were significantly correlated in a positive manner in the hippocampal region were as follows: GABA vs. Gln, and DA vs. 5-HT concentrations.

Conclusions reached: On the basis of our findings, significantly higher Gln concentrations and Gln/Glu, Gln/tCr, and GABA/Glu ratios in the SSP rats than in the CNTL rats may reflect the hyper activities of glutamine synthetase and GABAergic receptors while declined glutamatergic activity. Moreover, our main findings suggest that the GABA, Gln, and 5-HT signals in hippocampal region of the rats are particularly sensitive to stress-induced sleep perturbation. Our *in vivo*1H MRS and *in vitro* LC-MS/MS results suggested some novel metabolic markers for the cerebral neurochemical effects of stress-induced sleep perturbation in the rat brain.

PT659

Novel post-translational regulations of SK channel revealed by high-throughput and high-resolution ion channel profiling

Daisuke Tone[1], Koji L. Ode[1,2], Hiroki R. Ueda[1,2]

[1] Department of Systems Pharmacology, Graduate School of Medicine, The University of Tokyo, Bunkyo-ku, Tokyo, 113-0033, Japan [2] Laboratory for Synthetic Biology, Quantitive Biology Center, RIKEN, Suita, Osaka, 565–0871, Japan

Abstract

Calcium dependent potassium channels are important for afterhyperpolarization in neurons and regulate the cellular excitability. Small conductance potassium (SK) channels are members of calcium-dependent potassium channels. Previous studies suggests potential involvement of the dysregulated SK2/3 functions in psychiatric disorders including schizophrenia (Ref.1). Because the functions of ion channels are generally regulated through reversible phosphorylation, albeit so far only a single domain of SK2/3 has been demonstrated as a clear target of phosphorylation (Ref.2), we infer that multiple residues of SK2/3 undergo phosphorylation to control channels' function and such modification can be a target of pharmacological control for the disorders.

To achieve a comprehensive analysis of phosphorylation-dependent SK channel regulation, we systematically induced phospho-mimetic mutations throughout the entire SK2 plypeptide. The series of mutants were analyzed in 293T cells by a new 384-well based screening assay, in which we took the advantage of fluorescent dyes and reverse transfection technique to simultaneous monitoring of mutants' channel activity. We discovered phsopho-mimetic mutants that either supress or enhance the channel activity. We are now trying to identify kinase(s) responsible for the phosphorylation on the mutated residues. Interstingly, we found several kinases that suppress SK channel activity when they are co-expressed with SK2 in 293T cells. These post-translational SK2 regulation could have a role in switching neuronal excitability, and its dysfunction may cause neurological disorders.

References

1. Smolin B. et al, Int.J.Neuropsychopharmacol., 2012
2. Ren Y. et al, J.Biol.Chem, 2006

PT660

Cholinergic Neurons in the Basal Forebrain Promote Wakefulness by Actions on Neighboring Non-CholinergicNeurons: An Opto-Dialysis Study

Tae Kim, Kyung Hee University Hospital at Gangdong, Republic of Korea

Abstract

Understanding the control of sleep–wake states by the basal forebrain (BF) poses a challenge due to the intermingled presence of cholinergic, GABAergic, and glutamatergic neurons. All three BF neuronal subtypes project to the cortex and are implicated in cortical arousal and sleep–wake control. Thus, nonspecific stimulation or inhibition studies do not reveal the roles of these different neuronal types. Recent studies using optogenetics have shown that "selective" stimulation of BF cholinergic neurons increasestransitions between NREM sleep and wakefulness, implicating cholinergic projections to cortex in wake promotion. However, the interpretation of these optogenetic experiments is complicated by interactions that may occur within the BF. For instance, a recent in vitro study found that cholinergic neurons strongly excite neighboring GABAergic neurons, including the subset of cortically projecting neurons, which contain the calcium-binding protein, parvalbumin (PV) (Yang et al., 2014). Thus, the wake-promoting effect of "selective" optogenetic stimulation of BF cholinergic neurons could be mediated by local excitation of GABA/PV or other non-cholinergic BF neurons. In this study, using a newly designed "optodialysis" probe to couple selective optical stimulation with simultaneousin vivomicrodialysis, we demonstrated that optical stimulation of cholinergic neurons locally increased acetylcholine levels and increased wakefulness in mice. Surprisingly, the enhanced wakefulness caused by cholinergic stimulation was abolished by simultaneous reverse microdialysis of cholinergic receptor antagonists into BF. Thus, our data suggest that the wake-promoting effect of cholinergic stimulation requires local release of acetylcholine in the basal forebrain and activation of cortically projecting, non-cholinergic neurons, including, but not limited to, the GABAergic/PV neurons.

