift work was sometimes assigned.
Artificial lighting in the Heian era was the lamplight using vegetal oil. We reproduced an illumination tool of those days and measured the optical characteristics. The luminous flux of the flame light was less than quarter of a present incandescent 5W miniature bulb. Therefore, it is supposed that there was not the possibility of increasing vigilance level or circadian phase delay in the nighttime. On the other hand, also in the daytime, indoor illuminance was much lower than in the modern room.
In the Heian era, it is suggested that the sleep-wake cycle can be entrained by the astronomical twilight before sunrise. Regardless of whether people of those days were able to get regularity of bedtime, periodical awakening schedules would be maintained because the parametrical photic entrainment was not disturbed by excessive nocturnal light everywhere in the modern society. For the next generation lighting, it is considered necessary to secure gradually increasing dawn light with balanced spectral distribution after stable nocturnal darkness.

PO-2-167

WITHDRAWN

PO-2-168

SUBJECTIVE SLEEPING PROBLEMS AND SELF-REPORTED SLEEP LENGTH DURING FOUR SEASONS IN ARCTIC NORTHERN NORWAY

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Introduction: Arctic Northern is a natural laboratory for the study of seasonality of sleep. During two midwinter months the sun is below the horizon, and during two summer months the sun is above the horizon 24 hours a day, while at spring and autumn equinox, day and night are of equal length. If there were any effect of length of daylight on sleep, the population of Northern Norway, should experience this.
Material and methods: The study was part of a screening for cardiovascular disease, done by the National Screening Institute of Norway. All persons aged 23–71, living in Gamvik municipality, 460 persons, were asked to participate. Of 312 persons attending, 250 were invited to answer a questionnaire in January, March, June and September. The questionnaire asked about sleep length, subjective seasonal complaints, seasonal sleep complaints, and the actual time they woke up on the day of completion of the questionnaire. In December, the Centre for Epidemiologic Studies Depression Scale (CES-D) was added to the questionnaire.
Results: The sample was 196 persons, 108 (55%) women, mean age 50.7 (SD 10.7). Eighty-one persons (41%) reported subjective seasonal complaints, and 49 persons (21%) reported specific midwinter sleeping problems. Persons with midwinter sleeping problems slept more in all seasons, compared to persons reporting other problems, but only significantly more in spring (ANOVA, $df = 3$, $F = 3.158$, $p < .03$). Persons reporting midwinter sleeping complaints reported waking up later than persons with other complaints, but only significantly later in autumn (ANOVA, $df = 3$, $F = 5.313$, $p < .002$). Subjective seasonal complaints was significantly related to depressive symptoms (CES-D) (Beta −.092, $p < .000$) in a logistic regression modell controlling for age and gender.

PO-2-169 / AS-33 Presenter

SLEEP AND FATIGUE MANAGEMENT IN EXTREME ENVIRONMENT: CASE OF SOLO SAILORS

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Introduction: Solo offshore sailboat racing require skippers to face 24-hour/day readiness to perform under sleep loss. The objective was to measure the effectiveness of an Individual Fatigue Management Program (IFMP) during a solo-transatlantic race.
Method: Before a 3542 nm race, 15 sailors (men; 39 ± 9 yrs) completed a self-questionnaire about their sleep management in race. Following that, a 45-minute individual course about sleep regulation and consequences of sleep loss was given. In addition, they were offered to use an interactive sleep diary (software Scextan) that we designed to help users to manage fatigue during sleep restriction. Within 48 hours after arrival, sailors were asked to answer an interview based on a pre-established grid. A fatigue management feedback of the race was

individually made after the interview and sailors were re-tested with the same questionnaire. Interviews were transcribed by double-blind method. Results from self-questionnaire and interviews gave for each sailor Fatigue Management Scores (FMS).

Results: Variance analysis showed a light effect of the FMP ($p = .08$) by reducing the variance of the FMS between before and after the race. Interviews analysis revealed the difficulties that skippers had to adapt their fatigue management to what they thought to be the best for the performance. In particular, to rationally anticipate fatigue periods seems the most difficult to achieve. The winner of the race (18 days at sea) also had the best FMS in both questionnaires and interview. Analysis showed that he managed his fatigue in anticipation of the environment, more than other sailors. He was also the only one to almost constantly use the software to monitor his "sleep consumption" along the race. For 4 years, he systematically took into account fatigue management in the preparation of his races with a sleep specialist.

Conclusion: An IFMP associated to a dedicated tool is effective for better sleep management and helps to improve performance in solo sailing races. A tool which predicts individual alertness might reduce the gap between knowledge and behavior.

PO-2-170

SLEEP IN WINTERING EXPEDITION MEMBERS IN ANTARCTICA

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Antarctic environment is characterized by extremely low ambient temperature and seasonal variation in daylight time. In addition to those natural characteristics, psychological factors related to isolation with small number of members in the Antarctic base may have some influences on physiological and psychological functions. As previous studies have reported abnormalities in human circadian rhythms and deteriorated sleep in Antarctica, we evaluated sleep in the wintering members in Antarctica by using subjective and objective measurements. The subjects were ten males and two females recruited from the members of the 50th and 51st Japanese Antarctic Research Expedition (age: 39.7 ± 10.0 years; BMI: 25.2 ± 3.3). During their 13 months sojourn in the Antarctic base, data collection was conducted every 3 months (March, June, September, and December). The data collection was consisted of standardized sleep questionnaire answering past one month of sleep and wrist actigraphy for one week to evaluate sleep/wake rhythm. In 6 members of 51st expedition, instead of wrist actigraphy, the other type of activity monitoring device was attached to the waist of the subjects to evaluate sleep/wake rhythm and daily energy expenditure. Subjectively evaluated sleep maintenance showed mostly above the standard value throughout the sojourn. The results of objective sleep evaluation such as sleep efficiency, sleep period time and regularity of sleep time were individually differed, which might be associated with type of work and/or subjects' trait. On the other hand, sleep phase in June was significantly delayed from those in March for approximate one hour, which was accompanied by a decrease in daily energy expenditure of approximate 200 kcal. As the delayed sleep phase in June was thought to be related to lack of sunlight in winter, decreased physical activity might have adverse influences on sleep quality.

PO-2-171

SLEEP AFTER TOHOKU-PACIFIC OCEAN EARTHQUAKE IN 2011

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At 2:46 PM on March 11th, 2011, devastating earthquake shook northern part of Japan, which induced widespread severe damage. Wrist actigraphy and bed room temperature were accidentally measured for one week from March 9th. As the primarily objective of the data collection was a follow-up measurement examining the effect of sleep hygiene education for elderly, 6 of the 8 subjects completed one week actigraphy and the other two subject worn actigraph for 4 and 5 days including the night of earthquake. One to three weeks after retrieving the actigraphic data, the situation related to sleep was asked with informing of the individual results of actigraphy. The subjects were 3 men and 5 women (mean age, 73.1 ± 4.3 years) who were living in Sendai-city where the intensity of earthquake was registered as 6-lower. This intensity is defined by Japanese Meteorological Agency as degree of shaking as "Difficult to keep standing" and "A lot of heavy and unfixed furniture moves and falls". The area where the subjects were living did not suffer from Tsunami attacks. While some of the subjects' house suffered slight damage by the earthquake, two subjects moved to an asylum or her relative's house after the earthquake.

In the night of the earthquake, mean value of sleep efficiency was 72 ± 19%, and 5 out of 8 subjects showed the lowest value in the data collection period. A subject who showed the lowest value of 40% among the subjects slept in an asylum which was a school gymnasium without heating system. In the second night after the earthquake, time to go to bed tended to become earlier probably due to poor sleep in the last night and blackout caused by earthquake. Unusual situation possibly affecting nocturnal sleep reported by the subjects were aftershock earthquake, coldness, tight clothing able to go out, changing the bedroom for security. These results should be taken into account for considering future provision in case of disaster.

PO-2-172

ANNUAL CHANGE OF CIRCADIAN RHYTHM IN WINTERING EXPEDITION MEMBERS IN ANTARCTICA

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Background: Biological clocks synchronize and modulate circadian rhythms of systemic organs. Disruption of circadian rhythm are not only associated with an enhanced risk of insomnia, but also induce variety of other disease, such as metabolic disorder. Circadian rhythms are known to be affected by external stimulation, such as short sunlight and long darkness. However, it is uncertain how impact dose external environment gives the circadian rhythm. Antarctic environment is characterized by extremely low ambient temperature and seasonal variation in daylight time. To clarify the change of an accurate circadian rhythm from extreme circumstance, we evaluated continuous 24-hour RR intervals measurement in Antarctica.
Subjects and methods: The subjects were ten males and one female recruited from the members of the 50th and 51st Japanese Antarctic Research Expedition (Mean age: 40.6 years). Assessment of circadian rhythm using RR intervals obtained from Holter ECG under free living. During their 13 months sojourn in the Antarctic base, data collection was conducted every 3 months (March, June, September, and December).
Results: The mean annual circadian rhythm of HF and L/H were significantly different every season ($P < 0.0001$, ANOVA). Circadian rhythm of HF significantly prolonged in June than in September (June vs. September = 25.1 hour [20.4–27.0] vs. 30.2 hour [24.1–36.3], $P = 0.028$). And circadian rhythm of HF in June tended to prolonged than in March. Circadian rhythm of L/H significantly prolonged in June than in March (June vs. March = 26.1 hour [23.8–28.5] vs. 23.2 hour [20.8–25.6], $P = 0.046$). Sleep evaluation was delayed sleep phase from March to June for approximate one hour ($P < 0.05$).
Conclusion: The circadian rhythm prolonged in June in Antarctica and it might be related to the delayed sleep phase due to lack of sunlight in winter.

PO-2-173

CHANGES IN BLOOD AMINO ACID LEVEL ASSOCIATED WITH SLEEP DEPRIVATION IN RATS

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Introduction: Since some of critical neurotransmitters that control sleep/wake status are amino acids per se (i.e., GABA, glutamate, glycine) or synthesized from amino acids (i.e., monoamines), it is possible that an altered balance and quantity of amino acids can cause sleep disturbances. Similarly, sleep disturbances may induce changes in amino acid balances. In addition, since sleep disturbances are associated with changes in blood leptin and ghrelin levels, sleep disturbances may also cause metabolic changes in blood amino acids. However, there are no reports to directly address these questions. We therefore evaluated any changes in blood amino acid level associated with sleep changes using rodents.
Methods: Adult male Sprague-Dawley rats (n = 6) were acutely sleep deprived with gentle handling from ZT 0 (light on) to ZT 6 and then recovery sleep was allowed from ZT 6. The blood samples were collected from the tail vein every 3 hours from ZT 0 to ZT 12 in these rats. The same rats were used in a control test, and blood was also collected at each time point. Plasma amino acid concentrations were measured by an automatic amino acid analyzer.
Results: We could reliably measure more than 40 amino acids, including essential amino acids from small amount of plasma (7 ul). Most of the amino acids measured declined across time in both the baseline and sleep-deprived groups. Noticeable changes between the baseline and sleep-deprived groups were for glutamic acid (Glu), but no differences were seen in a large majority of amino acid measured. Of interest however, changes in Glu may have been due to the sleep deprivation, since the increase in Glu in the sleep-deprived rats was reduced when the rats were allowed to have recovery sleep.
Conclusion: Our results showed that acute sleep deprivation for 6 hours induced small changes in blood amino acid levels. Therefore, further investigations of chronic sleep restriction or sleep and circadian disease-oriented experiments will be required to substantiate the relationship between changes in amino acids and sleep.

PO-2-174

PHYSIOLOGICALLY BASED MODELING IN EXPLORATION AND PREDICTION OF SLEEPINESS ON ATYPICAL WORK SCHEDULES

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The effects of shift work on circadian entrainment and sleepiness are examined using a physiologically based mathematical model. The model accounts for the dynamics of the sleep-related brain nuclei in hypothalamus and brainstem according to Phillips & Robinson model (2007) and for entrainment of the circadian pacemaker to light as per St. Hilaire et al. model (2007). This approach allows studying entrainment to shift schedules in the long term and to probe the biological mechanisms underlying changes of sleepiness. In contrast to most of the earlier studies the present model accounts for the dynamic interactions between the circadian and homeostatic processes along with changes in external cues that are affected by the state of the model (sleep, wake-rest, wake-work), allowing a broader range of applications.
Here this model is applied to the simplest case of permanent shift schedules in order to understand the basic mechanisms and to lay the foundation for examining more complicated schedules and conditions, such as rotating shifts and natural light input. The results demonstrate that, in good agreement with experimental data, average sleepiness increases during the first days on the evening, night, and early morning shifts, but is unchanged for normal daytime work. This is explained by an inability to sleep enough during the active circadian phase and the resulting increase of homeostatic pressure. After this initial increase, sleepiness decreases and stabilizes due to circadian entrainment to the new external cues provided by the shifts. The simulations reveal the

presence of a critical shift onset time which depends on light conditions and circadian parameters, and separates the shifts leading to phase advance and those leading to phase delay of the circadian pacemaker. The shifts starting around this time take longest to entrain, and are expected to be the worst for the long term performance and well-being of the workers. The results are very robust to the presence of noise which was simulated as either random changes in ambient lighting or in mean potentials of the neuronal populations.

PO-2-175

SLEEP AND VIGILANCE OF ON-CALL PHYSICIANS IN JAPAN

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Objectives: Long work hours and work schedules may have a negative impact on vigilance. It is possible to raise drowsiness and lead poor work performance under insufficient sleep condition. In Japan, there is a custom to work on day duty after on-call. We examined sleep status and vigilance of physicians in Japan to investigate how these states would change before and after on-call duty.
Methods: A total of 28 physicians (13 at a university hospital and 15 at a municipal hospital, 20 men and 8 women) aged 26–43 years were followed by the wake-sleep study at before and after on-call duty. Total Sleep Time (TST) was obtained by wrist actigraphy. Vigilance was calculated from visual response time to random light signals for 10 minutes, measured using the Psychomotor Vigilance Task (PVT) monitor. PVT tests were conducted right before and after on-call duty. At the same time, subjective sleepiness was asked by Karolinska Sleepiness Scale (KSS).
Results: TST of the night during on-call duty was significantly shortened than the night before the on-call duty (273 ± 100 to 404 ± 80 min, $p < 0.001$). Compared with the morning before on-call duty, the subjective sleepiness was raised significantly after on-call duty (3.12 ± 1.1.21 to 5.15 ± 1.87, $p < 0.001$). The vigilance, the median reaction time by PVT, also showed a significant drop after the on-call duty (223 ± 30 to 249 ± 44 ms, $p = 0.039$).
Discussion and Conclusions: The results showed that on-call duty may affect on vigilance of the next day duty as the sleep restriction by on-call which would lead sleepiness. The day duty straight after on-call under the lower vigilance state could increase social risks which should be managed from sleep hygiene perspective.

