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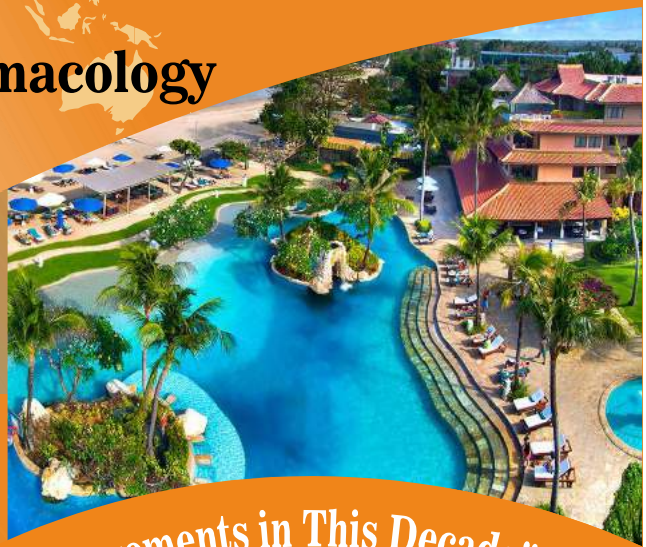

PROCEEDING BOOK

"Leap of Recent Neuropsychopharmacology Achievements in This Decade"

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Bali, Indonesia

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KEYNOTE LECTURE (KL-1)

Ketamine and The Pursuit of Rapid Acting Antidepressants

John H. Krystal[1], Robert L. McNeil, Jr.[2]
[1]Professor of Translational Research, Chair of Department of Psychiatry, Yale University School of Medicine, USA
[2]Chief of Psychiatry at Yale-New Haven Hospital, USA

There is a tremendous need for antidepressant treatments that work more rapidly and more effectively than available treatments. Our current antidepressant treatments (monoamine reuptake or metabolism modulators, lithium, ECT) have been in place for over 50 years. This presentation will review the path that led to the identification of ketamine as the first rapid onset antidepressant treatment. Ketamine is a short-acting NMDA glutamate receptor antagonist. A series of studies now demonstrate that a single intravenous dose of ketamine will produce reductions in depression severity within several hours and remission of depression in many patients within 24 hours. The antidepressant effects of a single dose of ketamine appear to last generally, from several days to several weeks. In light of evidence that suicidal ideation improves with other symptoms of depression, the potential role of ketamine and other rapid acting antidepressants will be considered briefly. Building on molecular insights into the mechanisms through which ketamine appears to produce its antidepressant effects, novel alternatives to ketamine will be discussed.

KEYNOTE LECTURE (KL-2)

Interactions between Neurotransmitters: The Key to Remission in Major Depressive Episodes

Pierre Blier
*Department of Psychiatry, University of Ottawa, Canada

Despite the availability of medications acting on a single neuronal element, like the selective serotonin reuptake inhibitors (SSRIs), all three main monoamine systems can be impacted in the brain. SSRIs produce an enhancement of serotonin (5-HT) transmission, but dampen the firing activity of norepinephrine (NE) and dopamine neurons. These data may help understand the low remission rates and in some instances residual symptoms, which may actually be iatrogenic side effects. Adding NE reuptake inhibition either with a NE reuptake inhibitor like a tricyclic, or switching the SSRI for high doses of a 5-HT/NE acting agent (SNRI), like venlafaxine, may be beneficial. Similarly, adding a dopamine agonist like pramipexole may also lead to an antidepressant response. There are now three partial dopamine agonists marked in some countries (aripiprazole, brexpiprazole, and cariprazine) that have been shown to be effective adjuncts in patients with inadequate response to a SSRI or a SNRI.

These three partial dopamine agonists as well as other “atypical antipsychotics” are also endowed with other properties that may contribute at low doses to produce an antidepressant response. Specifically, their 5-HT2A and 5-HT2C antagonism may contribute to restore NE and dopamine activity, respectively, in the presence of SSRIs. This is because SSRIs decrease NE activity through the activation of 5-HT2A receptors and dopamine activity through the activation of 5-HT2C receptors. Finally, several agents of that family are also potent of 5-HT1A agonists. The clinical relevance of this property is indicated by the antidepressant effect of the selective 5-HT1A agonist gepirone extended release.

Finally, laboratory studies in rats have shown that the rapidly-acting glutamate agent ketamine in depression increases the firing activity of DA and NE neurons in a time -course consistent with its prompt therapeutic action. These results underscore the importance of multi-targeted approaches to treat depression.

KEYNOTE LECTURE (KL-3)

Translating from Animal Models to Human Schizophrenia: Insights into Pathophysiology, Treatment and Prevention

Anthony A. Grace
*Distinguished Professor of Neuroscience, Professor of Psychiatry and Psychology, University of Pittsburgh, USA

There is considerable evidence that schizophrenia involves a dysregulated dopamine system, potentially driven by overactivity in the hippocampus. Furthermore, multiple postmortem studies of schizophrenia brains show a substantial loss of a particular type of inhibitory neuron known as the parvalbumin GABAergic interneuron; loss of this neuron is thought to drive the hippocampal hyperactivity and dysrhythmic activity, leading to an over-responsive dopamine system. Our studies suggest that when the hippocampus is hyperactive and dysrhythmic, the dopamine system is hyper-responsive to stimuli, which can underlie the resultant hallucinations and delusions. A major question is why there is interneuron loss in the hippocampus. Parvalbumin interneurons early in life are susceptible to damage due to stress. In a developmental disruption model of schizophrenia in the rat, we found that prepubertally these rats are hyper-responsive to stress, and furthermore relieving the stress early in life prevents the transition to “psychosis” in adulthood. This suggests that schizophrenia susceptibility may be due to heightened sensitivity to the deleterious effects of stress. Indeed, multiple stressors given during this sensitive period to normal rats can lead to the schizophrenia phenotype. Moreover, elimination of the ability of the medial prefrontal cortex to regulate stress makes normal rats hypersensitive to stressors that would not impact an intact rat. Given that identical twins are concordant for schizophrenia only 50% of the time, and that as much as half of schizophrenia is not familial, this leads to the intriguing possibility that genetic predisposition does not cause schizophrenia, but instead like the developmental disruption model causes the individual to be hypersensitive to the deleterious effects of stress. Therefore, controlling stress early in life in susceptible individuals may be an effective means to prevent transition to schizophrenia later in life.

PLENARY LECTURE (PL01)

Depression and Functionality

Kazuyuki Nakagome
*National Institute of Mental Health, National Center of Neurology and Psychiatry, Tokyo, Japan

Depression is a common mental illness that follows a chronic course and may cause serious functional disabilities. Only 20% of the patients recover and remain well, whereas 80% experience more than one depressive episode during their life course. Depression is associated with significant disability in work, school, family and society. Given its prevalence and multi-level impairments, WHO predicts depression to be the leading cause of disability by 2030. Although most of the patients desire not only to improve depressive symptoms but also to return to usual level of functioning, only 5% of clinical trials report functional outcomes. Level of functioning generally move in parallel with depressive symptoms and to achieve remission is critical to attain functional recovery. Moreover, it is acknowledged that functioning does not necessarily return to normal in patients who achieved remission of depressive symptoms. Residual depressive symptoms, insomnia, somatic symptoms and cognitive impairment, are the factors that affect psychosocial outcome after remission. Among these factors cognitive impairment has attracted increasing attention as a mediator between depression and functional disabilities. Cognitive impairment frequently persists during remission as equivalent as in the symptomatic phase, especially in the domains of attention, executive functioning and memory. Antidepressant treatment may improve functioning along with depressive symptoms, whereas its effect on cognition is, at least partially, independent from symptomatic improvement. However, improvement in cognition by antidepressants is incomplete, often failing to return to normal. Psychosocial treatment known as cognitive remediation therapy is gaining interest in the treatment of cognitive impairment in psychiatric disorders. Meta-analysis on cognitive remediation therapy for depression has shown significant effect in some cognitive domains as well as in functioning. More research is warranted to develop effective treatment methods and valid assessment tools that may lead to improvement in functioning and also possible mediators between depression and functioning.

PLENARY LECTURE (PL02)

Early Intervention in Bipolar Disorder: Does it impact Outcomes?

Lakshmi Yatham
*Professor of Psychiatry, University of British Columbia, Vancouver, Canada

Although bipolar disorder has a heterogeneous course of illness, the disorder is progressive in many patients with increasing risks of recurrence and a risk of long-term cognitive decrease. The question that remains unanswered is whether intervention in early stages of the disease improves outcomes. The objective of this presentation is to review the data on early intervention in bipolar disorder and its impact on patient outcomes.

Early intervention in bipolar disorder encompasses intervention at any of these stages of the disease: 1. In high- risk individuals to reduce the incidence of new cases; 2. In those with prodromal symptoms to reduce morbidity and incidence of new cases; and 3. In first episode manic patients to reduce morbidity and mortality and improve outcomes.

The available evidence for intervention in high-risk individuals and in those with prodromal symptoms is limited. However, there is good data from first episode cohorts. These data suggest that early intervention at disease onset has positive impact on outcomes. This presentation will review clinical, cognitive and brain imaging data, discussion clinical implications of these data, and suggest strategies for further research.

PLENARY LECTURE (PL03)

Psychotropic Drug Development Based on the Molecular Pathogenesis of Mental Disorders Starting from Rare Disease-Susceptibility Variants

Norio Ozaki
*Department of Psychiatry, Nagoya University Graduate School of Medicine, Japan

Research suggests that mental disorders lie along a spectrum instead of a dichotomized model. Many psychiatric symptoms such as cognitive disturbance are not only found in schizophrenia (SCZ) but also in autistic spectrum disorder (ASD), bipolar disorder, and even in depression. In addition, there is a definite overlap between genetic background between ASD, SCZ and bipolar disorder with high heritability of about 80%.