PT661

The effect of Yokukansan, a traditional herbal medicine, on sleep disturbances and anxiety symptoms in restless legs syndrome

Hideto Shinno[1], Nobuo Ando[1], Jun Horiguchi[2], Ichiro Ishikawa[1], Yu Nakamura[1]

[1]Kagawa University School of Medicine, Japan, [2]Shimane University School of Medicine, Japan

Abstract

Objective: Dopaminergic agonists such as pramipexole are now considered the first-line treatment for restless legs syndrome (RLS). Dopaminergic agonist, however, sometimes fail to treat RLS. It is important to identify the factors that may prevent therapeutic agents from improving RLS symptoms. This study aims to examine whether anxiety symptoms affect the control of RLS symptoms in patients treated with pramipexole. We also investigated the effect of a herbal prescription, *Yokukansan* (YKS), on RLS and comorbid anxiety symptoms.

Patients and Methods: Thirty-three patients with secondary RLS were enrolled in a prospective study. RLS symptoms and anxiety symptom were evaluated using the International RLS Study Group rating scale (IRLS) and Hamilton Anxiety Scale (HAM-A), respectively. Subjective sleep quality and daytime somnolence were also examined with Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS), respectively. After being treated with pramipexole for 4 weeks, the subjects were divided into 2 groups based upon the IRLS score. The responder

group included subjects whose IRLS scores were less than 10 after 4-week treatment, and the poor-responder group included those whose IRLS scores were 10 or over. (1) HAM-A scores were compared between the responder group and the poor-responder group. (2) In the poor-responder group, YKS was prescribed in combination with pramipexole. We also examined the effect of pramipexole and YKS (4 weeks) on IRLS, HAM-A, PSQI, and ESS. The local IRB approved this study. All patients gave written consent according to institutional guidelines and the tenets of the Declaration of Helsinki.

Results: There was no difference in basal IRLS scores between two groups. The mean HAM-A score after pramipexole treatment in the poor-responder group (n=9) was higher than that in the responder group (n=24). Treatment with pramipexole and YKS for 4 weeks improved RLS and anxiety symptoms.

Conclusions: Anxiety symptoms may affect the treatment outcome in patients with RLS. YKS was demonstrated to be effective for RLS and comorbid anxiety symptoms.

PT662

Risk factors of insomnia in cancer patients who referred to psychoonoclogy clinic

Changhyun Jang, Seok Joo Hong, Nam Hee Kim
Ajou University Hospital, Republic of Korea

Abstract

Purpose: Insomnia is one of the most prevalent symptoms experienced by cancer patients. The goal of this study was to investigate the severity of insomnia and the risk factors of insomnia in cancer patients who referred to specialized psychooncology clinic.

Method: A total of 167 cancer patients who referred to psychooncology clinic in Ajou University Hospital was investigated. Insomnia was measured using the Insomnia Severity Index (ISI). For the investigation of risk factors, we considered demographic factors, clinical factors, Distress Thermometer (DT), Functional Assessment of Cancer Therapy – General (FACT-G), and Hospital Anxiety and Depression Scale (HADS). The risk factors of insomnia were evaluated using multiple regression analysis.

Results: Of 167 patients, 132 (79.0%) were females and 35 (21.0%) were males, with the average age at presentation of 51.1 years old. Most common cancers were breast (42.1%), gastrointestinal (16.4%), and gynecologic (18.4%). We defined insomnia group with over 15 score of ISI. Insomnia group (N=73, 43.7%) had more psychiatric past history and showed significantly higher distress, anxiety, and depression and lower physical, emotional, and social wellbeing than non-insomnia group. After adjusting the effect of psychiatric past history, the significant risk factors of insomnia were distress, anxiety, physical wellbeing, and social wellbeing and accounted for 38.7% of the variance in insomnia.