PO-2-176

ASSOCIATED FACTORS OF POSSIBLE SHIFT-WORK DISORDER IN NURSES WORKING WITH RAPID ROTATION SCHEDULE IN JAPAN

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Previous studies showed that the workers who meet the criteria of shift-work disorder (SWD) are at a risk for health and behavioral problems, possibly leading to social and economic burden. We explored the associated factor of possible SWD in nurses working with rapid rotation shift-work schedule in Japan using a cross-sectional questionnaire survey. The eligible participants were 1493, and responses were obtained from 1202 nurses, including 727 two-shift workers and 315 three-shift workers. Questionnaire were consisted of the items relevant to demographic variables, family structure, household duties, job position, working schedule, existence of illness, food and physical exercise habits, and sleep problems. The participants with reported insomnia and/or excessive sleepiness subjectively related to their shift-work schedule for at least one month were categorized as possible SWD. The percentage of possible SWD participants in shift-worker was 24.4%. The result of multivariate logistic regression analysis to explore the associated factors for the existence of possible SWD in shift-worker showed that nurses who were younger, frequently missed a meal, and had eveningness-chronotype were likely to be associated with possible SWD. The result of this study was inconsistent with that of previous studies which suggested that eveningess-type individuals can tolerate shift-work. This inconsistency might be partly attributed to the rapid rotation schedule in which 87.5% of the subject shift-workers reported that night work shift was not inconsecutive. This result suggests that minimizing the delay of circadian rhythms might play a key role on the prevention of SWD in the shift-workers with rapid rotation schedule.

PO-2-177

ONE DAY OFF FOLLOWING CONSECUTIVE NIGHT SHIFTS IS ENOUGH TO MAINTAIN WAKEFULNESS AND COGNITIVE FUNCTION IN NURSES WORKING ON FAST AND FORWARD ROTATING SHIFT

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Objective: The three-shift working schedule with fast and forward rotation is common in the medical field in Taiwan. Nurses have one day off between the end of consecutive night shifts and the beginning of the next day shifts. During the off-day, one would be expected to overcome the feeling of physical and mental tiredness and to keep awake during the daytime for readjustment of their circadian rhythm. We explored the change of cognitive function and objectively measured sleep propensity in the daytime after three consecutive night shifts. Sleep-related hormones (growth hormone; cortisol; prolactin; thyrotropin, TSH) were also detected during the daytime. We further investigated the factors associated with mean sleep latency (MSL) of Multiple Sleep Latency Test (MSLT) and Maintenance of Wakefulness Test (MWT).
Methods: The study recruited 20 nurses (mean age 26.0 ± 2.0 years) from the acute psychiatric ward. We evaluated the changes on sleepiness vigilance, and performance on the day after three night shifts, using MWT, MSLT, Stanford Sleepiness Scale (SSS), Wisconsin Card Sorting Test (WCST), Digit Symbol Substitution Test, Symbol Searching Test, Taiwan University Attention Test, and collected sleep related endocrine. All of the tests were administered four times at 2 h intervals.
Results: The subjects had no increase in sleep propensity measured by MWT or MSLT despite of increased self-reported sleepiness by SSS. There was no time of day effect on the neuropsychological tasks. Age was negatively associated with the MSL of MWT and positively associated with the MSL of MSLT. The perseverative errors in WCST were negatively associated with the MSL of MWT. TSH level was significantly elevated during the daytime and positively associated with the MSL of MWT.

Conclusions: We conclude that nurses did not have increased sleep propensity and impaired neuropsychological performance in the daytime after three consecutive night shifts when they were trying to readjust circadian rhythm. This ability might be modulated by TSH and compromised by ageing and tasks which require a high attentive load.

PO-2-178

NURSES WORKING ON FAST ROTATING SHIFTS HAVE MORE IMPAIRED PERCEPTUAL AND MOTOR ABILITIES DURING THE END OF A NIGHT SHIFT

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Objective: A three-shift working schedule with faster rotation is common in the medical field in Taiwan. The aim of this study was to compare cognitive performance among three groups working two, three and four consecutive night shifts, respectively, at the end of the night shift and at the time of maximum fatigue (3–4 a.m.).
Methods: Sixty-two nurses (mean age 26.4 ± 2.0 years) were recruited from the acute psychiatric ward and randomly assigned into three groups. The exclusion criteria were current use of hypnotics, regular coffee drinker, psychiatric illness, major systemic disease, and sleep disorders. Cognitive performance included the State-Trait Anxiety Inventory, Stanford Sleepiness Scale, Wisconsin Card Sorting Test, Taiwan University Attention Test, Digit Symbol Substitution Test and Symbol Searching Test.
Results: The subjects working on consecutive two-night shifts had poorer performances in perceptual and motor abilities than those working on consecutive four-night shifts. There were no differences in demographic data, executive function, or attention among the three groups.
Conclusions: The routine duty of night shift nurses in our hospital is checking medical orders and prescriptions, which requires perceptual and motor abilities. Thus we suggest that rotating night shifts too fast may carry a risk of medical errors occurring.

PO-2-179

SLEEPINESS IN NURSES AND CARE WORKERS ENGAGED IN SHIFT WORK DURING CHILD REARING YEARS

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Objective and background of the study: Night shift can have a significant impact on the physical well-being of workers, mainly sleepiness, because this shift can last from 12 to 17 hours. Especially, working mothers rearing young children may suffer great physical effects, because they have a lot to do even after returning home. The objective of this study was to assess the sleepiness in nurses and care workers engaged in shift work during child rearing years.
Method: A self-administered questionnaire was administered to 19 nurses and care workers who worked in a chronic disease unit at Hospital A. The questionnaire included subject characteristics, PSQI, KSS, and the revised "Questionnaire of Subjective Symptoms" score, and was administered over 3 consecutive days. The KSS was completed 3 times per task before work, during breaks, and after work, and the revised "Questionnaire of Subjective Symptoms" was completed before and after work.
Results and Discussion: The mean KSS score for night shift was 2.77 before work, 4.21 during breaks, and 4.98 after work, with no difference between subjects rearing young children and those not. The corresponding score for day shift was 4.06 Before Work, 2.51 During breaks, and 3.59 After Work in subjects rearing young children and 3.11, 4.03, and 3.24 in those not. For day shift, there was no significant difference in the KSS during work between the subjects rearing children and those not. However, the mean score on the "Questionnaire of Subjective Symptoms" for day shift differed significantly between those rearing children and those not. Notably, the score before work was not related to whether or not they were rearing children, but there was a significant difference in the score after work between those rearing children (Factors I, 1.80, II, 6.40, III, 8.20, IV, 9.20, and V, 8.40) and those not (Factors I, 11.86, II, 12.00, III, 10.86, IV, 14.86, and V, 9.14), those not rearing children reported significantly more intense feelings of instability (Factor II) and local pain or dullness (Factor IV).

PO-2-180

IMPACT OF EXTENDED DURATION WORK SHIFTS ON DROWSY DRIVING, SUBJECTIVE SLEEPINESS AND DISTRACTIBILITY WHEN DRIVING

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Background: Acute and chronic sleep deficiency is an inherent part of medical training in the US due to the repeated exposure to extended duration work shifts, and is associated with increased medical errors and attentional failures, and increased incidence of crashes on the drive home. Here, we assess self-reported drowsy driving in trainee physicians on the commute to and from work.
Methods: A prospective, repeated measures design, whereby 16 trainee physicians (age 24–29 y) completed daily sleep diaries and drive diaries for each drive to and from the hospital over 3–6 weeks. For each commute to and from the hospital, participants completed the Karolinska Sleepiness Scale (KSS) ratings at the beginning and end of each drive, and reported sleep-related incidents (i.e. falling asleep at a stop light, hitting the rumble strip) and sleepiness-alleviating actions (i.e. winding down the window, using a cell phone).
Results: In comparison to the intervening day shifts, KSS levels were higher at the start and end of the drive on the commute home following an extended duration work shift ($p < 0.005$), with drowsiness levels increasing over the course of the drive ($p < 0.05$). More trainee physicians reported a drowsiness-related event on the journey home (98.2% vs. 50%), and were significantly more likely to report falling asleep at a stop light, being distracted having a lack of awareness and shouting aggressively ($p < 0.01$). They were also more likely change the music often, become mentally occupied, open the window, read and use the cell phone while driving their vehicle ($p < 0.05$). Finally, drowsiness levels at the beginning of the drive predicted the number and severity of incidence trainee physicians encountered in a dose-dependent manner.
Conclusions: Extended duration work shifts inherent in US physician schedules result in elevated levels of drowsiness while driving, which

in turn, leads to an increased likelihood of incident risk on the commute home. Sleepiness ratings prior to commencing the drive were predictive of the number and severity of sleepiness-related adverse driving incidents.

PO-2-181

SLEEP QUALITY AND ASSOCIATED FACTORS OF RADAR MONITORING WORKERS

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Background: Radar monitoring workers play an important role in aviation safety and military combat readiness. Sleeping quality and shift work may disturb the normal circadian rhythm and affect the decreased alertness and responsiveness of their duty. Furthermore, poor sleep quality may be associated with cardiovascular and neurological diseases in the long-term. The purpose of this study was to explore the correlation between sleep quality status and its associated factors (including job strain, fatigue, personal characteristic factors as well as environmental factors) among radar monitoring workers.
Design: A cross-sectional study of 242 radar monitoring workers and 431 office workers as a reference group were recruited. The Swedish occupational fatigue inventory (SOFI) was used to evaluate fatigue. While Demand-control-support model (JCQ), Effort-reward imbalance (ERI), and Stress-Satification Offset Score (SSOS) were used to evaluate job strain. Pittsburg Sleep Quality Index was used to measure the sleep quality. Questionnaire was used to collect personal characteristics, working types and duration, and disease history.
Results: There were significant sleep quality differences between these two groups. The multivariate analysis indicated that age (≥30 vs. <30) (OR 1.75, 95% CI 1.01 to 3.01), shift work (OR 1.67, 95% CI 1.05 to 2.67), current smoking habit (OR 1.88, 95% CI 1.11 to 3.17), coffee consumption habit (OR 1.82, 95% CI 1.13 to 2.9), high strain (vs. low strain) (OR 2.30, 95% CI 1.16 to 4.55), fatigue (OR 1.42, 95% CI 1.24 to 1.63), noisy environment (OR 2.16, 95% CI 1.28 to 3.65), and high temperature environment (OR 2.85, 95% 1.73 to 4.69) may be the influencing factors of poor sleep.
Conclusion: The poor sleep quality of radar monitoring workers may be associated with shift work, job strain, current life style factors, and sleeping environmental factors.

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SLEEPING ABOARD AIRPLANES: UNKNOWN RISKS

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Little is known about the physiological effects for crew and passenger when sleeping in airplanes under hypobaric conditions. At cruising altitude the cabin pressure equals an altitude of 8000 ft. At the DLR-Institute of Aerospace Medicine, 16 healthy subjects (8 female, average age 28 years±4 SD), slept in a pressure chamber furnished as crew-rest-compartment during a realistic flight simulation concerning atmospheric conditions and noise. Blood oxygen saturation (SpO2), heart rate, and Sleep-EEG were recorded during the 4 h sleep period. Morning performance was tested using an unstable tracking task reflecting typical operator demands. A control group of 16 subjects (8 female, average age 26 years±6 SD), slept 4 h in private sleeping rooms of the DLR-isolation unit in normobaric conditions. SpO2 and heart rate differed significantly between groups ($p < 0.0001$). During sleep period time (SPT) a mean SpO2 level of 96% (±1 SD) and a mean heart rate of 62 bpm (±8 SD) were measured in normobaric conditions, whereas mean SpO2 level in the pressure chamber was 88% (±1 SD) with a mean heart rate of 73 bpm (±7 SD). In hypobaric conditions for 83% (±5%) of SPT the average SpO2 dropped below 90% and for 4% of SPT even below 85% SpO2. The mean minimum SpO2-level was 81% (±3 SD). SPT and sleep efficiency did not differ between groups, but deep sleep ($p < 0.05$) and REM sleep ($p < 0.01$) were significantly reduced in hypobaric conditions in favor of the light sleep phases (N1 $p < 0.05$, N2 $p < 0.01$). Performance was significantly impaired in the experimental group ($p < 0.05$). The recuperative function for crew members sleeping in a crew-rest-compartment during flight seems limited since performance and sleep are impaired, and SpO2 drops considerably. Sleep aboard an airplane induced hypobaric hypoxia in young, healthy subjects. To date, the degree of arterial hypoxemia that should be considered as being harmful remains unclear. However, passengers with a SpO2 below 85% in the hypoxic challenge test are recommended to receive supplemental oxygen during flight. For risk groups sleep during flight should be regarded with care.

PO-2-183

FOOD INTAKE BEHAVIORS OF IRREGULAR SHIFT WORKERS AFFECTED THE CHRONOTYPE (MORNINGNESS-EVENINGNESS TYPE)

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Background: In modern society, shiftwork has many advantages, for example improvement of productivity and safety. So shiftwork is essential for our life. However, shiftwork hasn't only advantages but also many disadvantages. Previous studies suggested that shiftwork disturbed lifework, increased risks of various diseases as problems. As one of their problems, some previous studies showed that shiftwork affected shiftworker's food intake behaviors.
Purpose: The aim of this study investigates the affects of shiftwork to food intake behavior on chronotype (morningness-eveningness type) as chronobiological aspect.
Method: Participants were 225 irregular shift work nurses. This study was investigated by Questionnaire structured demographics of participants, the Morningness (M-type)-Eveningness (E-type) Questionnaire and the Food Intake Questionnaire. It was compared about food intake behaviors (food style, reason of selection, hunger before food intake, enjoyment during food intake, and satiety after food intake.) on breakfast and dinner with M-type and E type. On analysis, it was tested by chi-square test and Mann-Whitney test.
Result: Before day-work, there was a tendency difference by type of food among M-types and E-type ($p = 0.079$). E-type after night-work became significantly higher in the score of satiety afterward in comparison with M-type ($p = 0.016$). Sense of hungry before meal of E-type after day-work compared with M-type tended to be high ($p = 0.077$).
Conclusion: Therefore, it was suggested that M-type is more susceptible to the effect of shiftwork in food intake behavior than E-type.