The recent progress of molecular genetic analysis enabled researchers to search for large effect, rare disease-susceptibility variants, such as copy number variants (CNVs) and single nucleotide variants (SNVs). Thus, using array comparative genomic hybridization, we performed a high-resolution genome-wide CNV analysis in about 2,000 SCZ and identified clinically significant CNVs that were more frequent in cases than controls (odds ratio=3.04, 9.0percent of cases) [1]. Gene set analysis also replicated previous findings (e.g., synapse, calcium signaling) and identified novel biological pathways including genomic integrity. Furthermore, international collaborative ASD exome study identified 33 genes[2]. Many of the implicated genes encode proteins for synaptic formation and chromatin-remodeling pathways and also have been implicated in other disorders including SCZ.

In order to develop the new psychotropic drug for mental disorders such as SCZ and ASD, the next generation of research in these disorders must address the neural circuitry underlying the psychiatric symptoms, the cell types playing pivotal roles in these circuits, and common intercellular signaling pathways that link diverse genes. Therefore, now we are trying to elucidate the molecular pathogenesis of these neurodevelopmental disorders using cell or tissue-based models (induced pluripotent stem cell (iPSC) established from patients with rare variants–derived neurons or brain), as well as animal models with high construct validity.

PLENARY LECTURE (PL04)

The Role of Neuroinflammation in Psychiatric Disorders

Brian Dean
Florey Institute for Neuroscience and Mental Health, Australia

There is a significant body of evidence to suggest a role for neuroinflammation in the pathophysiologies of psychiatric disorders (Dean, 2011). Importantly, it is also becoming clear that different neuroinflammatory pathways or even different changes in the same neuroinflammatory pathways are contributing to the pathophysiologies of different psychiatric disorders. In this presentation, an overview of evidence supporting a role for changes in cytokine cascades in the pathophysiology of schizophrenia and major depressive disorders will be reviewed. Then, the complexities of differential changes in TNFα-regulated pathways in the cortices of subjects with schizophrenia, depression and bipolar disorder will be used to show how changes in the same cytokine pathway can lead to different pathophysiological outcomes. Finally, data suggesting that targeting TNFα-regulated pathways may have therapeutic benefits in depression will be presented to show how work on CNS cytokine pathways may lead to new classes of antidepressants.

MORNING LECTURE (ML01)

The Neurocircuitry of Depression: Focus on Dopamine System Dysregulation

Anthony A. Grace
*Distinguished Professor of Neuroscience, Professor of Psychiatry and Psychology, University of Pittsburgh, USA

Research suggests that mental disorders lie along a spectrum instead of a dichotomized model. Many psychiatric symptoms such as cognitive disturbance are not only found in schizophrenia (SCZ) but also in autistic spectrum disorder (ASD), bipolar disorder, and even in depression. In addition, there is a definite overlap between genetic background between ASD, SCZ and bipolar disorder with high heritability of about 80%.

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MORNING LECTURE (ML02)

Thalamo-Fronto-Temporal White Matter Connectivity in Schizophrenia and Schizotypal Personality Disorder: A Diffusion-Tensor Imaging Study

Jun Soo Kwon
*Department of Psychiatry, Department of Brain & Cognitive Science, Seoul National University, Seoul, Korea

The concept of “spectrum”, which pursues a more dimensional approach rather than a categorical approach is one of the most significant changes in DSM-5. Schizotypal personality disorder (SPD) is a schizophrenia spectrum disorder characterised by diverse psychopathologies including idea of reference, eccentric appearance and behaviour, unusual perceptual experience and social anxiety. Since SPD shares biological, genetic and phenotypical characteristics with schizophrenia (SCZ), studies on SPD may explain why only a fraction of SPD patients, who has a diathesis for schizophrenia, will develop full-blown schizophrenia. These studies will also increase our understanding of vulnerability and resilience mechanisms in developing psychosis. Although SCZ patients show deficits in thalamo-cortical and fronto-temporal connectivity, white matter (WM) connectivity has not been thoroughly investigated in SPD.

Structural and diffusion tensor imaging were obtained in 40 neuroleptic-naïve SPD patients, 60 SCZ patients and 100 healthy controls (HC), who were recruited from Seoul Youth Clinic in Seoul National University Hospital and the community by advertisements. Tract-based spatial statistics (TBSS) and probabilistic tractography were applied to analyse thalamo-fronto-temporal connectivity. We conducted two group comparisons, which are one between schizophrenia spectrum disorders (SCZ and SPD) and HC, and the other between either SCZ or SPD and HC. Correlations were also analysed for the connectivity measures and clinical scales, such as the Positive and Negative Syndrome Scale (PANSS) and the Global Assessment of Functioning (GAF) scale.

Widespread reduction in fractional anisotropy (FA) was observed in thalamo-cortical and fronto-temporal connections in SCZ compared to HC. SPD also showed FA reduction when compared to HC but to a lesser degree than SCZ. When compared as a schizophrenia spectrum disorder to HC, SCZ and SPD altogether showed decreased WM connectivity in left thalamo-orbital frontal pathway. However, only SCZ patients revealed FA reduction in orbito-temporal pathway, whilst SPD patients did not show this abnormality. There was a significant correlation between FA values and the negative symptom score of the PANSS and GAF scale score in SPD.

This is the first study to investigate thalamo-fronto-temporal connectivity in schizophrenia spectrum disorder patients and it also provides further evidences for SPD as a schizophrenia continuum. In summary, decreased WM connectivity in thalamo-orbital frontal pathway may be a shared biomarker in schizophrenia spectrum disorders, such as SCZ and SPD, and this observation, together with the preserved orbito-temporal frontal pathway in SPD suggests a possible role of fronto-temporal pathways in protecting SPD patients from the onset of psychosis.

MORNING LECTURE (ML03)

Early Intervention for Psychosis in Hong Kong: Data and Experience

Eric Chen
*Professor of the Department of Psychiatry, University of Hong Kong, Hong Kong

Early Intervention for psychosis has been propagated as a paradigm for service development in many locations in the last 20 years. It started with the realisation that despite good community services, there is still significant delays in the treatment of psychotic disorders, the delay being associated with a poorer long-term outcome. Early psychosis programmes aim to improve the long-term outcome for psychotic disorders by (1) earlier detection; (2) focused intervention in the early course of the disorder (critical period) and (3) prevention in the pre-psychotic stage. Using real-life data of such an initiative in Hong Kong in the last 15 years, we review with a series of controlled studies how this paradigm interacts with cultural and service delivery factors, and determined the extent to which outcome could be enhanced in a sustained manner. The result suggest that even with a relatively low-resource system, it was possible to significantly reduce treatment delay, as well as improve function outcome in a sustained manner, supporting the critical period hypothesis. However there also appears to be a limit to which functional improvements can occur, beyond this limit, improvement has proven more difficult to sustain.

MORNING LECTURE (ML04)

Low dose of ketamine, a novel, fast antidepressant, add-on trial for treatment resistant depression: from basic neuroscience study to clinical trial in Taiwan

Tung-Ping Su[1,2,3,4*], Mu-Hong Chen[2,4], Cheng-Ta Li[1,2,4], Wei-Chen Lin[2,4] , Chen-Jee Hong[1,2,4], Ralitza Gueorguieva[5,6], Pei-Chi Tu[1,2,3], Ya-Mei Bai[1,2], Chih-Ming Cheng[2], John Krystal[6*]
[1]Division of Psychiatry, Faculty of Medicine, National Yang-Ming University, Taipei, Taiwan, [2]Department of Psychiatry, Taipei Veterans General Hospital, Taipei, Taiwan, [3]Department of Medical Research, Taipei Veterans General Hospital, Taipei, Taiwan, [4]Institute of Brain Science, National Yang-Ming University, Taipei, Taiwan, [5]Department of Biostatistics, School of Public Health, Yale University, New Haven, CT USA, [6]Department of Psychiatry, Yale University School of Medicine, New Haven, CT USA

It has been well accepted worldwide that about 40% of major depression (MDD) were treatment refractory. The discovery and replication of the rapid and robust antidepressant effects of ketamine for treatment-resistant symptoms of depression may constitute an important treatment advance, addressing some of the limitations of current antidepressant treatment. Our study demonstrated that Intermediate dose of Ketamine (30mg/kg) reduced the immobility in the tail suspension test and forced swimming test for mice supporting its antidepressant-like effects in animal model. However, ketamine did not show effect on concentration of mTOR and Akt but increases of pGSK in the hippocampus of mice. Additionally, in patients with treatment refractory depression (TRD), we also found weaker theta and low alpha power in the prefrontal area of ketamine responders than non-responders, confirmed by ketamine induced reduction of sigma wave power in mice model. We also recruited 71 patients with TRD and equally randomized into three dose groups (0.5 mg/kg-ketamine, 0.2 mg/kg-ketamine and placebo (normal saline) in a double-blind manner. Mood and psychedelic ratings were assessed at baseline and 12 time-points post infusion until day 14. This is the first report to our knowledge to demonstrate a significant dose-related ketamine antidepressant effect on scores of the Hamilton Depression Rating Scale (HAMD-17), which is moderated by baseline depression severity. The responder analysis (> 50% reduction from baseline HAMD on at least two days between day2 and 5) also revealed a significant dose-related effect (0.5 mg/kg 45.8%, 0.2 mg/kg 39.1% and saline 12.5%). Of particular interest is that attenuation of symptom by ketamine was not only seen in depression but even greater than 50% in pessimism and suicidal thoughts, which lasted over a week, suggesting that acute low dose ketamine infusion may be useful in suicide prevention in the near future.

SPECIAL LECTURE 1 (SL01-1)

Direction of Psychiatric Research in DSM-5 Era

Masatoshi Takeda
*Aino University, Osaka, Japan

SPECIAL LECTURE 1 (SL01-2)

An American Perspective on US-Asia Partnerships: Opportunities and Challenges

John H. Krystal[1], Robert L. McNeil, Jr.[2]
[1]Professor of Translational Research, Chair of Department of Psychiatry, Yale University School of Medicine, USA
[2]Chief of Psychiatry at Yale-New Haven Hospital, USA

Psychiatric illness is a global challenge and the solutions to this problem are likely to emerge on a global basis. Partnerships between Asian and American scientists create opportunities for synergy at the level of access to research subjects, technology infrastructure, expertise, and funding. Successful collaborations create wonderful scientific opportunities and they may help to advance scientific careers and enhance the academic prestige of Departments and Medical Schools. Nonetheless, international collaborations bring special challenges related to sustaining long-distance collaborations and the potential clashing of different scientific and academic cultures. This presentation will be based on my personal experiences as well as the experiences of faculty within the Yale Department of Psychiatry in collaborating with groups in China, Taiwan, and elsewhere in the world and as well as in welcoming visiting scientists from around the world to Yale.