Conclusion: Insomnia is prevalent in cancer patients who referred to psychooncology clinic. The modifiable risk factors of insomnia in these patients were distress, anxiety, physical wellbeing, and social wellbeing. Early assessment and intervention strategies for these factors could prevent from becoming chronic insomnia in cancer patients.

PT663

Comparison of wearable activity tracker to actigraphy for sleep evaluation and circadian rhythm measurement.

Hyun-Ah Lee[1], Joung-Ho Moon[2], Heon-Jeong Lee[1, 2, 3], Taek Lee[4], Hoh Peter In[4], Chul-Hyun Cho[1, 3], Leen Kim[1, 3]*

[1]Department of Psychiatry, Korea University College of Medicine; [2]Department of Biomedical Sciences, Korea University College of Medicine; [3]Sleep-Wake Disorders Center, Korea University Anam Hospital; [4]Department of Computer Science, Korea University College of Information and Communications, Seoul, South Korea
[*]Corresponding author.
Leen Kim, MD, PhD,
Department of Psychiatry, Korea University College of Medicine, 73 Inchon-ro, Seongbuk-gu, Seoul 136–705, Republic of Korea
Tel: +82-2-920-5355, Fax: +82-2-927-2836,
E-mail: leen54@chol.com

Abstract

Actigraphy has been used to assess sleep wake cycles for over 20 years. Recently, various wearable activity trackers that are synced wirelessly to smartphone are commonly used to promote health by general population. The purpose of this study was to evaluate the reliability and validity of wearable activity tracker (Fitbit charge HR) for sleep evaluation and circadian rhythm measurement compared to actigraphy (Actiwatch 2). We compared wearable activity tracker and actigraphy for sleep and activity variables and circadian rhythm. 16 healthy adults wore Fitbit charge HR and Actiwatch 2 simultaneously on the same wrist. Also, participants went about their daily life and recorded sleep log during a 14-day period. The validity was assessed by comparing the output using Wilcoxon signed rank tests and Spearman's correlation. For sleep variables, both sleep start time ($r=0.869$, $p<0.001$) and sleep duration ($r=0.918$, $p<0.001$) are highly correlated between the two devices. However, Fitbit charge HR tends to overestimate sleep duration compared to actigraphy (mean±SD 409.7±97.6 vs 387.3±98.3). Although activity score showed low correlation between the two devices, period ($r=0.800$, $p<0.001$) and acrophase ($r=0.980$, $p<0.001$) of the circadian rhythm using Cosinor analysis are highly correlated. Fitbit charge HR showed strong validity for measurement of sleep variables and estimation of circadian rhythm. The results suggest that Fitbit charge HR can be used alternatively to measure sleep and circadian rhythm for psychiatric disorders, especially mood disorders.

Key words: Actigraphy, Fitbit, Validity, Sleep, Circadian rhythm

PT664

Associations between actigraphy-assessed sleep, inflammatory markers, and insulin resistance in the Midlife Development in the United States (MIDUS) study

Eun Lee[1], Suk Kyoon An[1], Judith Carroll[2], Taeho Kim[1], Kee NamKoong[1]
[1]Yonsei University College of Medicine, Republic of Korea, [2]University of California, USA

Abstract

Disturbed sleep_ENREF_23_ENREF_23 has been _ENREF_27 associated with increased insulin resistance in previous studies and there is growing body of evidence that activation of inflammatory pathways plays a crucial role in the development of insulin resistance. This study aimed to examine associations between objectively measured sleep, inflammatory markers and insulin resistance.

Cross-sectional data collected from 2004 to 2009 during the Midlife Development in the U.S. II (MIDUS II) biomarker project were used. The study was performed in the MIDUS Research Center at the University of Wisconsin–Madison and participants' homes. The study population included 374 community-based midlife subjects (138 men and 236 women) who completed 7