PO-2-184

COMPARISON OF SLEEP HABIT IN JAPANESE MEN STUDENTS BEFORE, DURING AND AFTER SCIENCE CRUISES

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Objective: This study aims to estimate effects of the life on the ship on sleep habit and diurnal rhythm during the cruise and the following period in Japanese university students.
Participants and Methods: Four men participants (22–28 yrs) continued to note the sleep diary and also to answer the questions on daily mood, falling in sleep, sleep quality, mood at waking up from one month before cruise(s) (Participant = P-A: Sep 1–15, P-B: May 5–Jun 28, Sep 1–15, P-C & P-D: May 5–Jun 28, Sep 1–Oct 15, Oct 21–Nov 21), during the cruise and till one month after the cruise. An integrated questionnaire including sleep habit and MEQ was also administered to them just before the cruise and one month later from the cruise.
Results: The regularity of sleep-wake rhythms were extremely higher during the cruise than that before or after the cruise in all four participants ($p < 0.01$). Sleep-wake schedule was more regular in two weeks after the cruise than that in two weeks before the cruise ($p = 0.016$) in P-A. Daily mood was significantly higher after the cruise than that before the cruise ($p = 0.002$) in P-B. In P-C, average wake-up time in week-end was 9:00 before the cruise, whereas the average value became earlier and 7:20. After the cruise, the wake up time was fixed for one week and then gradually delayed in P-D.
Discussion and conclusion: Fixed times of meals and works during the cruise might promote, in some extent, the regularity of sleep wake cycle and mental health at least in one or two weeks after the cruise.

PO-2-185

THE ASSOCIATION BETWEEN SLEEP PROBLEMS AND PERCEIVED HEALTH STATUS: A JAPANESE NATIONWIDE GENERAL POPULATION SURVEY

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Objective: Sleep problems have been reported to have a serious impact on daily functioning and to have an association with human well-being. To see the contribution of individual sleep problems on physical and mental health, we conducted a nationwide epidemiological survey and investigated the relation between sleep problems and perceived health status.
Method: The Nihon University Sleep and Mind Epidemiology Project (NUSMEP) was conducted in August and September, 2009, using face-to-face interviews. People aged 20 years or older were selected randomly from all areas of Japan, by using a three-stage stratified sampling method. Finally 2,559 people (response rate 54.0%) completed a questionnaire on perceived physical and mental health status, and sleep problems, including the presence or absence of insomnia symptoms (i.e., difficulty initiating sleep (DIS), difficulty maintaining sleep (DMS), and early-morning awakening (EMA)), excessive daytime sleepiness (EDS), short sleep duration (SSD), and insufficient rest by sleep (IRS).
Results: Poor perceived physical and mental health status were found in 16.9% and 11.4% of the participants. The prevalence of DIS, DMS, and EMA was 14.8%, 26.6%, and 11.7%. Subject having at least any of the three insomnia subtypes were 32.7%. The prevalence of EDS, SSD, and IRS was 1.4%, 4.0%, and 21.7%. Multiple logistic regression analyses revealed that DMS, SSD, and IRS were negatively associated with poor perceived physical health status, while DIS, EDS, and IRS were negatively associated with poor perceived mental health status.
Conclusion: These results suggest that individual sleep problems have their own significance with regard to perceived physical and/or mental health status.

PO-2-186

GENETIC ASSOCIATIONS BETWEEN SHORT SLEEP DURATION AND INCIDENCE OF HYPERTENSION: A SIX-YEAR FOLLOW-UP KOREAN GENOME EPIDEMIOLOGY STUDY

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Objectives: Hypertension is caused by complex interactions between genetic and environmental factors. Despite evidence for an association between short sleep duration and the development of hypertension, genetic factors associated with this effect have not been defined. Here we prospectively investigated the incidence of hypertension in subjects with short sleep duration over a 6 year follow up period, and identified associated genetic variants in a genome wide association study.
Methods: Hypertension was defined by systolic or diastolic blood pressure of >140 or >90 mmHg, respectively, or when participants reported using anti hypertensive medications. Sleep duration was determined by questionnaire. Three categories of sleep duration were established: <5 hours, 5–7 hours, and >7 hours. Genotyping was carried out using the Affymetrix Genome-Wide Human Single Nucleotide Polymorphism (SNP) Array 5.0.
Results: Of the 4,965 individuals included in our study, 1,071 (543 of 2,330 men and 528 of 2,635 women) developed hypertension. The cumulative incidence of hypertension during the 6 year study period was 21.6%. Sleep duration of <5 hours was associated with an increased risk of incident hypertension only in premenopausal women (adjusted hazard ratio 2.34, 95% confidence interval 1.30–4.21). The diplotypes of LRRC7, MYO1D, AUTS2, TGFBR3, JMJD2A, THSD4, SNTG2 and ACPL2 were associated with this increased risk.
Conclusion: This prospective population-based study showed that premenopausal women with short sleep durations had an increased risk of incident hypertension, and found associations with specific genomic markers.

PO-2-187

SOCIODEMOGRAPHIC AND SOCIOECONOMIC DIFFERENCES IN SLEEP DURATION AND INSOMNIA-RELATED SYMPTOMS IN THE FINNISH ADULT POPULATION

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Background: Poor sleep tends to be patterned by sociodemographic and socioeconomic circumstances. However, we lack nationally representative studies. The aim of this study was to examine the associations of sociodemographic and socioeconomic factors with sleep duration and insomnia-related symptoms.
Methods: Data were derived from the cross-sectional Health 2000 survey (2000–2001) representative of the adult Finnish general population (n = 5578, aged 30+ years). Sociodemographic and socioeconomic circumstances comprised gender, age, marital status, number of children, parental and own education, household income, employment status, and residential area. Insomnia-related symptoms over the previous month and average sleep duration were based on self-reports. Multinomial logistic regression models were adjusted first for gender and age, second for sociodemographic factors, and third for all covariates simultaneously.
Results: On average 71% of adult Finnish men and women slept 7–8 hours a day. Frequent insomnia-related symptoms were more prevalent among women (14%) than men (10%). Not being married, not having children, having low education, having low income, being unemployed, and on old age or disability retirement were associated with frequent insomnia-related symptoms. Short and long sleep duration were associated with similar factors. Additionally, living outside urban areas was associated with long sleep duration and low parental education with short sleep duration.
Discussion: Disadvantaged socioeconomic position in adulthood are associated with poor sleep. In promoting optimal sleep duration and better sleep quality, families with low income level, unemployed people and those on disability retirement should be targeted.

PO-2-188

DOES SLEEP POSITION AFFECT AROUSAL FROM SLEEP PATHWAYS IN INFANTS BORN PRETERM?

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Previous studies have shown that infants born preterm are more likely to succumb to SIDS, and also exhibit depressed total arousability when compared with term infants. As the final cortical element of the arousal process may be the most critical for survival, we hypothesised that the increased vulnerability of preterm infants to SIDS could be explained by depressed cortical arousal responses. We aimed to evaluate the effects of preterm birth on stimulus-induced arousal processes in both prone and supine sleeping positions. Ten healthy ex-preterm infants were studied with daytime polysomnography, in both supine and prone sleeping positions, at 2–4 wk, 2–3 mo and 5–6 mo post-term. Arousal from sleep was induced using a pulsatile jet of air at increasing pressures to the nostrils. Sub-cortical activations and cortical arousals (CA) were scored using standard criteria and expressed as proportions of total arousal responses. Data were then compared with data from 13 healthy term infants. In term infants at 2–3 mo of age, prone sleeping was associated with increased CA when compared to the supine position and the other ages studied. By contrast, in preterm infants this positional effect of increased CA when prone was evident at all three ages studied. We showed that prone sleeping promoted cortical arousal responses in healthy preterm infants throughout the first six months of post-term age. We have previously suggested that enhanced CA represents a critical protection against a potentially harmful situation; we speculate that such protection may be absent in SIDS victims.

PO-2-189

ALTERATION OF CHILD SLEEP IN JAPAN FROM 2000 TO 2010

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Introduction: In 2000, 49% of children in Japan aged 18 to 83 months fell into sleep 10 pm or later. The rate in 2010 was 30%. I am the founding member of web site named hayaoki site opened in 2002. Hayaoki means "wake up early in the morning" in Japanese. Hayaoki site is undoubtedly the first runner for the promotion to keep bedtime early, to wake up early, and to secure enough sleep duration for children in Japan. In this paper, I will look back these almost 10 years and view the next several years regarding child sleep in Japan.
Beginning of the campaign: Our campaign is consistent with recent scientific findings of the importance of sleep health practices (1. Increase exposure to morning light. 2. Engage in physical activity during daytime. 3. Sleep in the dark during the night. 4. Eat regular meals. + Avoid substances that disturb sleep (e.g., caffeine, alcohol, nicotine) and excessive media exposure.). We, members of hayaoki site, have had more than 100 lectures a year all around Japan. Since our promotion has been based on the scientific issues, many parents, health care takers, nursery school teachers and nurses have listened to our explanation.
Spread of the campaign: In 2006, we were asked to join the national-wide promotion to keep bedtime early, to wake up early and to take breakfast, organized by the Ministry of Education, Culture, Sports, Science and Technology. Tokyo Metropolitan has also begun promotion to keep bedtime early, to wake up early, and to secure enough sleep duration for children in 2008. Finally, 30% of children in Japan aged 18 to 83 months was found to fall into sleep 10 pm or later in 2010. It seems that our promotion have reached a goal.
Prospects: In spite of obtaining the goal, I am not satisfied on the sleep situation of children in Japan. I will indicate four points. 1. Short sleep duration. 2. Short nap duration. 3. Education on sleep. 4. Side effects of national-wide campaign.
Conclusion: We should keep spreading the basic knowledge on sleep to parents, pediatricians, family doctors, health care takers, nursery school teachers, nurses and policymakers.

PO-2-190

SIGNIFICANT RELATIONSHIP BETWEEN SLEEP CHARACTERISTICS AND BEHAVIORAL ATTRIBUTES IN JAPANESE SCHOOL CHILDREN

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Objectives: The total sleep duration of Japanese children is the shortest in the world. Sleep disturbance in children may be linked to daily school and cognitive performance. To clarify the relationship among children's sleep characteristics, behavioral attributes, school records, and their parents'sleep quality, we administered a questionnaire survey.
Methods: A total of 415 children(age range, 6–12 years; 221 boys and 194 girls) from one elementary school in Kurume city, Japan, participated in this study. We used the Japanese version of the Children's Sleep Habits Questionnaire (CSHQ-J), the Strengths and Difficulties Questionnaire (SDQ), and, for the parents, the Japanese version of the Pittsburgh Sleep Quality Index (PSQI-J), as well as each child's body weight, height, medication, school records and family history. The SDQ is a short screening instrument which addresses "Emotional symptoms", "Hyperactivity/inattention", "Conduct" and "Peer problems".
Results: The average values for the children's sleep duration, CSHQ-J, and SDQ, and the parents'PSQI-J were 9.1 hours, 44.7, 9.3, and 5.4, respectively. CSHQ-J showed a significant positive correlation with SDQ ($P < 0.01$) and the parents'PSQI-J ($P < 0.01$). However, CSHQ-J showed no correlation with body mass index or school records. School records showed a significant negative correlation with SDQ ($P < 0.01$). Children diagnosed with developmental disorders ($n = 43$) showed significantly higher CSHQ-J and subscales than other children. The collection rate was 95.2%.
Conclusion: The significant relationship between the children's CSHQ-J and SDQ and the parents'PSQI-J indicates that children's negative behavioral attributes may adversely affect children's and their parents'sleep quality. The poor sleep quality in children with developmental disorders suggests that behavioral attributes may play an important role in sleep quality.

PO-2-191

DEVELOPMENT & FEASIBILITY TRIAL OF A MINDFULNESS-BASED MULTI-COMPONENT IN-SCHOOL GROUP SLEEP INTERVENTION FOR POOR SLEEP & ANXIETY SYMPTOMS IN ADOLESCENT GIRLS

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Introduction: Existing literature links poor sleep, bedtime cognitive/physical arousal, and anxiety symptoms in adolescents. This pilot study examined the feasibility of a mindfulness-based, multi-component, in-school group intervention targeting poor sleep, using sleep and anxiety as outcome measures.
Methods: 62 Year 9 students (age 13–15) at a girl's college completed screening scales: Pittsburgh Sleep Quality Index (PSQI) and Spence Children's Anxiety Scale (SCAS). Self-reported poor sleepers were invited to a home interview for past/current psychopathology and suitability for the program, yielding a total of 10 participants. The 6-session program was based on Bootzin & Stevens (2005) with added stress/anxiety-specific components. Sessions ran weekly after school covering key aspects of: basic mindfulness concepts and practice, sleep hygiene, sleep scheduling, evening/daytime habits, stimulus control, skills for bedtime worries, and healthy attitudes to sleep. Treatment-related changes were measured by pre-post scores on the PSQI, SCAS, and objectively measured sleep on 7-day actigraphy.
Results: Mean (SD) baseline global PSQI and SCAS scores for group participants were 10.9 (2.5) and 38.3 (16) compared to 7.3 (3.7) and 27.9 (14.2) for the remaining screening sample. Based on effect-size analyses, participants who completed the program (90%) showed significant improvement on objective sleep onset latency (SOL), sleep efficiency, and total sleep time; actigraph data also showed significantly earlier bedtime, rise-time, and smaller daily bedtime variation. Post-intervention global PSQI and SCAS scores were 6.2 (3.6) and 27.3 (18.5), significantly lower than at baseline, and there was significant improvement on subjective SOL, sleep quality, sleep-related daytime dysfunction, and the SCAS Panic Agoraphobia subscale.
Conclusion: A mindfulness-based, multi-component, in-school group sleep intervention following brief screening is feasible, and has the potential to improve sleep and anxiety symptoms.