SPECIAL LECTURE 1 (SL01-3)

Present and Future Direction of Organizing a Multicenter Clinical Study in Asia

Jun Soo Kwon
*Department of Psychiatry / Department of Brain & Cognitive Science, Seoul National University, Seoul, Korea

Previous studies have explored the pathophysiology in psychiatric disorders including schizophrenia, major depression disorder, or bipolar disorder using various modalities. However, there is considerable variability in the findings due to relatively small samples, clinical heterogeneity of the population, or differences in data acquisition and processing protocols. A multi-center study using large samples and a wider range of population groups may help researchers to find more robust findings, increase the generalizability of the findings and identify illness-specific mechanisms. While multi-center collaborative work, especially in regards to psychosis, has been actively conducted in Europe and North America, such an approach in Asia is relatively rare. In this context, large Asian cohorts and consortium would be able to realize the unique advantages provided for psychosis research in Asia, and thereby offer insights into the current disparities in research.

SPECIAL LECTURE 1 (SL01-4)

Public awareness and anti-stigma approaches in an Asian setting

Eric Chen
*Professor of the Department of Psychiatry, University of Hong Kong, Hong Kong

Culture and language characteristics are important to the perception of mental illnesses and their treatment in the Asian Context. Some key issues about how language relevant to mental illness are reviewed using examples from Hong Kong. The impact of their use are discussed in the wider context of public awareness approaches for psychosis in order to facilitate early detection.

SPECIAL LECTURE 2 (SL02-1)

Drugs Used for Major Depressive Episodes

Pierre Blier
*Department of Psychiatry, University of Ottawa, Canada

The use of the word “antidepressants” has generated much confusion and contributed to the false notion of their excessive use. Indeed, the selective serotonin reuptake inhibitors represent the first-line pharmacological treatment for most anxiety disorders, which are more prevalent than major depressive disorder (MDD). Duloxetine was first introduced for the treatment of MDD, but is also indicated for chronic pain and in some countries for urinary incontinence. Low doses of tricyclic antidepressants have been used for decades in chronic pain, including amitriptyline for the prophylaxis of migraine. Immediate release trazodone is routinely utilized as a sedative. All these medications have been grouped under the umbrella of “antidepressants” and their combined use obviously far exceeds the prevalence of MDD.

The need for a mechanistically-based nomenclature is also crucial because the abovementioned drugs may be effective in distinct diagnostic entities at different doses. For instance, tricyclics “antidepressants” are generally effective in chronic pain at 25 mg/day, whereas about 150 mg/day is necessary to achieve a therapeutic action in MDD. *Per se*, this implies different mechanisms of action.

Finally, in treatment-resistant MDD, several medications that are not “antidepressants” have been used in combination with “antidepressants” to achieve remission. The best examples are low doses of atypical antipsychotics, which act on a variety of monoaminergic receptors without necessarily diminishing dopamine type 2 transmission.

In conclusion, a nomenclature using pharmacological targets rather than initial clinical indication must be implemented in order to span different diagnostic categories and remove any stigma associated with the term “antidepressant”.

SPECIAL LECTURE 2 (SL02-2)

The new classification of drugs used for mania and psychosis

Hiroyuki Uchida
*Keio University School of Medicine, Department of Neuropsychiatry, Japan

The current nomenclature of drugs used for mania and psychosis is based on clinical indications; they are classified as “mood stabilizers” and “antipsychotic drugs”, respectively. While this conventional nomenclature has been widely used, there are a number of limitations to this system. First, boundaries among various categories of psychotropic drugs, using the current nomenclature have become unclear. “Antipsychotic drugs” and “mood stabilizers” are good examples; antipsychotic drugs are used for not only schizophrenia, but also mood disorders, including bipolar disorder and treatment resistant depression. On the other hand, mood stabilizers are often prescribed for a mood component in any psychiatric disorder. This discrepancy between their names and indications often confuses patients and their caregivers and sometimes leads to a misunderstanding of the effects of prescribed medications. This misunderstanding could have negative consequences on medication adherence. Second, up-to-date scientific knowledge on these drugs has not been reflected in the current nomenclature. This is a serious issue since the current system was created nearly half a century ago. Third, unique and sometimes catchy labeling of particular drugs such as multi-acting receptor targeted antipsychotics (MARTA), serotonin dopamine antagonist (SDA), and dopamine system stabilizer (DSS), are proposed and initiated by pharmaceutical companies and often well accepted; however, they do not always accurately describe the mechanisms of action of those drugs. To overcome these limitations of the current nomenclature, the neuroscience-based nomenclature (NbN) was developed, which reflects our current neuroscience advances in a scientifically sound classification system. Antipsychotic drugs and mood stabilizers are now classified under the categories of “drugs used for psychosis” and “drugs for relapse prevention”, respectively. Moreover, within each category, drugs are classified based on their pharmacological profiles. In this presentation, examples of multidimensional classification with respect to medications used for the treatment of psychosis and mania will be presented.

JOINT AsCNP-CINP MEETING (JM01-1)

NMDA receptor channel subunit GluN2D: A dark horse molecule in Neuropsychopharmacology

Kazutaka Ikeda, Yoko Hagino, Soichiro Ide
*Department of Psychiatry and Behavioral Sciences, Tokyo Metropolitan Institute of Medical Science, Japan

N-methyl-D-aspartate (NMDA) receptors play crucial role in various brain functions, such as cognition, memory, learning, neural development, and pain. Phencyclidine (PCP) and ketamine, noncompetitive NMDA receptor antagonists, increases locomotor activity in rodents and causes schizophrenia-like symptoms in humans. Low dose of ketamine reportedly ameliorates anti-depressant resistant depression. Although activation of the dopamine (DA) pathway is hypothesized to mediate these effects of PCP and ketamine, the precise mechanisms by which these drugs induce their effects remain to be elucidated. We found that acute and repeated administration of PCP and ketamine did not increase locomotor activity in GluN2D knockout mice. GluN2D knockout mice did not show impairment of prepulse inhibition by PCP. We investigated the effect of PCP on extracellular levels of DA (DA_{ex}) in the striatum and prefrontal cortex (PFC) using *in vivo* microdialysis and locomotor activity in mice lacking the NMDA receptor channel GluN2A or GluN2D subunit. Gene expression changes in the brains were analyzed by using two different DNA arrays, array originally prepared in Kazusa DNA Research Institute and Illumina array. PCP significantly increased DA_{ex} in wildtype and GluN2A knockout mice, but not in GluN2D knockout mice, in the striatum and PFC. Furthermore, DNA array experiments revealed that PCP-induced *fos* expression was abolished in GluN2D knockout mice. These results suggest that PCP and possibly ketamine enhance dopaminergic transmission, increases locomotor activity, and induces *fos* expression by acting at GluN2D. GluN2D may be a new target for pharmacotherapy of PCP and ketaine dependence, schizophrenia and depression.

JOINT AsCNP-CINP MEETING (JM01-2)

Can we develop blood tests for psychiatric disorders?

Brian Dean
*Florey Institute for Neuroscience and Mental Health, Australia

The diagnoses of psychiatric disorders is still dependent upon careful clinical observations and the detection of specific symptom clusters(American Psychiatric Association, 2013). This contrasts to many other areas of medicine where diagnoses are based on results from biologically based measures which are often made by testing levels of blood components. Whilst some advances have been made in identifying potential biomarkers for psychiatric disorders(Scarr et al., 2015), there is still no widely used test that can assist with the diagnoses of psychiatric disorders. The CRC for Mental Health was form in Melbourne to manage a program of research to develop clinically useful tools for use in diagnosing or helping treatment decision making in subjects with disorders of the human CNS. Within psychiatry the CRC has had two major focusses for biomarker discovery. The first was to develop a mechanism to identify a sub-set of people with schizophrenia that are defined by a marked decrease in cortical muscarinic receptors(Scarr et al., 2009) when they are alive and, subsequently, to determine if they have specific symptom profiles or preferentially respond to certain drug treatments. The second was to validate the finding that changes in the levels of a panel of cortical genes can be used to separate people with schizophrenia from controls and to determine whether levels of expression of this panel of genes can effectively diagnose schizophrenia using RNA from white blood cells. This presentation will review potential advances in the field of biomarker discovery in psychiatric illness and then focus on findings by the CRC for Mental Health.

JOINT AsCNP-CINP MEETING (JM01-3)

Brain image and drug development: the past, present, and future

Yuan-Hwa Chou
*Department of Psychiatry, Taipei Veterans General Hospital, Taipei, Taiwan

Most people in the pharmaceutical industry estimate that typically 1 billion and take fifteen years must be spent to develop a compound. To help experimental medicine drive the development of drugs in humans faster and with greater confidence, one especially promising area for innovation lies in the use of new technology, brain image. Modern imaging that allows scientists to watch the functioning brain now relies primarily on two approaches. Magnetic resonance imaging (MRI) uses harmless magnetic fields and radio waves to map brain structures and brain physiology. Positron emission tomography (PET) uses safe, tracer doses of radioactive materials to follow the fate of individual molecules as they travel in the human body. These techniques promise to change the way drugs are developed. Future drug development will spend less time studying “models” of disease in animals and move quickly to more-informative experimental medicine in humans. The benefits of using neuroimaging in this way can already be glimpsed in six aspects of drug testing: time and cost, confidence in targets, integration of information, dosage, drug combination, and understanding of the placebo effect. In this presentation, I will summarize the current situation in the development of antipsychotics and antidepressants which applied the techniques. Given the state of the art knowledge, researchers could open a new way for their future study.

JOINT AsCNP-CINP MEETING (JM01-4)

Functional Neurosurgical Interventions for Drug Refractory Obsessive-Compulsive Disorder: Where We Are Now.