PO-2-192

WITHDRAWN

PO-2-193

SURVEY OF ACTUAL SLEEPING CONDITIONS IN MEDICAL UNIVERSITY STUDENTS: COMPARISON OF NURSING STUDENTS WITH THOSE OF OTHER FACULTIES

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Objective: To investigate sleep quality on awakening in medical university students and clarify the characteristics of sleeping.
Methods: We surveyed medical university students using the MA version of the OSA sleep questionnaire. The survey was conducted with the approval of the ethics review in an affiliated university. Subjects were provided with sufficient information, and those who consented were asked to complete the questionnaire and deposit it into a locked box. The standardized score of the OSA was compared.
Results: We surveyed 49 nursing students about one month after admission, and noted that they slept for about 5.3 hours on average. Eighty percent of the students felt drowsiness on awakening, and 45% of them felt difficulty in initiating and maintaining sleep, which suggested a tendency whereby they could not secure sufficient sleeping hours. Regarding dreams, they were divided into two groups (good or bad). Eighty percent of the students could not recover from fatigue. Meanwhile, 42 non-nursing students slept for 5 hours on average. Regarding evaluation of the OSA every five factors, 71% of the students felt drowsiness on awakening. Seventy-one percent of them felt difficulty in initiating and maintaining sleep, suggesting a tendency whereby they could not secure sufficient sleeping hours. Regarding dreams, they were divided into two groups (good or bad). Sixty-two percent of them could not recover from fatigue. Regarding nursing students, the rate of the total score for five factors being below and above 50% was 0 and 14%, respectively. However, regarding non-nursing students, that of below and above 50% was 14 and 12%, respectively. When performing

t-tests for both students, the rate for factor II was likely to be significantly lower in non-nursing students ($p = 0.01$).
Discussion: Both types of university student showed poor results concerning drowsiness on awakening, recovery from fatigue, and sleeping hours; therefore, it may be necessary for them to improve their lifestyle habits.

PO-2-194 / AS-16 Presenter

RECOMMENDED LEVELS OF WALKING PREDICT SLEEP AND HEALTH OUTCOMES AMONG OLDER PEOPLE

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The minimum level of physical activity likely to improve or maintain both health and sleep outcomes among older people has not been explored. The present analyses assess the contribution of physical activity, above and below the 150 minute international guidelines, to sleep and health outcomes reported at baseline.
Methods: Sleep, health, and physical activity data were obtained from a random community sample of 1042 people aged 65+ interviewed in 1985 for the Nottingham Longitudinal Study of Activity and Ageing. Baseline walking was categorized as below (<150 minutes/week) or above (=>150 minutes/week) international guidelines. In models adjusted for age, sex and health status at baseline, predictive relationships were examined between these activity categories and: 21-year all cause mortality (Cox regression); the prevalence of baseline insomnia (logistic regression);and subjectively reported time in bed (multiple regression). Mortality (cause/date of death) was monitored from baseline.
Results: At baseline 441 (48%) and 485 (52%) respondents were categorised as walking below and equal to/above the guidelines threshold respectively. During 1985–2006 the project was notified of 919 deaths. In the adjusted multivariate models, the higher level of walking was significantly associated with increased longevity (HR = 0.78, 95% CI = 0.67–0.89, $p < 0.01$), lower levels of reported insomnia (OR = 0.65, 95% CI = 0.46–0.92, $p < 0.05$) and shorter durations of 'time in bed' ($r^2 = .04$, $F_{(4,908)} = 10.25$, $p < 0.01$).
Conclusion: Internationally recommended levels of physical activity appear to provide a common threshold for superior health and sleep outcomes among older people. Results also suggest that time spent in bed may be an under-researched proxy for inactivity.

PO-2-195

THE JOINT ASSOCIATION OF SLEEP DURATION AND SLEEP PROBLEMS WITH DISABILITY RETIREMENT: A LONGITUDINAL REGISTER-LINKED STUDY

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Objective: To examine the joint association of sleep duration and sleep problems with subsequent disability retirement.
Methods: Baseline survey data were collected in 2000–2002 from 40–60-year-old employees of the City of Helsinki, Finland. Baseline data were linked with disability retirement data until the end of 2010, obtained from the Finnish Centre for Pensions registers (N = 6042). Sleep duration and sleep problems (Jenkins Sleep Questionnaire, assessing difficulties in initiating and maintaining sleep and non-restorative sleep) were derived from the baseline surveys. All-cause disability retirement (N = 561) and the most prevalent diagnostic groups, musculoskeletal diseases (43%) and mental disorders (26%), were examined. Cox regression analysis was used to yield hazard ratios (HR) with 95% confidence intervals (CI).
Results: A joint association of sleep duration and sleep problems with disability retirement was found, implying a higher risk for those with frequent sleep problems. HRs for all-cause disability retirement ranged among those with frequent sleep problems from 2.02 (95% CI 1.53–2.68, sleeping 7 h) to 3.92 (95% CI 2.57–5.97, sleeping 5 h or less). Adjusting for sociodemographic, work-related factors, and health attenuated the associations, which nevertheless remained. The associations were similar for the two diagnostic groups, although stronger for those with mental disorders.
Conclusions: Sleep problems dominate the joint association of sleep duration and sleep problems with subsequent disability retirement. Examining exclusively sleep duration would provide an incomplete understanding of the consequences of poor sleep.

PO-2-196

SLEEP AND ACTIVITY STATUS OF PSYCHIATRIC DAY CARE USERS IN JAPAN – A SURVEY OF A SLEEP AND ACTIVITY LEVEL USING ACTIGRAPHY

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Purpose: We conducted a study of a support program to enable homebound psychiatric patients to self-manage their sleep through the use of non-pharmacotherapy. The purpose of this study is to identify the sleep and activity status of homebound psychiatric patients as the first step of that program.
Method: The subjects of the study consisted of homebound psychiatric patients age 20 or older who were users of day care centers. Sleep and activity status was measured using sleep log, actigraph and self-administered questionnaires. Spearman's rho were determined between age, sleep indices and activity level. Data was collected during the period from September to December, 2009.
The survey was approved by the medical ethics committee of the facility with which the researchers are affiliated and by the day care centers.
Results: The subjects consisted of 9 psychiatric day care users comprised of 3 men and 6 women.
The majority of the subjects generally reported waking up and going to bed at regular times, but some of the subjects exhibited serious sleep disorders in which they repeatedly slept for short periods of time on an irregular basis. With respect to sleep health, all of the subjects were suspected of having at least one sleep problem. With respect to correlations among age, sleep indices, activity level and light exposure, significant correlations were observed between sleepiness scale and sense of having slept, and between activity level and daytime light exposure.
Discussion: Although many of the users of psychiatric day care centers in Japan generally exhibited regular sleep and biorhythms, all of the subjects were suspected of having some sleep disorders, thus suggesting the need to provide support for these subjects relating to improving their sleep. There were no significant correlations observed between

sleep indices and daytime activity levels or light exposure levels. We intend to conduct a study on a specific support program for this purpose by increasing the number of subjects.

PO-2-197

ASSESSING THE RELIABILITY OF A QUESTIONNAIRE TO ASSESS LIFETIME SLEEP QUALITY IN A CASE-CONTROL STUDY OF BREAST CANCER

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Sleep diaries and/or questionnaires are the most cost-effective and realistic option for measuring sleep in large population based studies. There have been a number of formal questionnaires designed for the detailed assessment of sleep quality. However, these instruments have been designed predominantly to assess recent exposures and short term outcomes. The Breast Cancer Environment and Employment Study (BCEES) team has developed a sleep questionnaire that addresses some of the limitations of previous sleep quality questionnaires in assessing lifetime sleep quality. The aim of this study is to assess the reliability of the BCEES sleep questionnaire. Women participating as controls in the BCEES study were invited to participate in the sleep reliability study once they had completed the lifestyle questionnaire, which included the sleep questions. Consenting participants completed the BCEES sleep questions again at least two weeks later. Categorical responses to the two questionnaires were compared using weighted kappa statistics. Preliminary results were based on 189 people who had data available for analysis from both the test and re-test questionnaires. Of these 189 people, 3 had missing data on hours of sleep duration and 8 had data missing on subjective sleep quality. Kappa values for usual duration of sleep on work days was 0.71 (p-value < 0.001) and for usual sleep duration on non-work days was 0.70 ($p < 0.001$). Kappa values for subjective usual sleep quality was 0.75 ($p < 0.001$). Our study found good test-retest reliability on individual items of the BCEES sleep questionnaire. The reliable and valid assessment of sleep quality is critical in providing an accurate assessment of the relationship between sleep quality and health outcomes.

PO-2-198

DIFFERENCES IN OBJECTIVE AND SUBJECTIVE SLEEP IN FIRST-TIME AND EXPERIENCED MOTHERS

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Introduction: Changes in sleep are common across pregnancy and the postpartum period, with poor sleep potentially contributing to postnatal distress. Previous findings have reported differences between objective and subjective measures of sleep, subjective sleep being a better predictor of postpartum mood in healthy women than objective sleep, thus suggesting that subjective sleep is an indicator of overall wellbeing. Sleep differences have also been observed in first-time (FM) and experienced mothers (EM), however subjective and objective measures of sleep have not been compared as a function of parity.

Methods: During the third trimester of pregnancy (Time-1) 36 FM and 35 EM completed measures on mood and sleep, and wore actigraphs for 7 days. Among these participants, 30 FM and 31 EM completed the same procedure within 2 weeks postpartum (Time-2). Mood scales included the Edinburgh Postnatal Depression Scale, the Depression Anxiety Stress Scale, and the Hospital Anxiety Depression Scale. Subjective sleep was assessed using the Pittsburgh Sleep Quality Index.
Results: Analyses confirmed previous findings that both objective and subjective sleep worsen from late pregnancy to the postpartum period. During T-2 both Mood and objective sleep were significantly better in EM than in FM; however, no differences were observed in subjective sleep. Regression analyses revealed an overall significant association between subjective sleep and mood. Comparisons of regression coefficients between FM and EM showed a significantly stronger relationship of subjective sleep and postpartum stress in FM, no significant differences were observed in other variables.
Conclusion: Discrepancy between FM and EM in objective sleep may indicate more effective strategies to cope with sleep disruption in EM. Results support the notion that subjective sleep might reflect psychological wellbeing rather than actual sleep, especially in the case of postnatal stress levels in FMs.

PO-2-200 / AS-13 Presenter

WORK-FAMILY CONFLICTS AND SLEEP MEDICATION: A LONGITUDINAL REGISTER-BASED STUDY

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Background and aims: Work-family conflicts are prevalent among employees and potentially detrimental to health and well-being, including sleep problems. However, longitudinal studies using objective measures on sleep are lacking. This study examined the longitudinal association of work-family conflicts with subsequent sleep medication adjusting for covariates.
Methods: Data were derived from the Helsinki Health Study baseline mail surveys in 2001–2002 (3137 women, 849 men). Data concerning sleep and other psychotropic medication were derived from the Finnish Social Insurance Institution's registers covering all reimbursed prescribed medication in 1995–2007 (ATC-codes). Those currently using sleep or other psychotropic medication at baseline were excluded from all analyses (n = 319). Previous sleep medication five years before baseline was adjusted for in the analyses. Four work to family items measured whether job responsibilities interfered with family life, and four family to work items measured whether family responsibilities interfered with work. Cox proportional hazard models were fitted, adjusting for age, sleep medication five years before baseline, and social, family-, and work-related covariates.
Results: During a five year follow-up, 16% of participants had at least one purchase of prescribed sleep medication. Strong conflicts between family and work were reported by 8%, whereas 16% of participants reported strong conflicts between work and family. Strong family to work conflicts were associated with subsequent sleep medication after full adjustment for social, family- and work-related covariates association (HR = 1.77, 95% CI 1.34–2.33). Strong work to family conflicts were also associated with subsequent sleep medication after full adjustment (HR = 1.37, 95% CI 1.01–1.85). Control analyses excluding those with prior sleep medication (16%) produced slightly stronger results.

Conclusion: Better balance between work and family likely helps prevent sleep medication and underlying sleep problems.

PO-2-201

SLEEP DEPRIVATION RELATED SMOKING, DRINKING AND FATIGUE AMONG MIDDLE-AGED JAPANESE MEN

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Background: Sleep deprivation is one of the biggest health problems in Japan. According to the Japanese National survey in 2006, mean sleeping hours of Japanese male worker was 7.5 hr that was 40 min shorter than in 1976. We are concerned with aggravation of the problem because the 24-hour society is progressing very rapidly.
Purpose: This study investigates the sleep habits of healthy middle-aged men. We focused on smoking, drinking and fatigue which are related to sleep deprivation.
Subjects and Methods: The subjects were 3256 middle-class male employees aged 30 to 59 years old. They attended medical check ups in our clinic from January to December in 2007. The data were gathered from a self-administered questionnaire that investigated lights-out time, getting up time, and the number of awakening times. The relationship between these data and symptoms such as fatigue and not having energy was evaluated. Moreover, the influence of smoking and drinking on sleeping hours and the quality of sleep was investigated.
Results: The mean [±SD] sleeping hours were 6.87 ± 0.02 hours. The younger subjects slept shorter [6.57 ± 0.05 hours in their thirties]. Significant relationship was observed between lights-out time and fatigability [$p < 0.01$], but there was no apparent relationship between getting up time, sleeping hours and fatigability. The number of cigarettes and amount of alcohol consumptions were significantly related to the data on sleep. Particularly, there was an apparent relationship between smoking and getting up time [$p < 0.01$]. The amount of alcohol consumption is significantly related to sleeping hours [$p < 0.01$], lights-out time [$p < 0.01$] and interruption of sleep. Drinking and smoking were also related to fatigue.
Discussion: In our study, sleeping hours were shorter than that in the earlier study. Middle-aged Japanese males may have been cutting down on sleep because of changes in society. Sleep deprivation among middle-aged men in Japan should be considered seriously.

PO-2-202

THE CONTRIBUTION OF SLEEP QUALITY TO SELF-RATED HEALTH AND PHYSICAL AND MENTAL FUNCTIONING: THE JAPANESE CIVIL SERVANTS STUDY

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Introduction: While it is well-known that poor sleep quantity (i.e. short sleep duration) is associated with the development of various diseases, research on the associations of sleep quality with physical and mental health is relatively few.
Methods: The subjects were 3684 public sector employees (2471 men and 1213 women: Mean age 42.8) aged 20–65. Questionnaire survey was conducted in 2003. Sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI) which generates 7 components of sleep quality and one overall sleep quality. Physical and mental health was evaluated using Short Form 36 (SF-36) and subjects with a score below 25 percentile were considered to have poor physical and mental functioning. Self-rated health was evaluated using one item in SF-36. Logistic regression analysis was used to evaluate whether poor sleep quality is associated with poor self-rated health and poor physical and mental functioning. In multivariate analysis, age, socioeconomic status, and personality (affect balance) were adjusted for.
Results: In general, the poorer the overall sleep quality, the poorer the self-rated health and physical and, in particular, mental functioning. All of the subscales of the PSQI (i.e. subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, use of sleep drug, daytime dysfunction) was independently associated with poor self-rated health and poor physical and mental functioning.
Conclusions: Self-rated health and physical and mental functioning are affected by sleep quality. Improvement in sleep quality may have beneficial effects on physical and mental health.

PO-2-203

ASSOCIATIONS OF SLEEP QUANTITY WITH SLEEP QUALITY: THE JAPANESE CIVIL SERVANTS STUDY

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Introduction: This study aims to evaluate the associations of sleep quantity with sleep quality and evaluate whether characteristics of poor sleep quality differ between short and long sleepers.
Methods: The subjects were 3769 public sector employees (2517 men and 1242 women: mean age: 42.6) aged 20–65 working in a local government in Japan. Questionnaire survey was conducted in 2003. Sleep hours was defined as hours between bedtime and rising time and divided into 6 groups, ranging from less than 5 hours to 9 hours or longer. Sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI). Analysis of covariance (ANCOVA) was used to evaluate the associations of sleep quantity (i.e. sleep hours) with poor sleep quality.
Results: Average sleep hours was 7:03 for men and 6:39 for women. The prevalence of poor sleep quality was, in average, 21.5% for men and 31.6%. The lowest prevalence of poor sleep quality was observed for men taking 7–8 hours sleep and women taking 8–9 hours sleep(15.6% and 17.1%, respectively). Both short and long sleepers had poorer sleep quality than average sleepers. While 77.8% of men and 68.6% of women taking less than 5 hours sleep (i.e. short sleepers) had poor sleep quality, 23.6% of men and 29.4% of women taking 9 hours sleep or more (i.e. long sleepers) had poor sleep quality. The reasons of poor sleep quality differed between short and long sleepers. While poor sleep quality among short sleepers was mainly attributable to poor subjective sleep quality and daytime dysfunction, poor sleep quality among long sleepers was mainly attributable to long sleep latency, poor sleep efficiency and sleep disturbance.
Conclusions: The lowest prevalence of poor sleep quality was observed among men and women taking around 8 hours sleep. Both short and long sleepers had poor sleep quality but the underlying causes differed between short and long sleepers.

PO-2-204

EFFECT OF FIVE DAYS SLEEP SHORTAGE ON SPORT RELATED PERFORMANCES

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Introduction: Sports related activities need not only physical but neural and psychological abilities. It has been studies that sleep shortage deteriorate cognitive performances. However, there have not been studies examining how sleep shortage affect sports related activities. In this study, we examined physical and cognitive performances on healthy young subjects to investigate how sleep shortage affect sleep sports related activities.
Methods: Subjects were six healthy young students. In order to measure regular sleep length, subjects wore wrist actigram for 14 days. Experiment was performed on two conditions (regular sleep condition: RSC, sleep deprivation condition: SDC). Subjects took normal sleep in the RSC first two days. On the second day after regular sleep, exercise performances (EX) (aerobic and anaerobic) and cognitive tests (COG) (PVT and dexterity test) were examined. In the SDC, sleep was shortened to 50% of regular sleep length for each subject. EX was measured at 18:00 of the 1, 3, 5 day, and COG was measured at 9:00 every day. Standard PSG was done on the second regular sleep night and 1, 3, 5 shortened sleep nights.
Results: There were no significant differences in exercise performances and cognitive performances between regular sleep and sleep deprivation condition. However number of PVT-false (RT × 500 ms, RT < 150 ms) have an increasing trend. However, sleep variables were significantly different in the sleep consecutive deprivation conditions. Percentage of sleep stage 1 decreased and percentage of slow wave sleep increased in the sleep deprivation conditions ($p < 0.05$).
Conclusion: Results of experiment suggested that five days shortened sleep didn't affect exercise performances and cognitive performances. It may be because improved sleep quality (increased SWS) substitute insufficient sleep to time.

PO-2-205

INDIVIDUAL DIFFERENCES INFLUENCE ON THE EFFECTS OF SLEEP DEPRIVATION DURING FACE RECOGNITION

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Sleep deprivation affects a range of cognitive functions, including those related to social interaction. However, it is currently unclear whether sleep deprivation specifically affects the neural basis of understanding others' emotional states, an essential component of effective social functioning. We used fMRI to examine subjects in sleep-deprived and well-rested states to examine the effects of sleep deprivation on neural activity related to emotional facial expression processing, predicting that activity in empathy-related brain areas would be significantly affected. Taken together, the present study thus aimed to investigate the influence of interindividual psychological differences on patterns of activation in the neural network associated with the perception of facial expression, under conditions of sleep deprivation and normal sleep.
Well-slept participants exhibited significantly greater activation increases in the fusiform gyrus (FG) and insula while observing happy faces. In contrast, neural responses to fearful faces in the inferior frontal gyrus and insula were significantly greater following sleep deprivation. Moreover, higher levels of depression were associated with higher FG responses to happy faces under normal sleep conditions. However, a lower mental health state was associated with higher insula activation in response to fearful faces under sleep-deprived conditions. Our findings suggest that individual differences in mental health (and levels of depression in particular) in healthy individuals can impact on the effects of sleep deprivation on face processing.
These results provide novel evidence supporting the hypothesis that empathy-related brain areas involved in emotion processing are affected by sleep deprivation, consistent with the notion that sleep deprivation affects the processing underlying emotion understanding.

PO-2-206 / AS-11 Presenter

CAN RELATIVE VULNERABILITY TO THE EFFECTS OF SLEEP DEPRIVATION ON PSYCHOMOTOR VIGILANCE BE ESTIMATED USING FEATURES OF DAYTIME PERFORMANCE?

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Some individuals show severe cognitive impairments during sleep deprivation, whereas others are able to maintain high levels of performance. At present, there is no reliable method for predicting how well a person will cope with sleep loss. Here, we examined whether daytime performance on the psychomotor vigilance test (PVT) can be used to estimate a person's relative vulnerability to the effects of sleep deprivation on sustained visual attention. Healthy volunteers (n = 48, ages 21–30) were kept awake for at least 26 hours in a controlled laboratory environment. Every two hours, participants completed a 10-minute PVT. In a retrospective analysis, we stratified participants into top, intermediate, and bottom performance groups based on number of PVT lapses during the usual hours of sleep (i.e., between 16–24 hours after wake). Compared to the top tertile of performers, subjects in the bottom tertile exhibited an earlier wake-dependent decline in PVT performance and had about twice as many lapses during sleep deprivation. Chronotype, circadian phase, and actigraphy-based sleep measures were similar between groups, despite differences in performance vulnerability to sleep loss. We found that some measures of PVT performance variability during the day correlated with lapses during sleep deprivation (Spearman's rho > 0.70; P < 0.05). Participants with the highest number of lapses during sleep deprivation had the most variable PVT response times during rested wake, whereas subjects with the fewest number of lapses during the usual hours of sleep showed relatively lower variability in daytime PVT performance. Our findings raise the possibility that it may be possible to estimate a person's relative vulnerability to sleep loss by assessing features of his/her daytime performance.Research was supported by the Duke-NUS Signature Research Program funded by A*STAR and the Ministry of Health, Singapore; National Medical Research Council, NIG09may007; SingHealth Foundation, SHF/FG410P/2009.

PO-2-207 / AS-15 Presenter

EFFECT OF SLEEP DEPRIVATION ON SLEEP, MOOD AND EMOTIONAL PROCESSING

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Objectives: To investigate the effect of total sleep deprivation on the response to an analogue depressing event in terms of mood and emotional processing, in healthy young subjects.
Methods: Subjects (aged 18–25 yrs) where shown a depressive film followed by either 24 hrs total sleep deprivation or normal sleep. Subjects were screened to ensure no personal history of psychiatric conditions, no smoking and no illicit drug intake. Before watching the film all subjects underwent a two-week screening period of actigraphy, including melatonin and cortisol profiling. Polysomnographic recordings were done before and after watching the film. Mood was assessed by a visual analogue scale (VAS), state anxiety scale and positive and negative affect scale. Emotional processing was measured by participants reporting the number of intrusive memories relating to the film experienced.
Results: This study is ongoing. The two groups, sleep deprived (n = 17) and non sleep deprived (n = 20) show no difference in age, sex, caffeine or alcohol intake, subjectively rated sleep quality, morningness/eveningness, or type of personality. All participants were found to have a significant decrease in mood after watching the film, reflected in increased anxiety and sadness, feelings of being horrified, decreased happiness and calmness. A poison distributed generalized linear model shows that group (sleep versus sleep deprived) has a significant effect on the number of intrusions generated, with the sleep deprived group having fewer intrusions than the non sleep deprived group ($p = 0.003$). To date no significant effect of the film has been found on sleep over the anticipated effects of sleep deprivation.
Conclusion: We have found that within a homogenous young healthy population, sleep deprivation causes fewer intrusive memories to an analogue depressive event, than sleeping normally. This correlated with clinical data suggesting that sedation after trauma can lead to an increase in post traumatic stress disorder, which is characterized by the presence of intrusive memories (Matar et al 08).

PO-2-208

BEHAVIOURALLY INDUCED INSUFFICIENT SLEEP SYNDROME AND ITS BORDERLAND

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Behaviourally induced insufficient sleep syndrome (BIISS) occurs when an individual chonically fails to obtain the amount of sleep required to maintain normal levels of alertness and wakefulness. Its significance is mostly unappreciated by the patient. Some patients may develop secondary symptoms which may even become the main focus of the patients, serving to obscure the primary cause of the difficulties. This study presents the results of the post hoc evaluation of 47 consecutive patients who received the diagnosis of BIISS in our Center of Sleep Disorders.
Mean age of the BIISS patient was 40 ± 12 years (mean ± SD). Only 30% were females. Patients mostly complain symptoms of hypersomnia with excessive daytime sleepiness, however, many individuals reported other symptoms as sleep attacks without general daytime sleepiness, fatigue, sleep drunkenness, concentration and attention deficits or cognitive impairment. Mean ESS was 14.1 ± 3.6. Time in bed (TIB) estimation based on the SQ revealed TIB of 7:10 h ± 1:03 h during weekdays and 8:29 h ± 1:16 h on weekend. TIB estimation based on actigraphy recordings revealed significantly shorter TIB on weekdays and on weekends (weekday: 6:25 h ± 0:57 h, weekend: 7:56 h ± 1:13 h) compared to TIB taken from the SQ. In this population the PSG recording revealed short sleep latency 8.4 ± 7.9 minutes and high sleep efficiency (91.5 ± 16.7%). Mean sleep latency of MSLT was 5.5 ± 3.3 minutes. Sleep onset REM (SOREM) episodes with 2 and more SOREM were present in 8 patients. Mean sleep latency of MWT was very variable. A clear reduced ability to maintain wakefulness (sleep latency <12 min) was present in 34% of patients.
To conclude, the results of this case series indicate that there are a noticeable large number of patients who were not aware that their sleep duration was insufficient and that there is a substantial clinical overlap between BIISS, narcolepsy without cataplexy and idiopatic hypersomnia without long sleep. A positive response to increased sleep time is diagnostic of BIISS and an important feature to differentiate between these three entities.

PO-2-209

THE EFFECT OF SLOW WAVE ACTIVITY DEPRIVATION DURING AN AFTERNOON SHORT NAP ON PERFORMANCE

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Purpose: To take an advantage of recuperative effects of short nap, slow wave sleep (i.e., slow wave activity, SWA; ×2.0 Hz) would be necessary. However, it has also been reported that SWA would worsen performance immediately after awakening. The aim of the present study is to investigate whether SWA deprivation during a short nap can improve performance and subjective sleepiness.
Method: Ten healthy men (28.7 ± 6.4 years old) took part in the five experimental conditions, which were (1) control condition (rest on the chair for 30 min), (2) 15 min nap condition, (3) 20 min nap condition, (4) SWA condition (the participants slept for 30 min), and (5) SWA deprived condition (SWA-DEP). In the SWA-DEP condition, participants were stimulated by tactile vibrations immediately after the experimenters confirm the sleep stage 3 during a 20 min nap. The vibration devices were installed in the chair in the location of back area (around L2). Before and after the nap or rest, participants carried out a simple reaction time (RT) task and answered questionnaires (sleepiness, fatigue, tension and relax). The order of the conditions was counterbalanced among the participants. All the participants were explained the procedures of the experiment and signed for participation.
Result: It was confirmed that SWA was suppressed by the vibration in the SWA-DEP condition. RT was shorter in the SWA-DEP condition than in the other conditions. Subjective sleepiness was lower in the SWA-DEP condition than in the 20 min nap condition. These results suggest that the technique of SWA deprivation using tactile vibration was effective on increasing the effect of afternoon short nap on performance and subjective sleepiness.

PO-2-210

SELF-AWAKENING PREVENTS SLEEP INERTIA UNDER THE PERIOD OF PARTIAL SLEEP DEPRIVATION

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The ability to awaken at a predetermined time without an alarm is known as self-awakening. Self-awakening has been reported to prevent sleep inertia after undisturbed normal sleep (Ikeda & Hayashi, 2010), but whether it can improve sleep inertia after partial sleep deprivation is unknown. The aim of this study was to examine the effects of self-awakening on sleep inertia after partial sleep deprivation. This study included 15 healthy workers (age, 27–49 years) without the habit of self-awakening. Two conditions were employed in this study: the forced-awakening and self-awakening condition. In each condition, participants slept in their homes for 5 h for 4 consecutive nights. Nocturnal sleep was monitored using Actiwatch (Actiwatch AW64, Mini-Mitter Co. Inc., Bend, Ore.). Vigilance performance was analyzed using a psychomotor vigilance task (PVT-192, Ambulatory Monitoring, Ardsley, New York, USA) and subjective sleepiness, motivation, fatigue, and feeling were rated using the 5-point Likert scale before bedtime and immediately after awakening. The order of the conditions was counterbalanced across the participants. There were no significant differences in the sleep variables without body movement time. PVT reaction times were significantly shorter in the self-awakening condition than in the forced awakening condition. In addition, motivation was significantly improved in the self-awakening condition than in the forced awakening condition. These data indicate that self-awakening can prevent sleep inertia under the period of partial sleep deprivation.