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Despite continued therapy, a substantial portion of patients with obsessive–compulsive disorder (OCD) continue to experience persistent symptoms and remain functionally impaired. Although the etiology of OCD remains unknown, there is growing evidence suggesting a neurobiological basis for OCD, such as dysfunctional cortico-striatal-thalamic-cortical (CSTC) circuits. In the hope of reducing the disability and debilitation of patients with refractory OCD, neurosurgery is used as a therapeutic tool to modulate specific targets or nodes within these circuits. The development of stereotaxis allows for more targeted, precise interventions that produce discrete subcortical lesions. Ablative stereotactic neurosurgical interventions (anterior cingulotomy, limbic leukotomy, subcaudate tracotomy and anterior capsulotomy) have been attempted. Although the advent of stereotactic radiosurgery (e.g. the “Gamma knife”) has provided a means to produce accurate lesions without subjecting the patient to a surgical operation, surgical complications must also be considered, and may occur in up to 20%. Deep-brain stimulation (DBS), which has emerged as an evidence-based option for the treatment of movement disorders such as Parkinson's disease and dystonia, is a well-accepted alternative to ablative therapy. DBS is adaptable, adjustable and reversible and demonstrates efficacy comparable to lesioning, as well as a favorable safety profile. Although DBS for OCD has received United States Food and Drug Administration approval as a "humanitarian device exemption", but the results are limited by small sample size and insufficient randomized controlled data. Magnetic Resonance guided Focused Ultrasound Surgery (MRgFUS) is novel treatment using non-invasive high intensity focused ultrasound guided and monitored by MR thermal imaging. Non-invasive tissue ablation by MRgFUS may reduce risks of tissue damage, improve clinical outcome and have better accessibility to target. Recent clinical trial demonstrates the promising results of bilateral thermal capsulotomy with MRgFUS without inducing side effects to treat patients with refractory OCD.

Key Words: Cortico-striato-thalamo-cortical, Obsessive-compulsive disorder, Deep brain stimulation, Psychiatric surgery, magnetic resonance-guided focused ultrasound

JOINT AsCNP-JSNP MEETING (JM02-1)

Molecular genetics for psychostimulants addiction in Asian countries

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Genetic contributions to substance dependence vulnerability are supported by data from twin studies, linkage studies, candidate gene association studies and, more recently, Genome Wide Association Studies (GWAS). Animal studies including genetically modified mice have also attempted to identify the genes that may contribute to responses to addictive drugs and addiction liability, initially focusing upon genes for the targets of the major drugs of abuse. Based on the results of the human candidate gene and mouse KO studies, it might be thought that those genes are clearly implicated in substance dependence. There were thoughts that GWAS might identify some of those genes, and also that many were unlikely to harbor variants that altered their functions to the extent found in KO mice. GWAS that examined methamphetamine dependence with collaborative studies of Taiwan and Japan found a substantial overlap of positively associated genes that examined substance dependence. Like those studies, genes for cell adhesion molecules, enzymes, transcriptional regulation, cell structure and RNA, DNA and protein handling/modifying genes were included. GWAS for substance dependence have attained a high degree of replication, e.g. the same genes or gene loci being associated with substance dependence across a large number of studies and suggest that substance dependence is highly polygenic; each allelic variant contributing in a small, additive fashion to addiction vulnerability.

JOINT AsCNP-JSNP MEETING (JM02-2)

Addiction clinical trials in Taiwan and researches in Asian country collaborations

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Taiwan has experienced a long history of substance abuse for more than one hundred and fifty year, began with opium misuse. The first clinical trial dated back to eighty years ago when Dr Du used tapering dose of morphine to detoxify opium addicts. He also invented the method of urine test of morphine. In recent era, lofexidine, naltrexone, venlafaxine, dextromethorphan, buprenorphine has been trialed in the management of heroin withdrawal and dependence, whereas naltrexone and disulfiram for alcohol dependence. Currently, lamotrigine is trialed for ketamine dependence. For international collaborative research, alcohol and methamphetamine are the mostly studied substances, especially in genetic field, and some involved the survey of drug use pattern and smoking behavior. We suggest that further international collaborative researches in addiction across Asian countries are warranted.

JOINT AsCNP-JSNP MEETING (JM02-3)

Complex interplay between pain relief and opioid addiction: chronic pain diminishes the mesolimbic dopaminergic network

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The mesolimbic dopaminergic pathway begins in the ventral tegmental area (VTA) of the midbrain and connects to the limbic system via the nucleus accumbens. This system is widely believed to be a "reward" pathway. Since the mesolimbic dopaminergic pathway is shown to be associated with feelings of reward and desire, this pathway is heavily implicated in neurobiological theories of addiction, schizophrenia, stress and depression.

On the other hand, the maxim “no pain, no gain” summarizes scenarios in which an action leading to reward/euphoria also entails a cost. Although we know a substantial amount about how the brain represents pain and reward separately, we know little about how they are integrated during goal-directed behavior. Two theoretical models might account for the integration of reward/addiction and pain. Recently, clinical studies in Japan have suggested that in only a few cases can psychological dependence on opioid analgesics be considered to be a serious side-effect, when patients suffer from severe pain. Then, at the present symposium, I will present the topics for the molecular changes in rewarding networks under chronic pain.

JOINT AsCNP-JSNP MEETING (JM02-4)

Novel molecules, Shati/Nat8l, Piccolo and TMEM168, Protect Methamphetamine Depedence in Mice

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We have identified a novel molecule SHATI/NAT8L, PICCOLO and TMEM168 in the nucleus accumbens (NAc) of mice treated with methamphetamine. Shati/Nat8l is N-acetyltransferase like 8 protein (NAT8L) to produce N-acetylaspatate (NAA) from aspartate and acetyl-CoA. Shati/Nat8l protects the methamphetamine preference via mGluR3. Further Shati/Nat8l CpG island methylation ratios were lower in the patients with schizophrenia than in the healthy controls, which is consistent with our findings in the mice model. PICCOLO, a presynaptic scaffolding protein, was overexpressed in the nucleus NAc of the mice repeatedly administrated with METH. Piccolo downexpression by antisense technique augmented METH-induced behavioral sensitization, conditioned reward and synaptic dopamine accumulation in NAc. Expression of Piccolo C2A domain attenuated METH-induced inhibition of dopamine uptake in PC12 cells expressing human DAT. Consistent with this, it slowed down the accelerated DAT internalization induced by METH. Further, to characterize rs13438494 in the PCLO gene, we constructed plasmids carrying either the C or A allele of the SNP and transiently transfected them into SH-SY5Y cells to analyze genetic effects on the splicing of PCLO mRNA. The C and A allele constructs produced different composition of the transcripts, indicating that the intronic SNP does affect the splicing pattern. We also transfected DA and serotonin (5-hydroxytryptamine; 5- HT) transporters into cells and analyzed their uptakes to elucidate the association to psychiatric disorders. In the cells transfected with the C allele, both the DA and 5-HT uptake were enhanced compared to the A allele. We also conducted a clinical study, in order to clarify the genetic associations. PCLO rs13438494 exhibits a relationship with the dependence-like behaviors in human. TMEM also protects methamphetamine preference in mice. Interestingly, TMEM has interaction with osteopontin. Hire we would like to introduce our three molecules for drug dependence in bacsis and clinical field.

JOINT SYMPOSIUM REAP (RS-1)

Understanding drug treatment of schizophrenia in Asia through pharmacoepidemiological research - the REAP studies

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Background: Pharmacoepidemiology research in Asia is relatively new when compared to the Western societies. Using reliable method of ascertainment and quantifying drug exposure, the REAP (Research on Asian Psychotropic Prescription Pattern) is a large scale psychopharmacopeidemiological study with aims to evaluate its impact on the efficacy and safety of drugs treatment on different populations in Asia. This report summarized findings of the REAP study on antipsychotic prescription pattern of schizophrenia inpatients that were undertaken from 2001 to 2016.
Methods: Four consecutive surveys with a total of 14,660 inpatients with schizophrenia were involved. The subjects were initially recruited from various centers of 6 countries (China, Hong Kong, Japan, Korea, Singapore and Taiwan) but were extended to 15 countries and including Bangladesh, India, Indonesia, Malaysia, Myanmar, Pakistan, Sri Lanka, Thailand and Vietnam in the last survey (2016). They were assessed by their attending psychiatrists for psychiatric symptoms, adverse events and other clinical information, and all the prescribed medications using a unify standardized protocol. The WHO-ATC system was used to classify the drugs.
Results: The type and dosages of antipsychotics used and the pattern of polypharmacy differed from one country to the other and across the time. There is an increasing trend of using mono-antipsychotic therapy and the rate was higher than in most Western counterparts. The second-generation antipsychotics (SGAs) have been gradually replacing the first-generation antipsychotics (FGAs) as the mainstream treatment of schizophrenia. Adjunctive use of antiparkinsonian drugs decreased significantly with the decreasing use of FGAs and antipsychotic polypharmacy. Significant increasing concurrent use of mood stabilizers and antidepressants was however observed. Most adverse events were similar with in other studies, but with a lower reported rate of sexual dysfunction. The younger patients had generally higher prevalence of violence behavior and had higher prescription of SGAs and adjunctive mood stabilizers.
Conclusion: In applying epidemiological methods of investigation, the REAP has demonstrated a plausible way of understanding schizophrenia through pharmacological intervention.

JOINT SYMPOSIUM REAP (RS-2)

Changing trend of the use of antipsychotics

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Aim and objectives: This paper describes the characteristics of prescription patterns of antipsychotic medication in patients with schizophrenia in Asian countries from 2001 to 2016.
Method: Authors of this study collaborated with psychiatrists in Asia to undertake an international survey reviewing prescription patterns of psychotropic medications in Asia. Using a unified research protocol and questionnaire, the REAP (REsearch on Asian Psychotropic Prescription patterns) study reviewed the prescription of a large number of inpatients from China, Hong Kong, Japan, Korea, Singapore and Taiwan in 2001 (N=2399), 2004 (N=2136), and in 2008 (N=2226). In 2016, we surveyed both in- and out-patients with schizophrenia from Bangladesh, China, Hong Kong, India, Indonesia, Japan, Korea, Malaysia, Myanmar, Pakistan, Singapore, Sri Lanka, Taiwan, Thailand and Vietnam (N=3744).
Results: Prescription patterns of antipsychotic drugs differ from country to country and have recently experienced rapid changes since the introduction of second-generation antipsychotic drugs in some countries. Our survey over the years shows that as the use of first generation antipsychotics has reduced, the use of second-generation antipsychotics has increased drastically. The presentation of patient psychopathology varies greatly from country to country. Moreover, the use of antidepressants has increased. The cause of these need further exploration. The rise in the endocrine disorders and metabolic syndrome in many countries warrant systematic study.
Conclusion: The changing prescription patterns of psychotropic drugs in patients with schizophrenia have created multiple challenges for psychiatrists in Asia that need an urgent outcome study and review.