PO-2-211

SCENT REDUCES THE DELETERIOUS EFFECT OF SLEEP INTERRUPTION ON CIRCADIAN RHYTHM AND SKIN CONDITIONS

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OBJECTS: This study investigated (1) the deleterious effect of brief-interruption of sleep on circadian rhythms, and on mental, physical and skin conditions, and (2) the reduction of deleterious effect by scent.
SUBJECTS: Twenty females in their thirties were equally divided into two groups; scent using and control groups.
METHODS: A newly developed fragrance which depresses sympathetic nervous activity was used at bedtime every night over one menstrual cycle by scent using group. As brief interruption of sleep, the subjects were asked to wake up temporarily at 2:00 and to answer some quiz questions for approx. 5 min under a light condition, and allowed to sleep again. This procedure was repeated continuously 2 nights. Psychological stress level was evaluated by STAI, and the sleep quality was measured by sleep questionnaires. Diurnal changes of clock gene expression and salivary cortisol level were measured by QPCR using salivary total RNA and by ELISA respectively. Autonomic nervous activity was measured by heart rate fluctuation analysis under orthostatic stress. The skin conditions were evaluated by sebum-secretion level, skin moisture value, skin barrier recovery and cold stress response.
RESULTS: In spite of no change in the score of STAI, the brief interruption of sleep reduced the score of sleep quality, and disturbed the diurnal change of clock gene expression and salivary cortisol level. Also it stimulated the sympathetic nervous activity. The interruption was found to decrease the sebum secretion and moisture levels of the skin, and disturb the recovery of skin barrier and cold stress response. In contrast to the control group, the deleterious effect of sleep interruption on the scent using group was significantly mitigated by inhalation of the fragrance.
CONCLUSION: Environmental change in daily life such as brief-interruption of sleep causes the deleterious effect on mental, physical and skin conditions, and scent inhalation reduces the deleterious effect and leads to good conditions.

PO-2-212

PREPROHYPOCRETIN/PREPRO-OREXIN POLYMORPHISM PREDICTS INDIVIDUAL DIFFERENCES IN MWT LATENCY, SLEEP PHYSIOLOGY AND HOMEOSTASIS DURING SLEEP RESTRICTION

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The orexin-hypocretin system is involved in normal regulation of sleep and wakefulness and is disturbed in narcolepsy. The −909 C/T polymorphism of the prepro-hypocretin/prepro-orexin (HCRT) gene is associated with an increased risk of sudden onset of sleep (SOS)/sleep attacks in Parkinson's patients, though it is not associated with narcolepsy. We evaluated the role of this polymorphism in mediating sleep and wake responses during baseline and chronic partial sleep deprivation (PSD). 16 C/C, 59 C/T and 54 T/T healthy adults (29.9 ± 6.9 y; 63 females) completed 2 baseline (10 h TIB) nights, followed by 5 consecutive PSD nights (4 h TIB) in a laboratory experiment assessing physiological sleep responses (including NREM slow-wave energy [SWE]) and neurobehavioral outcomes (i.e., cognitive tests, subjective sleepiness and fatigue, and sleep propensity as measured by MWT). Comparisons were made across the 3 genotypes. T/T genotypic and T allelic frequencies were higher in Caucasians than African Americans; results were significant after controlling for ethnicity. At baseline, the C/C group showed decreased sleep homeostatic pressure (SWE) during the night ($p < 0.05$), but comparable SWE elevation to PSD. Relative to T allele carriers, C/C subjects also had more stage 2 sleep and less SWS during baseline (p's < 0.05) and during PSD (p's < 0.05) and greater REM latency reductions ($p < 0.05$) during PSD. C/C subjects showed longer MWT latencies during PSD ($p < 0.05$) but not at baseline. No differences were found for circadian phase typology, habitual sleep, demographics, subjective sleepiness, or cognitive performance. All genotypes demonstrated similar cognitive performance (PVT, Digit Span) decreases, and increases in subjective sleepiness (KSS) in response to PSD. The HCRT −909 C/T polymorphism is associated with differences in sleep homeostasis during fully-rested conditions, as well as in physiological sleepiness and sleep structure during PSD. The C/C genotype appears particularly buffered from the physiological, but not the cognitive performance effects of sleep restriction.

PO-2-213 / AS-14 Presenter

SLEEP DEPRIVATION INCREASES SEROTONIN 2A RECEPTOR DENSITY IN THE HUMAN BRAIN: A [18F]ALTANSERIN PET STUDY

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When wakefulness is extended beyond the usual in animal models, an elevation of the serotonin level is observed. It is an open question whether this difference in neurotransmitter release is accompanied by changes in the respective serotonin receptor (5-HT2AR) densities. The aim of the present study was to investigate the effect of prolonged wakefulness on 5-HT2AR availability in the human brain and its linkage to EEG measures of sleep deprivation (SD) and substrates of cognitive performance impairment. 18 healthy subjects (39–58 years) without sleep disorders participated in two subsequent dynamic [18 F]altanserin bolus/infusions positron emission tomography (PET) scans before and after 24 hours of SD. The binding potential relative to the plasma concentration corrected for metabolism (BPP), proportional to the 5-HT2AR density, was chosen as outcome parameter. Subjects performance was screened with the psychomotor vigilance task (PVT). Wake EEG was recorded. SD significantly increased the specific binding of [18 F]altanserin in the following ROIs (ranging from 8 to 11%, $p < 0.05$): anterior and posterior cingulate cortex, insula, parietal cortex, medial inferior temporal gyrus, sensomotoric cortex, and ventrolateral prefrontal cortex. Correlation of the relative change of PVT performance and BPP showed a significant linear relation for several cortical regions (e.g. insula: $r = 0.59$, $p = 0.01$). We found no correlation of wake EEG power and receptor binding changes. The findings point to an upregulation of 5-HT2AR density caused by a single night of prolonged wakefulness. Furthermore 5-HT2AR density and psychomotor performance correlate. These results suggest that SD may trigger plastic changes in cortical 5-HT2AR density. These and our previous findings of increased A1-adenosine receptor density after SD in humans and rodents support the general hypothesis of an increase in synaptic strength during wakefulness and downscaling during normal sleep as a maintenance mechanism of synaptic functionality.

PO-2-214

SLEEP DEPRIVATION ALTERS VALUATION SIGNALS IN THE VENTROMEDIAL PREFRONTAL CORTEX

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Sleep-deprivation (SD) has long been known to impair vigilance and attention, factors that can contribute to poor decision making. Yet the most insidious effects of SD might be on preferences themselves, such that deprivation changes the very values that underlie our decisions. Here we employed functional magnetic resonance imaging (fMRI) in human participants to examine how SD affects the neural mechanisms underlying economic decision making. We identified decision value (DV) signals predictive of each participant's willingness to exchange money for brief views of attractive faces in a separate task. SD altered these DV signals in VMPFC in proportion to the corresponding change in economic preference. To explore the neural mechanisms underlying this SD-related change in DV we analyzed value signals related to monetary and social rewards independently, which presumably correspond to a stage prior to integration in VMPFC. We observed changes in response to social rewards in the amygdala, frontal pole, striatum and insula that correlated with changes in DV signals in VMPFC. No such changes were observed in response to monetary rewards. These results provide evidence that SD can have selective effects on valuation of specific reward types, which may in turn alter economic decision making. In addition, these changes in preference were uncorrelated with altered vigilance after a night of SD, which warns us that attempts to ameliorate the cognitive effects of SD may leave unaffected important changes in neural signals for value.

PO-2-215 / AS-14 Presenter

CEREBRAL BLOOD FLOW FOLLOWING ACUTE SLEEP RESTRICTION MEASURED USING ARTERIAL SPIN LABELING

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Sleep restriction is common due to shift work and extended work hours. Sleep restriction can substantially increase sleepiness during monotonous situations. In this study, we investigated changes in cerebral blood flow (CBF) after a night restricted to 4 hours time-in-bed (actual sleep 3.6 ± 0.26 h (mean±SD)) compared to after a normally-rested night (actual sleep 7.9 ± 0.94 h) using a relatively new perfusion measurement technique called arterial spin labeling (ASL).CBF was measured in 18 individuals after both rested and sleep-restricted nights using ASL in a GE 3 T MRI scanner. Individuals were asked to keep their eyes open during the 5-min ASL scans. The CBF images were co-registered with anatomical scans, normalized to a standard MNI template, and smoothed using a 10-mm FWHM Gaussian window. CBF following sleep restriction was compared with rested CBF using a voxel-wise paired t-test. There was no difference in global CBF values between rested (43.1 ± 7.2 mL/100 g/min) and sleep-restricted (43.0 ± 6.7 mL/100 g/min) sessions. Regional CBF decreased ($p < 0.05$, $Z \times 2.3$, Cluster-based correction) in the right inferior/middle gyri and intra-parietal sulcus, and bilaterally in the superior frontal, precentral, paracentral, and superior parietal lobules. Increased CBF ($p < 0.01$, uncorrected, extent threshold of 100 voxels) after sleep restriction was observed in the right occipital gyrus, left inferior lateral occipital gyrus, left middle temporal gyrus, and bilateral frontal pole.We have shown that the ASL-based perfusion imaging can be used to detect changes in CBF following acute sleep restriction. We observed decreased CBF in the right parietal and frontal areas important for alertness and attention. The decreased CBF in these areas reflects the reduced alertness and cognitive deficits observed after sleep loss.

PO-2-216 / AS-4 Presenter

PREDICTORS OF SLEEPING DIFFICULTIES IN YOUNG WOMEN

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Some studies have concluded that the gender disparity in sleep difficulties in young adults may be driven by higher rates of affective disorders in women. Other have argued that sleep related gender disparities are largely due to socio economic inequalities. This paper investigated a range of factors as potential predictors of "difficulty sleeping" in 9061 Australian women aged from 24 to 30 years, using survey data. Variables that covered socio-economic status (SES); lifestyle; abuse history and affective issues (depression and anxiety) were investigated. Odds ratio (OR) analyses showed that symptoms of depression and intense anxiety were more significant predictors of difficulty sleeping than SES variables, with ORs at least 5 times larger. Regression analyses were consistent with this, with depression and anxiety symptoms being strong predictors of difficulty sleeping. However, four other variables (binge drinking, lower qualifications, dissatisfaction with excessive weight and a history of abuse) also made significant contributions to sleep difficulty in this sample, even when depression and anxiety symptoms were statistically controlled. On the other hand, analyses suggested that having a lower household income, a recent major illness, and ever having combined alcohol and drugs only predict sleeping difficulty in this sample via a co-existing relationship with depression and anxiety. The current findings argue for the primacy of affective problems in predicting sleep disruption in young women, although several other predictors are also independently important.

PO-2-217 / AS-12 Presenter

CELLULAR EFFECTS OF SLEEP RESTRICTION IN HEALTHY YOUNG MEN

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To elucidate the detriments of cumulative sleep restriction at cellular level. Find pathways and single genes that react to sleep restriction in controlled environment.
Study participants (N = 13) spent one week in laboratory conditions. The experiment consisted of two nights of baseline sleep (8 h/night), sleep restriction for five nights (4 h/night) and two nights of recovery (8 h/night). The control subjects (N = 6) spent the time in laboratory sleeping normally (8 h/night). Blood samples were collected and total cholesterol was measured after baseline, sleep restriction and recovery phases. Total RNA was extracted from blood mononuclear leukocytes. RNA expression was analyzed using Affymetrix whole genome microarrays complemented with pathway and transcription factor analysis of differentially expressed genes.
We saw significant increase of immune response pathways after sleep restriction. The significant up-regulated pathways included T-cell activation, NF-kappaB signaling and IL-8 production pathways ($P < 0.001$). Known immunological transcription factor binding site was enriched in up-regulated transcripts and its transcription was shown to increase in sleep restriction ($P < 0.05$). Circadian rhythm and lipid transport and synthesis pathways were down-regulated. Several expression changes did not return back to baseline after recovery phase.
Our data suggest that sleep restriction has a strong pathophysiological effect on signaling pathways related to the immune system and energy metabolism. Sleep restriction disrupted the function of molecular clock, and recovery from sleep deprivation was a long-term process also at cellular level. The findings may explain why prolonged sleep deprivation may predispose to cardiovascular diseases and obesity.

PO-2-218 / AS-21 Presenter

THE EFFECTS OF SLEEP DEPRIVATION ON SYMPATHOADRENAL SYSTEM AND HYPOTHALAMIC-PITUITARY-ADRENOCORTICAL AXIS USING SALIVARY STRESS MARKERS

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Introduction: People often experience sleep deprivation due to our modern around-the-clock lifestyle, increased work load and various other challenges. It is reported that sleep deprivation-induced stress can negatively influence on human health. However, it is unknown potential mechanisms underlying the impact of sleep deprivation on stress system. The saliva sample testing can evaluate stress responses accurately with a non-invasive sampling method. The purpose of this study was to investigate the effects of sleep deprivation on sympathoadrenal system (SAS) and hypothalamic-pituitary-adrenocortical axis using salivary stress markers.
Methods: Ten healthy young males completed two, 2-day trials (i.e. control and sleep deprivation trials) separated by more than five days each. For the control trial, participants were allowed normal sleep from 23:00 to 7:00; for the sleep deprivation trial, they did not sleep for 34 hours. These experimental trials were performed under supervision by the investigators. On both trials, saliva samples were collected at 9:00, 13:00 and 16:00 before each meal on both days. Salivary samples were analysed for α-amylase, secretory immunoglobulin A (sIgA), chromogranin A (CgA) and cortisol concentrations.
Results: Changes in salivary α-amylase, sIgA and cortisol concentrations were not significantly different between trials on both days. Changes in salivary CgA concentrations on the first-day were not significantly different between trials, but changes in CgA concentrations on the second-day were significantly higher in the sleep deprivation trial than the sleep trial ($P < 0.05$).
Discussion: CgA co-released with catecholamines from the adrenal medulla and sympathetic nerve endings seem to be a better index of sympathetic activity. Increased salivary CgA concentrations in the sleep deprivation trial suggest the activation of SAS. Sleep deprivation may represent as an index of psychosomatic stress response and mediate the stress system.

PO-2-219 / AS-21 Presenter

ENDOTHELIAL FUNCTION IN HEALTHY ADULTS WITH INSUFFICIENT SLEEP

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Background: Many community-based studies have shown that short sleep duration is linked to an increased risk of hypertension and all-cause mortality, but its effects on atherosclerosis are not well characterized. Endothelial dysfunction may contribute to the progression and complication of atherosclerosis. Flow-mediated dilation (FMD) has been used as a noninvasive tool to evaluate endothelial function. We assessed endothelial function in healthy adults with insufficient sleep by FMD.
Methods: Seven healthy subjects (26.2 ± 4.2 years) were studied. Brachial-ankle pulsed wave velocity (baPWV), systolic blood pressure (SBP), and diastolic blood pressure (DBP) were measured using a plethysmography (form PWV/ABI; OMRON COLIN Co., Ltd., Japan). High-resolution ultrasound (Prosound α10; ALOKA, Co., Ltd., Japan) with a 7.5 MHz linear array transducer was used to measure the diameter of the right brachial artery after the subject had rested for at least 10 min in the supine position. We evaluated the maximum intima-media thickness (maxIMT). Heart rate variability (HRV) is used as an index to evaluate the autonomic activity. The power spectra were quantified at 0.04~0.15 Hz (low frequency power; LF) and 0.15~0.40 Hz (high frequency power; HF). On natural sleep nights, the subjects were in bed for 8 hours (sufficient sleep), while on the controlled sleep nights, the subjects were allowed to be in bed between 3 am and 7 am, and their total sleep time was limited to <4 h (insufficient sleep).
Results: FMD was found to be significantly lower after insufficient sleep than after sufficient sleep. No significant differences were observed in baPWV, SBP, DBP and maxIMT between insufficient sleep and sufficient sleep. HF was significantly lower, while LF/HF was significantly greater after insufficient sleep than after sufficient sleep.
Conclusion: Insufficient sleep is considered to negatively affect the endothelial function as a consequence of an elevated sympathetic activity.

PO-2-220 / AS-18 Presenter

MELATONIN CHANGES IN THE PINEAL GLAND OF SLEEP DEPRIVED RATS FOLLOWING HABENULAR NUCLEUS LESION

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Melatonin changes in the pineal gland of sleep deprived rats following habenular nucleus lesion Huijuan Jin, Meiying Song, Min Huang, Manli Wang, Hua Zhao*Department of Physiology, Norman Bethune College of Medicine, Jilin University, Changchun 130021, ChinaSleep deprivation (SD) is considered a risk factor for various disorders involving behavior, emotion, attention, learning ability, and immunological functions. It has been reported that SD-induced physiological functional disturbances are associated with reduction of melatonin. Animal experiments unequivocally show that SD can lead to melatonin reduction in the pineal gland of rats. However, the underlying mechanism remains unknown. The habenular nucleus (Hb) is an important structure that regulates the function of the pineal gland, which may affect melatonin content in the pineal gland after SD. The experiment aim is to investigate that the reduction of melatonin in pineal gland after SD is related to the changed activity of the Hb, revealing a central mechanism of sleeping regulation. In the present study, high performance liquid chromatography showed that the melatonin content in the pineal gland was significantly reduced, and *f*Á-aminobutyric acid content in the Hb was significantly increased after SD. Furthermore, the melatonin content in the pineal gland was markedly reduced after Hb lesion under normal sleep and SD conditions. Immunohistochemistry showed that the number of Fos-positive neurons was significantly decreased in the lateral and medial Hb after SD. The results demonstrate that the reduction of melatonin in the pineal gland after SD is related to decreased activity of Hb neurons, and that the Hb can regulate sleep-wake rhythm by influencing melatonin secretion in the pineal gland.
Key Words: Habenular nucleus; melatonin; pineal gland; sleep deprivation; rat*Email to zhua@jlu.edu.cn

PO-2-221

ACUTE SLEEP DEPRIVATION AFFECTS DIURNAL RHYTHMICITY IN GRANULOCYTES

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The sleep/wake cycle and circadian timing system affect circulating numbers of immune cells, with highest lymphocyte levels being observed at night. The aim of this study was to provide an in-depth characterisation of diurnal rhythms in the levels of different human blood cell populations obtained under strictly controlled laboratory conditions and to investigate the impact of acute total sleep deprivation on any observed rhythmicity.
Eleven healthy male subjects (25.0 ± 5.8 (SD) years) participated in a 72 h laboratory session which included an 8 h sleep episode followed by 29 h of continuous wakefulness. Blood samples (every 3 h over a 48 h period) were taken for flow cytometry to determine circulating numbers of different blood cell subsets. The impact of condition (sleep versus sleep deprivation) on peak time and amplitude of the blood cell rhythms was investigated. Inter-individual variation of, and correlation between, the different cell populations was also assessed.
Cosinor analysis revealed significant diurnal rhythmicity for 3–9 (out of 11) subjects per cell population (B cells, T cells (and subsets), granulocytes, monocytes). Non-linear curve fitting of normalised data from all individuals showed significant diurnal rhythmicity in circulating levels of all the blood cell types investigated. Both methods found that naive-CD4 cells exhibited the most robust rhythms independent of sleep condition (sleep versus sleep deprivation). Furthermore, granulocytes showed the lowest correlations with any other cell type while exhibiting the largest inter-individual variation in abundance. Granulocyte levels and their diurnal rhythmicity were severely affected by acute sleep deprivation and likely reflect the body's immediate immune response to the stress of sleep loss.
Support: Netherlands Forensic Institute (NFI), and the Netherlands Genomics Initiative (NGI) / Netherlands Organization for Scientific Research (NWO) within the framework of the Forensic Genomics Consortium Netherlands (FGCN).

PO-2-222

PER3 AND ADORA2A POLYMORPHISMS IMPACT NEUROBEHAVIORAL PERFORMANCE DURING CHRONIC SLEEP RESTRICTION

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We examined the contribution of PER3 and ADORA2A polymorphisms to individual vulnerability to chronic sleep restriction. Nineteen healthy adults (ages 18–39, 11 men, 7 women) underwent 7 nights of sleep restricted to 3 hours nightly time in bed (TIB), preceded by 7 in-laboratory nights of 10 hours nightly TIB and followed by 3 nights of 8 hours nightly TIB. Volunteers performed the psychomotor vigilance test (PVT) throughout and were genotyped for PER3 VNTR and ADORA2A polymorphisms ($PER3^{4/4}$ n = 7; $PER3^{4/5}$ n = 10 [$PER3^{5/5}$ n = 2, not included in the analyses]; $ADORA2A^{C/T}$ n = 9; $ADORA2A^{T/T}$ n = 9 [$ADORA2A^{C/C}$ n = 1, not included in analyses]). Mixed-model ANOVAs with repeated factors day and time of day and between-subjects factor PER3 or ADORA2A genotype were performed for PVT lapses (reaction time [RT] 500 msecs) and reciprocal RT (1/RT *1000). $PER3^{4/4}$ individuals presented with significantly fewer lapses on SR4 – SR7 (DAY X PER3, $p < 0.05$). During recovery (R), $PER3^{4/4}$ individuals presented with significantly fewer lapses on R1 and R2 (DAY X PER3, $p < 0.05$) compared to $PER3^{4/5}$ individuals. For reciprocal RT, $PER3^{4/4}$ individuals displayed significantly faster RTs compared to $PER3^{4/5}$ individuals overall. Compared to $ADORA2A^{C/T}$ individuals, $ADORA2A^{T/T}$ individuals displayed faster RTs on SR6 (Day X ADORA2A interaction, $p < 0.05$). Our results indicate that individuals expressing $PER3^{4/4}$ and $ADORA2A^{C/T}$ polymorphisms are less vulnerable to chronic sleep restriction than are individuals expressing $PER^{4/5}$ and $ADORA2A^{T/T}$ polymorphisms. In light of previous failure to show that these polymorphisms impact performance during chronic sleep loss, we suggest that PER3 and ADORA2A polymorphism only become behaviorally relevant only under conditions of more persistent sleep restriction.

PO-2-223

HEART RATE VARIABILITY AND ENDOTHELIAL FUNCTION AFTER SLEEP DEPRIVATION AND RECOVERY SLEEP IN SHIFT WORKERS AND NON-SHIFT WORKERS

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Sleep deprivation, shift work, endothelial dysfunction and changes in heart rate variability (HRV) have all been associated with cardiovascular disease. The aim of this study was to compare the effect of total sleep deprivation (TSD) and recovery sleep on HRV and endothelial function in experienced shift workers and matched non-shift workers under identical laboratory settings.
Eleven male shift workers (shift work > 5 years) and 14 non-shift workers were matched for age, BMI and cholesterol. Endothelial function was assessed by flow-mediated dilatation (FMD) using ultrasound at 0.75 and 10.75 h after habitual wake up time, following baseline sleep, TSD and recovery sleep (controlled posture, lighting and food intake). HRV parameters (e.g. HR variance and low frequency/high frequency (LF/HF) ratio) were derived from 5-min electrocardiogram bins at 0.25, 4.25, 11.5, 12.5 and 13.5 h after habitual wake up time. Circadian phase was assessed before baseline sleep by salivary dim light melatonin onset (DLMO).
There was no difference in circadian phase between both groups. HR variance was greatest at 0.25 h following TSD and lowest after recovery sleep. A significantly higher LF/HF ratio, significantly lower HR variance and a trend for a lower%FMD ($P = 0.08$) were observed in the shift workers compared to the non-shift workers.
These differences in endothelial function and HRV observed in the shift workers may reflect higher sympathetic and/or lower parasympathetic activity, and may explain the increased cardiovascular risk reported in the shift workers.

PO-2-224

THE EFFECT OF A SLEEP RESTRICTION ON THE PUPILLARY LIGHT REFLEX

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Purpose: We indicated the effects of the mild sleep restriction for a week on the amplitude of the central neural system by the light reflex. The amplitude on the pupillary light reflex was seem to relate to the serotonin neuron (Koudas, 2009). However, it's not detected the relation between the subjective sleepiness of the people with sleep loss and the pupillary reflex.
Methods: The subjects were 7 healthy males (age 21 ± 1.0, range 20–23), who have no medical histories. All the subjects were non-smokers. They had two sleep schedules, 8 h and 5 h, for each 7 days. They were assigned the schedules randomly. The sleep durations were identified by the sleep diary and the actigraph using the wrist-watch type action monitor (AMI, Micro Mini Actigraph). They wrote the values of the sleepiness by the visual analogue scales each 3 h for 14 days, 9:00, 12:00, 15:00, 18:00, 21:00. We measured their pupils on the last day each the schedules by the machine with the CCD camera using the infra-red radiation (Hamamatsu, C7364). According to the Shapiro-Wilks test, we used the non-parametric statistical test.
Results: The average of the VAS scores of the sleepiness on 8 h was 134.6 ± 36.3, the average of 5 h was 215.3 ± 38.3. The VAS scores of the 5 h sleep restriction was significantly higher ($p < 0.04$, Wilcoxon signed rank test). The average of the amplitudes on 8 h was 3.3 ± 0.3 mm, the average of 5 h was 2.9 ± 0.7 mm. The difference of the amplitudes between the sleep schedules was not significant ($p > 0.1$, Wilcoxon signed rank test). The correlation between the amplitudes and the VAS scores was not reached the level of significance in statistics ($r = -0.71$, $p > 0.07$, spearman rank correlation).

PO-2-225 / AS-8 Presenter

TIRED AND INSIGNIFICANT

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Introduction: Sleep affects a variety of subjective measures of mood and affect, such as sociability, optimism, irritability, and general mood. fMRI-data suggests a neural foundation for less rational social judgements in sleep-deprived individuals, with an amplified amygdala

response to negative emotional stimuli as well as a loss of functional connectivity with the medial prefrontal cortex. But what happens when the negative emotional stimuli is of a social nature? Social exclusion is known to have a powerful negative effect on people, and based on the relationship between sleep deprivation and emotional reactivity we hypothesized that being excluded affects a sleep-deprived person even more negatively than someone who has had a good night's sleep.
Method: 24 healthy individuals (11 males) with a habitual sleep need between 7 and 8.5 h/night were randomly divided into a sleep restriction group (4 h/night for 2 nights) or a control group. After the second night they played a computerized ball tossing game, ostensibly with two other people over a network, but the participant was, in reality, the only player. The game consisted of two sessions, one where the participant was included and one where the other two "players" excluded the participant by not tossing them the ball. A questionnaire was completed after both sessions assessing participants' feelings of belongingness, meaningfulness, control, and self esteem.
Results: Compared to the control group, the sleep-restricted group was more negatively affected by exclusion in terms of meaningfulness ($p = 0.001$). The sleep-restricted and the control group did not differ significantly in belongingness, control, or self-esteem.
Conclusion: When sleep restricted, people are more sensitive to social exclusion, at least in terms of feeling more meaningless. These findings suggest that sleep restriction may have an important impact on how we interact with other people. The relation between suboptimal sleep and feelings of meaninglessness may be of relevance to understand the link between disturbed sleep and depression.

PO-2-226 / AS-21 Presenter

CONSISTENT INCREASES OF DELTA SLEEP IN INDIVIDUALS EXPOSED TO CHRONIC SLEEP RESTRICTION

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There is still a debate whether chronic sleep restriction results in an allostatic or homeostatic responses of deep sleep. An animal study showed a striking allostatic response among rodents exposed to chronic sleep restriction (1), although we could later confirm that humans increase their deep sleep in a homeostatic manner (2). A possible explanation for the different findings could be large individual differences in the response to restricted sleep. Thus, we investigated whether the increase of delta sleep (in response to repeated sleep restriction) is consistent across individuals or whether some individuals fail to respond with an increase of delta power.
Nine healthy males (age range 23–28 yrs) went though a laboratory protocol including 2 baseline days (sleep 23–07 h) and 5 days with sleep restriction (03–07 h). The first 3.8 h hours of NREM-sleep EEG was analysed with respect to spectral analysis. The first step included observation of raw data. However, since raw data are contaminated by measurement errors a model based approach was also used to produce empirical Bayes estimates of individual response patterns (in the 0.75–32 Hz band) to restricted sleep across five days with restricted sleep. A linear mixed effect model was used with (polynomial) fixed effects for days of sleep deprivation and frequency response profiles. The final model included 8 fixed and 8 random effects, the latter accounting for individual differences.
Results: The raw data indicate that sleep restriction resulted in increased delta sleep in 52 out of 54 sleep episodes occurring after restricted sleep. The empirical Bayes estimates suggested that all participants reacted with an increase of the delta band after 2 days of restricted sleep with continued increased delta sleep power until recovery (p's $< .01$ for all fixed effects).
To conclude, the uniform increase of delta sleep amongst individuals supports the notion of a very robust and stable homeostatic response to restricted sleep.
1) Kim et al., (2007) *PNAS* 104:10697–702
2) Akerstedt et al., (2009) *Sleep* Feb 1;32(2):217–22