JOINT SYMPOSIUM REAP (RS-3)

Polypharmacy and psychotropic drug loading in patients with schizophrenia in Asian countries: the REAP-AP4 study

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Purpose: In the treatment of schizophrenia, polypharmacy refers to the use of two or more antipsychotic medications, while combined medications as additional use of other psychotropic drugs. Methods: By using the results from the fourth survey of Research on Asian Prescription Patterns on antipsychotics (REAP-AP4), the rates of polypharmacy and combined medication use in each country were analyzed. The online website-based data key-in system was used for data collection, which took place from March to May 2016. Daily medications prescribed for the treatment of inpatients or outpatients with schizophrenia, including antipsychotics, mood stabilizers, anxiolytics, hypnotics, and antiparkinson agents, were collected. Fifteen countries participated in this study, namely Bangladesh, China, Hong Kong, India, Indonesia, Japan, South Korea, Malaysia, Myanmar, Pakistan, Singapore, Sri Lanka, Taiwan, Thailand, and Vietnam, with 3744 surveyed patients. Results: The prescription patterns differed across these Asian countries, with the highest and lowest rates of polypharmacy noted in Vietnam (59.1%) and Myanmar (22.0%), respectively. Furthermore, the highest rates of combined use of mood stabilizers, antidepressants, anxiolytics, hypnotics, and antiparkinson agents were noted in China (35.0%), South Korea (36.6%), Pakistan (55.7%), Japan (61.1%), and Bangladesh (87.9%), respectively, whereas the lowest rates were noted in Bangladesh (1.0%), Bangladesh (0%), Myanmar (8.5%), Myanmar and Sri Lanka (0%), and Vietnam (10.9%), respectively. Conclusions: The average psychotropic drug loading of all patients was 2.01 ± 1.64, with the highest and lowest loadings noted in Japan (4.13 ± 3.13) and Indonesia (1.16 ± 0.68), respectively. Differences in psychiatrist training as well as the civil culture and health insurance system of each country may have contributed to the differences in these rates.

JOINT SYMPOSIUM REAP (RS-4)

Proposing the REAP Vignette-base survey among Asian psychiatrists

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EDUCATIONAL WORKSHOP (EW-1)

A brief report on a treatment program for problematic internet use among South Korean youth

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Background/Objective: Studies of Internet gaming addiction outline the negative consequences of excessive gaming, its prevalence, and associated risk factors. Mounting evidence indicates that those, who are vulnerable to these problems, suffer from multiple comorbid psychiatric disorders. There is a general consensus that total abstinence from the Internet should not be the goal of the interventions and that instead, an abstinence from problematic applications and a controlled and balanced Internet usage should be achieved. The aim of the treatment is to help the patient manage the inappropriate behavior and still be able to use the technology.
Method: We designed and tested the HORA (Happy Off to Recovery of Autonomy) program at the National Center for Mental Health in Seoul, S.Korea. The HORA program is an inpatient Internet addiction recovery program which integrates technology detoxification(no technology for 14 days), bibliotherapy, cognitive behavioral therapy, motivational interviewing, sociodrama, animal assisted therapy, individualized treatments for co-occurring disorders, psycho-educational groups(addiction education, social skill, life visioning), forest therapy, aftercare treatments(monitoring of technology use, homecoming day), and continuing care(outpatient treatment) in an individualized holistic approach.
Results/Discussion: Participants' scores on the Korean version of WEMWBS(Warwick-Edinburgh Mental Well-being Scale) and VAS(Visual Analogue Scale) regarding degree of craving for game use showed a statistically significant change after 2 weeks of intervention(Wilcoxon signed-ranks test). The HORA program helps patients relearn healthy coping skills in a contained environment. In addition, the HORA program is set up to address a wide variety of underlying issues which may contribute to the excessive internet game by connecting patients with integrative community service providers knowledgeable in these areas during a stay at the center.
Conclusion: This study is presenting evidence that individuals with internet gaming addiction can successfully regain their control on a multimodal treatment approach, HORA program.

EDUCATIONAL WORKSHOP (EW-2)

Dealing with arising ketamine abuse in Taiwan

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Ketamine use has been identified as a grave issue in public safety and health in many Asian societies. The number of young adults who use or misuse ketamine has rapidly increased during the past 5 years in Taiwan. Because harms associated with ketamine use, ketamine in Taiwan is regulated as Schedule III drug in Article 2 of Statute for Narcotics Hazard Prevention and Control. In Article 11-1, using or holding ketamine < 20 grams without prescription is fined 10,000 to 50,000 New Taiwan Dollars (approximately 300 to 1,500 US dollars) with 4 to 8 hours of compulsory drug education/workshop.

For dealing with the emerging problem of ketamine abuse in Taiwan, many researches were carried out the explore the characteristics of ketamine abusers, the harm of long-term ketamine exposure, and the effective treatment modalities. Studies shows most of the ketamine abusers are male, relative young, have full-time job, and nicotine dependence. They have higher prevalence of HIV infection and risky behaviors. Neuroimaging and cognitive studies demonstrates that long-term ketamine users have brain volume decrease, imapired attention and impulse control. Group therapy and life skill training show some effects to the patients with ketamine abuse. However, there is still lack of consensual effective treatment at present.

There are still arguments about ketamine Schedule catogries and the policy of management. We should keep steps on facing the challenges of ketamine and other substances abuse problem, especially among young population. There more comprehensive evaluation we have, the more we can help the patients with addiction problems.

EDUCATIONAL WORKSHOP (EW-3)

Assessment of maternal drug use and impact on child safety and parenting

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Abuse of alcohol and drugs by parents can have negative effects on the well-being and safety of children. Researches demonstrate a correlation between drugs use during pregnancy and inadequate prenatal care, linked to maternal and neonatal risks including a lack of postnatal care, and well-child visits. For drug-using pregnant women, prenatal care is especially valuable as it facilitates monitoring of drug uses and linkages with physical and mental health while assessing psychological and social problems.

In antenatal care unit or obstetric unit, the health care team or practitioner should screen and assess all pregnant and postpartum women for alcohol and drug uses. After screening and assessing, the health care team should give an advice or arrange an appropriate response and individualized specific plan for pregnant woman and family. The important dimensions for assessment composed of 1) current and past experiences of drugs or alcohol use and amount, 2) problems of alcohol and drugs use of partner and family member, 3) supporting system and capacity for parenting and 4) maternal and newborn urine toxicologic analyses.

In conclusion, adequate assessment of maternal drug use from the prenatal period is associated with positive perinatal and postnatal development outcomes. Understanding the relationship between maternal drugs abuse and child maltreatment is important because it is necessary for providing better assessments of families at risk, and planning for prevention and intervention strategies.

EDUCATIONAL WORKSHOP (EW-4)

The Preventive Measure Against Alcohol Use Disorder Among the Working Persons with Habitual Drinking

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As one of the big problems regarding alcohol use disorder in Japan is their late onset of it after their retirements, we developed the pereventive method for it. This method includes the two-steps interventions, first ones conducted after the lecture, and the second in about 6 months after them, to prevent working persons with habitual drinking from suffering from alcohol use disorder. Then, to study the effectiveness of them, we took self-administrated questionnaires about their frequencies and quantities of alcohol, their self-efficacy in drinking, and their motivation for moderation in drinking, before and after the first interventions, and after the second one. Seventy-nine working persons responded our questionnaires. Forty-three participants (54.5%) had habitual drinking more than 4 times per week. Twenty-four participants (30.4%) drank more than 6.1 drinks. Except for 9 ones chose less than once drinking per month or unanswered, we investigated 70 persons about their changes in amount of alcohol (Participation; once 22; twice 48). 8 of 22 first participants and 25 of 48 ones in the both reduced amount of alcohol. Regarding their attitudes about their habitual drinking and their frequencies and quantities of alcohol, those who tried to change their alcohol related habits were significantly higher among participants in both sessions than ones among those who participated only in the first interventions ($P<0.05$). Although the both participants had high motivation for their improvements of drinking, we suggested the booster interventions were more effective on them.

SYMPOSIUM (S01-1)

Quality of life and social function in patients with schizophrenia or bipolar disorder receiving long-acting antipsychotics

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Purpose: Long-acting injectable antipsychotics (LAIs) provide a potential solution to overcome poor adherence to medication in patients with schizophrenia and bipolar disorder. In this study, we compared the subjective experiences and clinical features of patients receiving LAI treatment for schizophrenia and bipolar disorder. Methods: Overall, 449 patients with schizophrenia and 45 patients with bipolar disorder who regularly received LAI treatment for at least 6 months were administered the brief version of the World Health Organization Quality of Life (WHOQOL) questionnaire, Subjective Well-Being Under Neuroleptics (SWN) scale, Personal and Social Performance (PSP) scale, Clinical Global Impression of Severity (CGI-S) scale, and lack of insight scale. A retrospective chart review was conducted in all patients to determinate the frequency of hospitalization during their illness course. Results: The frequency of hospitalization (times/year) decreased significantly after LAI treatment in patients with schizophrenia (from 0.26 ± 0.42 to 0.12 ± 0.45) and bipolar disorder (from 0.53 ± 0.65 to 0.16 ± 0.40). The overall WHOQOL scores and the scores of the four domains were significantly lower than the Taiwanese norm in both groups. In total, 47.0 % and 35.6 % of the patients with schizophrenia and bipolar disorder were judged as having lack of insight. Conclusions: LAI treatment can efficaciously prevent the relapse of psychotic or mood episodes in patients with poor adherence to medications. Although approximately half the study patients had poor insight, they nevertheless received LAI treatment regularly. LAI treatment is recommended as an extensive regiment in patients with bipolar disorder or schizophrenia.

SYMPOSIUM (S01-2)

The picture of long-acting injectable antipsychotics in Japan

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Five kinds of long-acting injectable antipsychotics (LAIs)—aripiprazole, pariperidone, risperidone, fluphenazine, and haloperidol—are available in Japan. Despite their reported advantages and recommendation in *The Guidelines of Pharmacological Therapy for Schizophrenia* by the Japanese Society of Neuropsychopharmacology, LAI use among antipsychotics is low. The estimated number of patients with schizophrenia in Japan is about 700,000, and the estimated rate of LAI use is around 10%. This rate is low compared with 23% in the United States or 35% in Europe. Reasons may include differences in health care systems and concerns about side effects. There are 350,000 psychiatric hospital beds, and average hospital stay is approximately 300 days in Japan. Current consensus is that patients with a long hospital stay do not require LAIs. Some psychiatric service providers and families are concerned about side effects, such as sudden death. There reported 32 deaths between 6 months since pariperidone LAI is launched in Japan, and government released a letter about attention and proper use. According to this letter and report there requires attention to their physical conditions such as arrhythmia and abnormal glucose tolerances, and requires proper use of LAI such as dose adjustment and avoidance of multiple combination use of antipsychotics.This presentation describes the picture of LAI use in Japan and includes this background information.

SYMPOSIUM (S01-3)

Major adverse effects of long-acting injectable versus oral antipsychotics in schizophrenia patients: a population-based retrospective cohort study

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Objective: Long-acting injectable (LAI) antipsychotics (LAI-APs) have been found to improve medication compliance and reduce admission rates. However, the side effects of long-term LAP-APs in schizophrenia patients remains unclear.Methods: Using a nationwide database, the Taiwan National Health Insurance Research Database, subjects who had first been diagnosed with schizophrenia between 2002 and 2013 were identified. The schizophrenia patients receiving LAI-APs were designated as the LAI group. A 1:2 ratio was used to select age-, gender-, and index-year -matched control without LAI use. Patients who had major adverse effects before enrollment were excluded. The 2 cohorts were observed until December 31, 2013. The primary endpoint was occurrence of major adverse effects including metabolic syndrome (DM, Hypertension, Hyperlipidemia), cerebrovascular events, and acute myocardial infarction (AMI).Results: Among 13,937 newly diagnosed schizophrenia patients, we identified 1,443 patients with LAI-APs use, and 2,886 matched patients without LAI-APs use between January 2002 and December 2013. Of the 4,293 patients, 516 (11.92%) suffered from major adverse effects during a mean follow-up period of 5.14±2.96 years, including 147 (10.19%) from the LAI-APs cohort and 369 (12.79%) from the control group. In schizophrenia patients, the Cox multivariate proportional hazards analysis showed that the risk decreased with LAI-APs use 0.751 (95% confidence interval (CI), 0.618 to 0.912; p = 0.004). Moreover, in LAI-APs cohort, patients receiving secondary generation LAI-AP treatment had lower risk than those with first generation LAI-APs treatment (adjusted hazard ratio 0.689, 95% confidence interval (CI), 0.480 to 0.989; p = 0.043).Conclusions: LAI-APs use was associated with a reduced risk of major adverse effects among schizophrenia patients.

SYMPOSIUM (S01-4)

Potential Treatment Strategy of Long-acting Injectable Antipsychotics for Treatment-Resistant Schizophrenia

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Patients with schizophrenia experiences varying symptoms, severity and clinical courses, and 20%-30% of the patients eventually become treatment-resistant. Although there are no universally accepted criteria for defining the subtype of treatment -resistant schizophrenia (TRS), it may be possible to diagnose TRS subtypes based on the patient's clinical course and symptoms. Dopamine supersensitivity psychosis (DSP) has been described as a cause of TRS; it accounts for approx. 70% of TRS cases. However its treatment has not been established. It has been suggested that an excess of D2 receptor occupancy induces DSP and that treatment with high doses of antipsychotics with short half-lives is likely to result in DSP compared to treatment with long half-lives such as long-acting injectable (LAI) antipsychotics. In our recent study, which we conducted to investigate the efficacy of LAI antipsychotics for DSP patients, risperidone long-acting injectable (RLAI) was given as an adjunctive medication to oral antipsychotics in 108 patients with TRS: 72 patients with a history of DSP (the DSP group) and 36 patients without such a history (the NonDSP group). Although both groups showed significant improvements in the total Brief Psychotic Rating Scale (BPRS) score in the 2-year follow-up period, greater improvement was observed for the DSP group compared to the NonDSP group. The total dose of antipsychotics including the dose of RLAI and/or oral antipsychotics did not changed in either group throughout the study period. It should be noted, however, that the severity of extrapyramidal symptoms, including tardive dyskinesia, was significantly improved only in the DSP group. These findings suggest that RLAI treatment provides relief from refractory schizophrenia symptoms, particularly for patients with a history of DSP.

SYMPOSIUM (S02-1)

The effects of social stress on prefrontal cortical function in rodents

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Prefrontal cortex (PFC) is thought to be the site for high cognitive function that enables the organisms to consciouslyconstruct goal-directed behavior while simultaneously inhibiting emotional and habitual behaviors. We have shown that the glutamatergic synapses of rodent PFC pyramidal neurons possess the large capacity to undergo use-dependent synaptic plasticity, which we believe serves to shape the PFC cognitive function at the cellular level. Our decade-long effort suggests that for the induction of synapticplasticity, the neuromodulator dopamine has to act through a certain manner. Thus, dopamine enables the induction of long-term potentiation (LTP) and long-term depression (LTD) in rodent PFC neurons through the “inverted-U shape” function, where only optimal levels of dopamine enable the induction of LTP and LTD. Under too high or too low levels of dopamine, LTP and LTD inductions are impaired. These results indicate the possibility that the behavioral deficits seen in psychiatric disordersassociated with changes in dopamine levels in the PFC may result at least partly from synaptic plasticity dysfunctions in the PFC. More recently, as one way to modulate PFC function, we adopted chronic social isolation stress model in mice, where mice are kept individually for 4-6 weeks. It was found that the isolated mice show increased anxiety as well as increased aggression towards other mice. Our preliminary data suggest that there are some changes in the levelof frontal cortex neuromodulators. We will discuss possible relation between PFC plasticity and the behavioral deficits associated with social isolation stress.

SYMPOSIUM (S02-2)

The roles of dopamine in social hierarchy of rodents and primates

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Humans and many animals living in social groups organize into hierarchy. Neural substrates underlying such social hierarchy have largely remained unknown. Dopamine (DA) is a neurotransmitter whose roles have been suggested in a umber of cognitive and affective functions including regulation of social behaviors. Thus, we investigated whether and how DA might be involved in construction of social hierarchy in rodents and non-human primates. Pharmacolgical manipulations of both DA D1 and D2 receptors altered social dominance of the drug administered subjects in socially housed mice and macaques. In particular, the D1 antagonsit faciliated social dominaince in the middle ranked mice, whereas the D2 antagonist attenuated social dominance in higer ranked mice. In macaques, the effects of the D1 antagonist were different from those of rodents, with its administration not altering social domaince in the drug adminsiterd subject, but other non-treated subjects in the group, whereas the effects of the D2 antagonsit were similar to those of rodents, but with additional effects with which social hierarchy could be more stablized when the drug was given into the low ranked subject. These changes observed in macaques appeard to involve alterations of social affiliatin tactics between subjects in the groups. These results suggest that DA may play substantial roles in social group dynamics such as construction of social hierarchy, but their roles may be different between rodent and primate species.

SYMPOSIUM (S02-3)

Dopamine innervation in the cortico-basal ganglia pathway of humans and nonhuman primates and its relevance to social cognition

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One of the most distinctive features of our species is a dramatic increase in relative brain size. However, we still have only a rudimentary understanding of the specific neuroanatomical features that could underlie our unique behavioral and cognitive specializations. Comparative neuroanatomical studies are useful in identifying phenotypical traits that may contribute to the human condition. Ideally, comparisons can be made between human brains and those of our closest living relatives, including the great apes. Neurotransmitter systems are excellent candidates for evolutionary modification as the integrity of these systems is critical to higher cognitive functions. Further, neurotransmitter systems are compromised in human-specific neuropathological processes that are associated with devastating cognitive deficits. There is also an experience-dependent plasticity in neurotransmitter concentrations that may extend to hard-wired differences among species. Dopamine is important for executive functions, including speech and language and learning and memory processes. Our recent analyses of dopaminergic innervation in various cortical regions and within the basal ganglia revealed human-specific patterns and densities that may have been important in the evolution of human cognitive and behavioral specializations.

SYMPOSIUM (S02-4)

Dopamine regulation of social information processing in non-human primates

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Accumulating evidence from rodent studies suggests that dopmaine (DA) plays importnat roles in regulation of social behaviors. However, how DA transmission is involved in social cognition in primates has remained unclear. To provide an insight on this issue, we investigated how social and nonsocial information is processed and modulated by DA signaling in macaques using the visual preference paradigm. We found that Japanese macaques exhibited preferred attention to social visual stimuli (monkey faces with and without affective valences) than nonsocial visual stimuli (e.g. landscapes, objects). Both D1 and D2 receptor antagonsit adminisration decreased perferred attention to social stimuli. However, the D1 anatgonsit also increaed attention to nonsocial stimuli at the same time, whereas the D2 antagonist did not affect attention to nonsocial stimuli. There was no difference in preferred attention its modulation by the DA receptor antagonsits between social stimuli with and without affective valanece. These results suggest that DA transmission may mediate preferred attention to social over nonsocial visual stimuli; however, the role of D1 signaling appears to maintain the balance of visual attention to social and nonsocial cues, whereas the role of D2 signaling is specifically associated with social information processing. We are currenlty investigating cortical activities associated with such DA-dependent visual preference to social over nonsocial stimuli using the near-infrared spectroscopy (NIRS).