PO-2-227

FEATURES OF TIREDNESS

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Objectives: It is generally believed that looking tired entails a number of characteristics such as dark circles under the eyes, pale skin and droopy eyelids. Since this has never been scientifically studied, we set out to investigate how sleep affects facial traits and what it is about a face that makes it look tired.
Methods: The faces of 10 participants (5 women), mean age of 23 yr, were photographed between 14.00–15.00 h during two conditions in a balanced design: after normal sleep (23.00–07.00 h and 7 hours of wakefulness) and following sleep deprivation (sleep 02.00–07.00 h and 31 hours of wakefulness). These photographs were then presented in a randomised order to 40 naive observers (20 women, mean age 25 yr) who rated the faces (on VAS scales) with respect to dark circles under the eyes, red eyes, glazed eyes, hanging eyelids, swollen eyes, pale skin, wrinkles/fine lines, rash/eczema, corners of the mouth pointing down, tense lips, inclination of the head, and tiredness.
Results: During sleep deprivation the participants were judged to have more dark circles under the eyes, redder eyes, more hanging eyelids, more swollen eyes, paler skin, more wrinkles/fine lines, and corners of the mouth pointing more downwards (p's < 0.01), compared to after a night of good sleep. Sleep deprivation did not affect glazed eyes, rash/eczema, tense lips or inclination of the head significantly (p's $> .05$). Looking tired was positively correlated with the factors affected by sleep deprivation, but also with glazed eyes (p's < 0.01).
Conclusions: Our findings show that there are facial features reliably correlated with sleep deprivation and looking tired, hence adding to recent findings on sleep and judged appearance (1). Further studies are warranted to understand if these factors affect situations such as mate choice, clinical decision making, and other social interactions.
1) Axelsson et al. Beauty Sleep: Experimental study on the perceived health and attractiveness of sleep deprived people *BMJ* 2010, 341:c6614

PO-2-228

SLEEP IN ANTARCTICA

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Sleep in Antarctica Antarctic environment is characterized by extremely low ambient temperature and seasonal variation in daylight time. In addition to those natural characteristics, psychological factors related to isolation with small number of members in the Antarctic base may have some influences on physiological and psychological functions. As previous studies have reported abnormalities in human circadian rhythms and deteriorated sleep in Antarctica, we evaluated sleep in the

wintering members in Antarctica by using subjective and objective measurements. The subjects were ten males and two females recruited from the members of the 50th and 51st Japanese Antarctic Research Expedition (age: 39.7 ± 10.0 years; BMI: 25.2 ± 3.3). During their 13 months sojourn in the Antarctic base, data collection was conducted every 3 months (March, June, September, and December). The data collection was consisted of sleep EEG by portable EEG device, from obtained electroencephalographic data, we analyzed it and considered all sleep variables. The sleep state was associated with environment outside the seasonal daylight hours or temperature change, we formed an initial hypothesis. The quality of the sleep was good quality in starting for March. However, the quality of the sleep worsened over time, it became good quality in December. By the questionnaire survey, the motivation of the member gradually worsens after peaking in March and corrects it and increases just before return home again. This sleep electroencephalogram analysis results were similar to the questionnaire results, too. The stress that could not meet a family and had much work may have an influence on the sleep from external environment.

PO-2-229

THERAPEUTIC DECISION-MAKING FOR SLEEP APNEA AND HYPOPNEA SYNDROME USING HOME RESPIRATORY POLYGRAPHY

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Rationale: Home respiratory polygraphy is an alternative to polysomnography for sleep apnea-hypopnea syndrome diagnosis. However, therapeutic decision-making is a different process than diagnosis. This study aimed to determine the efficacy of home respiratory polygraphy compared to in-hospital polysomnography for therapeutic decision-making in a large sample.
Methods: Patients with an intermediate or high sleep apnea-hypopnea syndrome suspicion were included in a multicenter study (eight sleep centers) and assigned to home and hospital protocols in a random order. Therapeutic decisions (continuos positive airway pressure, no continuos positive airway pressure or impossible decision) were made by an investigator in each center, based on using either home respiratory polygraphy or polysomnography and a single set of auxiliary clinical variables. Patients and diagnostic methods (home respiratory polygraphy and polysomnography) were assessed in a random order using an electronic database. After a month the same therapeutic decision-making procedure was repeated with the same method.
Results: Of 366 randomized patients, 348 completed the protocol. The impossible decision case was not observed with either polysomnography or home respiratory polygraphy. Therapeutic decisions using home respiratory polygraphy had a sensitivity of 73%, a specificity of 77%, and an agreement (sum of true positives and negatives) of 76%. Patients with higher home respiratory polygraphy apnea and hypopnea index scores (major or equal than 30)(40% of the total sample) had a sensitivity of 94%, a specificity of 44%, and agreement was 91%.
Conclusion: The home respiratory polygraphy-based therapeutic decision was adequate when apnea and hypopnea index was high, but deficient in the large population of patients with mild to moderate apnea and hypopnea index. Therefore, both selecting patients with a high suspicion/severity of sleep apnea-hypopnea syndrome and future prospective cost-effectiveness studies are necessary.

PO-2-230

NEUROGLIAL METABOLIC COUPLING DURING THE SLEEP-WAKE CYCLE

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During sleep-wake cycle, cortical neuronal firing pattern changes rapidly and considerably. This implies that adaptations in brain energy metabolism are likely to occur throughout the sleep-wake cycle to match such variations. Astrocytes are ideally suited to play a key role in neuro-metabolic coupling since they present two main metabolic features: their ability to store glucose under the form of glycogen and the possibility to produce lactate as an energy substrate to neurons through the "Astrocyte-Neuron Lactate Shuttle"(ANLS). Moreover, astrocytes form connexin-mediated networks through gap junctions (GJs) and energy metabolites can diffuse across GJs thus contributing to neuronal activity. Therefore, we tested the involvement of astrocytes in the metabolic adaptation during sleep deprivation (SD) induced by the "gentle-SD" method (GSD) and by administration of Modafinil (MOD), in mice. Moreover, functionality of GJs after MOD application was studied using diffusion of gap-junction channel-permeable dyes in acute cortical slices. We also performed instrumental SD on transgenic mice expressing GFP in astrocytes (Tg(GFAP-GFP)) to determine astroglial regulation of ANLS-related genes expression.
We founded that glycogen metabolism was directed towards a "synthesis mode" to maintain glycogen levels in spite of the wakefulness continuation. Moreover, increase in mRNA encoding specific astroglial connexin, in SD mice and enhanced GJ-mediated intercellular communication in astrocytes treated with MOD, suggest a dynamic effect of wakefulness on astroglial networking. Finally, mRNA encoding proteins related to ANLS in cortical astrocytes from (Tg(GFAP-GFP)) displayed a significant induction after SD.
Altogether, these results indicate that metabolism and GJ-mediated networking in cortical astrocytes are dynamically regulated when wakefulness is prolonged.
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Hypnotic agent 〈Zolpidem tartrate tablets〉

Listed in the NHI drug price list.

Myslee® Tablets 5mg·10mg

Psychotropic drug, Habit-forming drug(Caution: Habit-forming.)
Prescription drug(Caution: Use only pursuant to the prescription of a physician, etc.)

• Please refer to package inserts for ‘‘Indication’’, ‘‘Dosage and Administration’’ and ‘‘Precautions’’.

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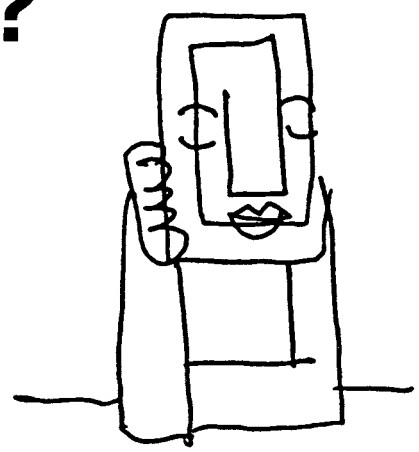
What would Florence Nightingale have done?



Whenever we see our mark in her handwriting, this question comes to mind.

Florence Nightingale fulfilled her personal aspirations as a nurse caring for soldiers during the Crimean War. Her course of action determined by the needs of the suffering and wounded, she gave each patient her undivided attention, above and beyond the call of duty. From her life work, we can learn the importance of looking at health care from the patient's point of view. Florence Nightingale's efforts exemplify a deep concern for others, a commitment that we at Eisai have dubbed "Human Health Care." We are dedicated to promoting her ideals.

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Human Health Care
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Kyorin

Therapeutic agent for overactive bladder NHI Listed

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URITOS® OD Tablets 0.1mg

〈Imidafenacin tablets〉

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Caution：Use only pursuant to the prescription or directions of a physician etc.

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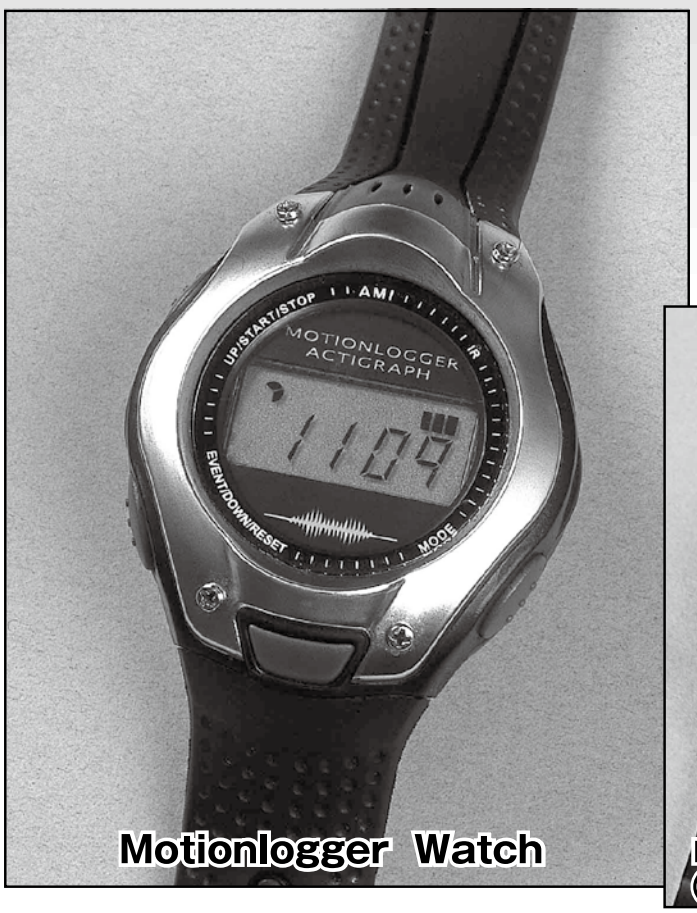
“Motionlogger Actigraph”



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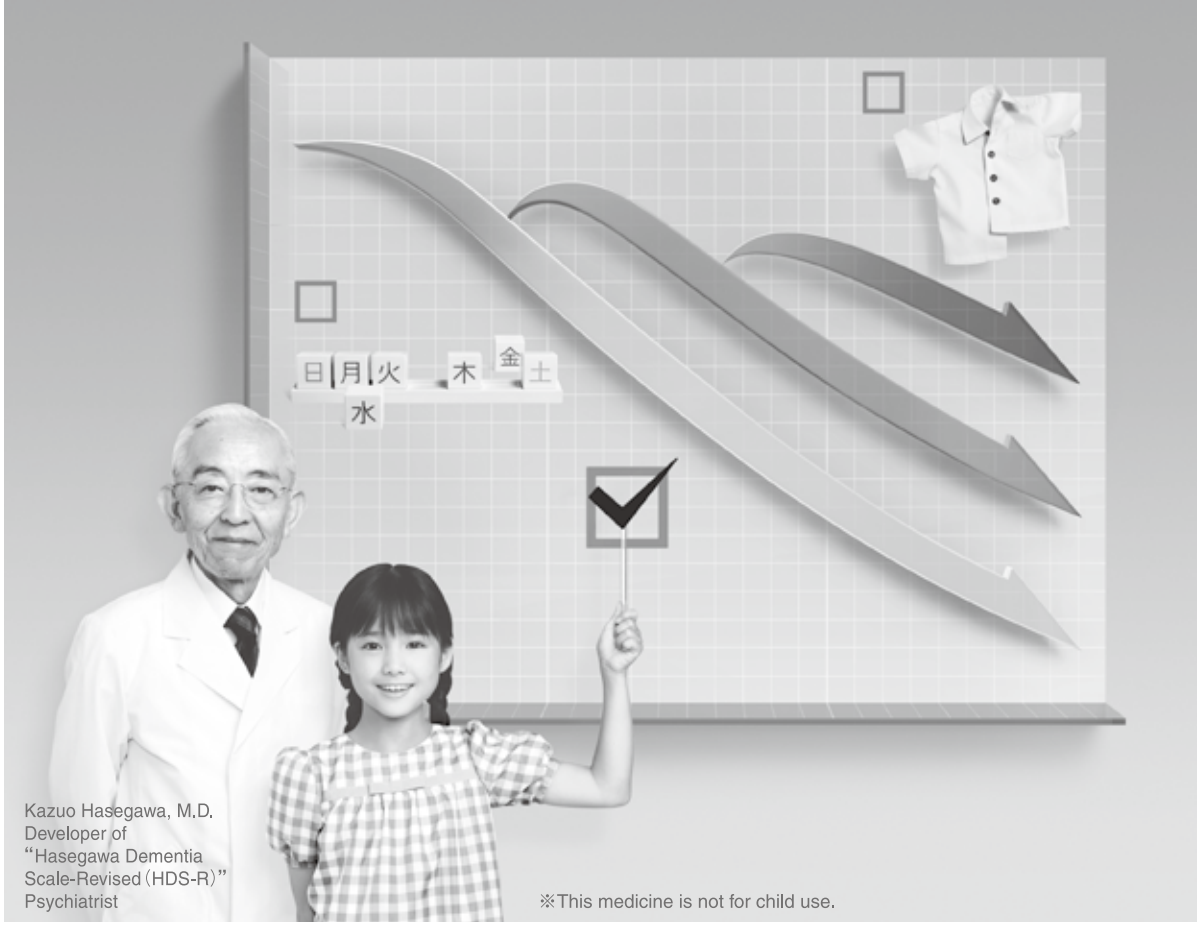

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Developer of
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Psychiatrist

※This medicine is not for child use.

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Prescription drug (Caution: Use only as directed by a physician)

-For the treatment of dementia of the Alzheimer's type-

[Listed on the NHI Drug Tariff]

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5mg TABLETS
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10mg TABLETS

〈Donepezil Hydrochloride Orally Disintegrating Tablets〉

Aricept® 3mg JELLY
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10mg JELLY

〈Donepezil Hydrochloride preparation〉

www.aricept.jp

● For "Indications", "Dosage and Administration", and "Precautions including Contraindications", please refer to the package insert.

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