SYMPOSIUM (S03-1)

Schizophrenia and idiopathic unconjugated hyperbilirubinemia (Gilbert's syndrome)

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Idiopathic unconjugated hyperbilirubinemia (Gilbert's syndrome, GS) is a relatively common congenital hyperbilirubinemia occurring in 3-7% of the world's population. It has been recognized as a benign familial condition in which hyperbilirubinemia occurs in the absence of structural liver disease or hemolysis, and the plasma concentration of conjugated bilirubin is normal. Recently, it was reported that unconjugated bilirubin exhibited neurotoxicity in the developing nervous system. The 'neurodevelopmental hypothesis' of schizophrenia proposes that an yet as unidentified event occurs in utero or during early postnatal life. We have observed that patients suffering from schizophrenia frequently present an increased unconjugated bilirubin plasma concentration when admitted to the hospital. Therefore, we noticed a relation between unconjugated bilirubin and the etiology of and vulnerability to schizophrenia. Our reported findings suggest that there are significant biological and clinical character differences between schizophrenic patients with and without GS. From the viewpoint of the heterogeneity of schizophrenia, there may be a poor outcome for the subtype of schizophrenia with GS.

SYMPOSIUM (S3-02)

Prediction Model of Metabolic Syndrom Induced by Olanzapine in Schizophrenia Patients

Khamelia Malik
Indonesia

SYMPOSIUM (S03-3)

Autoimmune Limbic Encephalitis Like Schizophrenia

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Background/objective: Antibody-mediated limbic encephalitis presents with various psychiatric conditions including schizophrenia-like symptoms. In this session, we focus on anti-NMDA (N-methyl-D-aspartate) receptor antibody encephalitis. We will provide an up to date review of these disorders, and highlight the role of psychiatry in diagnosis, symptomatology, and treatment through our experimental cases.
Methods: We evaluated the clinical features of, and performed neuropsychological examinations on patients with antibody-mediated encephalitis.
Results/Discussion: Our series of six patients showed subacutely progress clinical phase as follows: prodromal symptoms of upper respiratory infection, subsequent various neuropsychiatric symptoms including transient schizophrenia-like symptoms developing transient catatonic syndrome, subsequent status epilepticus and sustained consciousness disturbance with respiratory failure. Patients treated successfully with immunotherapy although some patients continuously suffered residual higher brain dysfunction. Cerebral spinal fluid of the patients showed positive for anti-NMDA receptor antibody and/or anti-VGKC antibody. Patients showed no specific lesion on MRI studies. It is reported that approximately 80% of patients with anti-NMDA receptor encephalitis are women, and, close to half in those over than 18 years of age have an ovarian teratoma. Anti-NMDA receptor encephalitis is a complex disease, which required cooperation with psychiatrists, neurologists, and gynecologists. As for molecular mechanism of anti NMDA receptor encephalitis, it was previously reported that autoantibodies bind the NMDA receptor, leading to its internalization from the cell surface and a state of relative NMDA receptor hypofunction.
Conclusion: Anti-NMDA receptor encephalitis is potentially lethal but possibly treatable disease. Patients with anti-NMDA receptor encephalitis exhibit high rates of psychiatric conditions. Psychiatrists need to have increased awareness and keep a high degree of suspicion for this disease.

SYMPOSIUM (S03-4)

Salivary alpha-amylase (sAA) as a biomarker for the response of therapy in schizophrenia patients

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Background: Reliable biology indicators for stress reaction and psychopathology are valuable markers for both psychological research and clinical practice. Recently, the measurement of salivary alpha-amylase (sAA) was introduced as a non-invasive and more convenience protocol. Several studies showed the high sensitivity of sAA level in various mental disorders, unfortunately there still no data on how the level of sAA in naïve-drugs of schizophrenia patients.
Objective: To determine whether sAA level could be as potential biomarker for therapeutic response in schizophrenia patients.
Methods: Using the cohort study, we collected 30 samples that met the inclusion criteria and 30 normal control samples. sAA level and PANSS score were taken 5 times at baseline, 3 days after treatment of antipsychotics, 5 days after treatment, 7 days, and 14 days after treatment of antipsychotics.
Results: Schizophrenia patients showed significant higher sAA levels compared to normal control group. sAA levels showed significant decline in correlation with the improvement of PANSS score within 2 weeks of antipsychotics therapy.
Conclusion: The measurement of sAA levels can be used as potential biomarker of therapeutic response in schizophrenia patients.

SYMPOSIUM (S04-1)

Pro-inflammatory cytokines as the biomarkers of clinical outcome and neuroimaging abnormalities in bipolar disorder

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Gathered evidence suggested bipolar disorder and unipolar depression are both related to dysregulated inflammatory reaction. We compared the levels of pro-inflammtory cytokines between 130 patients with bipolar disorder, 146 patients with unipolar depression and 130 age, gender matched normal controls, and found the patients with bipolar disorder were with a more severe inflammatory dysregulation than the patients with unipolar depression, with significantly higher levels of soluble interleukin-6 receptor (sIL-6R), C-reactive protein (CRP), soluble tumor necrosis factor receptor type 1 (sTNF-R1), and monocyte chemotactic protein-1 (MCP-1). We further found the patients with bipolar I disorder had significantly higher levels of sTNF-R1 than the patients with bipolar II disorder; the patients in a depressive state had significantly lower levels of sTNF-R1 than the patients in manic/hypomanic and euthymic states. The results indicated sTNF-R1 may be potential biomarkers for bipolar disorder. We further found the patient with metabolic syndrome were with higher levels of pro-inflammtory cytokines and associated with more previous hospitalizations, more tardive dyskinesia, poorer insight, poorer global function, and more impaired executive function (conceptual level response on the Wisconsin Card Sorting Test). We further investigated the associations between the levels of pro-inflammatory cytokines and neuroimaging abnormalities among 75 patients with bipolar disorder. With controlling of age, gender, BMI, intracranial volume, and duration of illness, we found higher level of sTNF-R was associated with reduced grey matter volume over bilateral Crus II, occipital pole and occipital cortex inferior division, planum temporale, posterior division of supramarginal gyrus, , and higher level of sIL-6R was associated with reduced cortex thickness over the left middle temporal. The results supported that pro-inflammatory cytokines could be biomarkers of clinical outcome and neuroimaging abnormalities in bipolar disorder

SYMPOSIUM (S04-2)

Do human plasma metabolites predict severity of depression and suicidal ideation?

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Evaluating the severity of depression (SOD), especially suicidal ideation (SI), is crucial in psychiatric settings to prevent suicidal accidents. Traditionally, SOD has been assessed on interviews such as the Hamilton Rating Scale for Depression (HAMD)-17, and/or self-administered questionnaires such as the Patient Health Questionnaire (PHQ)-9. However, these evaluation systems have completely relied on a person's subjective information, which sometimes lead to difficulties in clinical settings. To resolve this limitation, a more objective SOD evaluation system is needed. Here, we collected clinical data including HAMD-17/PHQ-9 and blood plasma of psychiatric patients from three independent clinical centers. We performed metabolome analysis of blood plasma, and 123 metabolites were detected. Interestingly, five metabolites are commonly associated with SOD in all three independent cohort sets regardless of the presence or absence of medication and diagnostic difference. Moreover, we successfully created a classification model to discriminate depressive patients with or without SI, using the technique of machine learning. The present multi-center study offers a potential utility for measuring blood metabolites as a novel objective tool for assessing SOD in clinical situations.

SYMPOSIUM (S04-3)

Pharmacogenetics of SSRI Therapeutic Response among Patients with Major Depression

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As with all antidepressant therapies, there is variability among major depressed patients in terms of response to selective serotonin reuptake inhibitor (SSRI) treatment. Of the factors causing this inter-individual variability in response, differences in genetic components may play a major role. Our studies in patients with major depression treated with SSRI (fluoxetine or citalopram) have focused on the associations between genetic polymorphisms in candidate genes related to SSRI therapeutic response. Several genetic polymorphisms were found to be associated with SSRI therapeutic response, including genetic variants of the serotonin transporter, serotonin-1A-receptor, monoamine oxidase A, plasminogen activator inhibitor-1, tryptophan hydroxylase 2, brain-derived neurotrophic factor, G-protein beta3 subunit and interleukin-1beta. A better understanding of the SSRI response-related genes by combining whole genome approaches with case-control association studies may allow for a personalized treatment in depressed patients.

SYMPOSIUM (S04-4)

Central Mechanism and Ketamine's Biological Effects of Treatment-Resistant Depression

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Patients with major depressive disorder who fail to respond to adequate trials of antidepressant treatment are common and have worsened quality of life and increased disease burden. Many factors could reliably predict such treatment-resistant depression (TRD), such as a history of poor-responses to antidepressants, high level of insomnia or hypnotic uses, and more painful symptoms. In recently years, we conducted several neuroimaging studies to investigate neuro-pathophysiology of TRD. We found brain abnormalities in the dorsolateral prefrontal cortex, supplementary motor areas, and thalamus are highly predictive of TRD. In today's talk, I would like to review the central mechanism of TRD. Additionally, low-dose ketamine has been shown to be effective in treating TRD and BDNF seems to play a key role in the clinical efficacy of ketamine. I will also present the findings of ketamine and BDNF from our recent ketamine study.

SYMPOSIUM (S05-1)

Distinguishing MDD from bipolar depression: Implications for diagnosis and treatment

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Despite contemporary classificatory systems not acknowledging differences between major depressive disorder (MDD) and bipolar depression, there is a growing acceptance of symptomatic and life course differences between these two presentations. In 2008, a taskforce of the International Society for Bipolar Disorders published guidelines on the diagnosis of bipolar depression, proposing a 'probabilistic' (likelihood) approach to the distinction between MDD and bipolar depression. The features identified by that 'Probabilistic Approach' include specific symptoms (hypersomnia, increased weight and/or appetite, psychomotor retardation, psychotic features and/or pathological guilt, other atypical features, and mixed features), longitudinal characteristics (onset before age 25 and at least five lifetime depressive episodes) and a positive family history of BD. Our group has since reported from validation studies that an empirically-derived cut-off of ≥4 'Probabilistic features' most optimally differentiates bipolar depression from MDD, with the most robust specific distinguishing features being psychomotor retardation, psychotic features, and mixed features. Similar findings have been reported from large UK, Chinese and US cross-sectional datasets . Our group has recently investigated whether young people at increased familial risk to bipolar disorder (BD) similarly manifest such 'probabilistic' features when depressed, even before the onset of mania, and whether such 'probabilistic' features predict the later onset of mania. 287 participants aged 12-30 (163 HR with a first-degree relative with BD and 124 controls) were followed annually for a median of five years. At baseline, HR participants were significantly more likely to report ≥4 Probabilistic features (40.4%) when depressed than controls (6.7%; $p<.05$). The presence of ≥4 Probabilistic features was associated with a seven-fold increase in the risk of 'conversion' to threshold BD (hazard ratio=6.9, $p<.05$) above and beyond the fourteen-fold increase in risk related to major depressive episodes (MDEs) per se (hazard ratio=13.9, $p<.05$).

SYMPOSIUM (S05-2)

Similarities and Differentiations in Cortico-Limbic Neural System in Major Depressive Disorder and Bipolar Disorder

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Background: It is often difficult to differentiate major depressive disorder (MDD) and bipolar disorder (BD) merely according to clinical symptoms. Similarities and differences in neural activity between the two disorders remain unclear. In current study, we use amplitude of low-frequency fluctuations (ALFF) to compare neural activation changes between MDD and BD patients.

Methods: One hundred and eighty-three adolescents and young adults (57 MDD, 46 BD and 80 healthy controls, HC) were scanned during resting state. The ALFF for each participant was calculated, and were then compared among all groups using voxel-based analysis.

Results: There was a significant effects of diagnosis in the core regions of cortico-limbic-striatal neural system. Furthermore, MDD showed left-sided abnormal neural activity while BD showed a bilateral abnormality in this neural system.

Conclusions: Differences in lateralization of ALFF alterations were found. Alterations predominated in the left hemisphere for MDD, whereas alterations were bilateral for BD.

SYMPOSIUM (S05-3)

The dysfunctioning of rewarding circus in Major Depressive Disorder and the effects of antidepressants on the rewarding circus

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Growing evidence has implicated dysfunction of the thalamus and its projection cortical targets in depression. However, the anatomical specificity of thalamo-cortical connectivity in MDD remains unknown due to the regional heterogeneityof the thalamus and limited methods to examine this. In this study, resting-state fMRI was collected on MDD and healthy controls. The thalamus was parcellated based on connectivity with six predefined cortical regions of interest (ROIs). The segmented thalamic nuclei were used as seeds to map connectivity with the rest of the whole brain.The results shows that the cortical ROIsdemonstrated correlations with spatially distinct zones within the thalamus. We founda trend towards reduced parietal ROI-to-thalamus connectivity in MDD. This may clarify the anatomical specificity of thalamo-cortical connectivity abnormalities in MDD. We therefore speculate that selectively modulating the connectivity of thalamo-cortical circuitry may be a potential novel therapeutic mechanism for MDD.

SYMPOSIUM (S05-4)

The 33-item Hypomania Checklist (HCL-33): a new self-completed screening instrument for bipolar disorder in depressed patients

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Background: Bipolar disorder (BD) is often misdiagnosed as major depressive disorder (MDD). This study tested the psychometric properties and the accuracy of the Chinese version of the 33-item Hypomania Checklist (HCL-33) to identify BD in Chinese clinical settings.

Methods: A total of 350 depressed patients were consecutively interviewed in a major psychiatric hospital in China. The patients' socio-demographic and clinical characteristics were recorded using standardized protocol and data collection procedures. The HCL-33 was completed by patients to detect symptoms characteristic of mania and hypomania. DSM-IV diagnoses were established using the Mini International Neuropsychiatric Interview (MINI).

Results: The HCL-33 showed high internal consistency with two-factorial dimensions. The optimal cut-off point on the HCL-33 to differentiate BD from MDD was 15, while cut-off points of 14 and 13 differentiated BD-I and BD-II from MDD, respectively. The maximum sensitivity was 0.62, 0.67 and 0.72 for differentiating BD, BD-I and BD-II from MDD, respectively.

Conclusions: The psychometric properties of the Chinese version of the HCL-33 are acceptable when tested in depressed inpatients. The routine clinical use of the HCL-33 as a screening instrument for BD in depressed patients needs to be further examined.

SYMPOSIUM (S06-1)

Neural substrates in the limbic forebrain underlying ketamine addiction

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Background/Objective: Ketamine, an NMDA receptor antagonist, displays a diverse pharmacological profile. Sub-anesthesia dose with chronic consumption induces addiction, as well as symptoms that model for schizophrenia or ketamine psychosis. The action of anti-depressant effect of ketamine has been explored extensively; however, the cellular mechanism of ketamine addiction has been rarely addressed. The specific aim of this study is to explore the neural substrates of ketamine addiction and its rewarding properties.
Method: Male B6 mice administered with sub-anesthetic ketamine (30 mg/kg, i.p.) for continuous 7 days were used to establish ketamine behavioral sensitization. Pairing of 5 mg/kg ketamine with non-preferred compartment in a conditioned place preference (CPP) paradigm was used to evaluate ketamine reward. Western blot and drug manipulations were used to identify the significance of designated signal regulators on development of ketamine sensitization.
Result and Discussion: After 7 days of 30 mg/kg ketamine, mice displayed a clear behavioral sensitization and a marginal place preference in the drug-paired compartment. In ketamine-sensitized mice, levels of AMPA receptor, ERK1/2, Akt and GSK3 phosphorylation were readily enhanced in the ventral striatum and prefrontal cortex at withdrawal period. Pharmacological blockade of AMPA receptor suppressed ketamine-induced behavioral activation. Systemic injection of MEK inhibitor SL327 potentiated the degree of behavioral sensitization. Administration of GSK3 inhibitor SB216763 prevented KET-induced behavioral sensitization. We speculate that chronic ketamine exposure readily precipitates drug craving, rather than rewarding. Of which, ventral striatal and prefrontal AMPA receptors are required for the behavioral effect of ketamine, and downstream ERK1/2 and GSK3 signaling might play a crucial negative feedback role in ketamine sensitization.
Conclusion: Current results suggest that ketamine induces behavioral sensitization via signaling modulation in the nucleus accumbens and prefrontal cortex at a sub-anesthesic dose.

SYMPOSIUM (S06-2)

Symptom dimensions of ketamine-associated psychosis in comparison with schizophrenia

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Background: Our primary goal was to evaluate the dimensions of the Positive and Negative Syndrome Scale (PANSS) in ketamine users (acute and chronic) compared to schizophrenia patients (early and chronic stages).
Method: We conducted exploratory factor analysis for the PANSS from four groups: 135 healthy subject administrated ketamine or saline, 187 inpatients of ketamine abuse; 154 inpatients of early course schizophrenia and 522 inpatients of chronic schizophrenia. Principal component factor analyses were conducted to identify the factor structure of the PANSS.
Results: Factor analysis yielded five factors for each group: positive, negative, cognitive, depressed, excitement or dissociation symptoms. The symptom dimensions in two schizophrenia groups were consistent with the established five-factor model. The factor structures across four groups were similar. The factors in the chronic ketamine group were more similar to the factors in the two schizophrenia groups rather than to the factors in the acute ketamine group. Symptom severities were significantly different across the groups (Kruskal-Wallis $\chi 2(4) = 540.6$, $p < 0.0001$). Symptoms in the two ketamine groups were milder than in the two schizophrenia groups (Cohen's d=0.7).
Conclusion: Our results provide the evidence of similarity in symptom dimensions between ketamine psychosis and schizophrenia psychosis. The interpretations should be cautious because of potential confounding factors.

SYMPOSIUM (S06-3)

Comparison of cognitive function and psychotic profile of patients with ketamine dependence who had transient or persistent psychosis and schizophrenia

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Background: Ketamine, an NMDA antagonist, has been applied to probe the pathophysiological process of schizophrenia. We previously reported that chronic heavy ketamine abuse is associated with persistent psychotic symptoms that resemble the symptomatic domains in schizophrenia. Here, we report a cognitive profile of persistent ketamine associated psychosis (PKAP) with comparisons of cognitive function with ketamine abuse non-psychosis (KNP) and chronic schizophrenia (SZ) patients.

Method: We recruited 136 inpatients including KNP (N = 44), PKAP (N = 17), and SZ (N = 75). Each subject was assessed cognitive function using CogState and psychotic symptoms using Positive Negative Syndrome Scale (PANSS).

Results: Consistent with our previous findings, the psychotic profile of PKAP resembled the symptomology of SZ patients. More importantly, we found significant difference of cognitive impairments among KNP, PKAP, and SZ groups. Verbal learning, problem-solving, and emotional regulation were worse in the PKAP and SZ groups relative to the KNP group. Furthermore, cognitive impairments were associated with psychotic symptoms, but not ketamine use.

Conclusion: Our results confirm a rare clinical phenomenon of PKAP that is more similar to schizophrenia than KNP. These findings suggest that future research of neurobiology of PKAP may provide meaningful insights of schizophrenia.

SYMPOSIUM (S06-4)

The efficacy of lamotrigine in the treatment of ketamine dependence

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Background: Ketamine has become a popular abused substance worldwide including Taiwan in recent years, especially in young and adolescent population. Currently there is no effective medication available to treat ketamine dependence. Lamotrigine is an anticonvulsant drug used in the treatment of epilepsy and bipolar disorder, with the main pharmacological mechanism sodium channels blocking and also inhibits the release of glutamate through modulation of high voltage-activated calcium currents and sodium channels. Recently glutamatergic medications have been proposed for the treatment of drug and behavioral addictions.This study is to investigate the efficacy of lamotrigine in the treatment of ketamine dependence. We present the study design of this study and the preliminary data without unblinding.

Method: This is a double-blind, placebo controlled study.Current users of ketamineare randomly assigned by computer-generated numbers either to the lamotrigine or placebo group in a 1:1 ratio.The dosage of study medication istitrated from 25 mg/HS initially to a range of 100mg to 200mg /day at the end of 12 weeks.The negative result of urine screen is the primary endpoint comparison between trial drug and placebo.

Results: We have currently recruited 16 patients with ketamine dependence, including 9 males and 7 females.The age (S.D.) was 31.2 (4.7). At baseline, all subjects tested positive for ketamine. At week 12, 50% of the subjects who completed the study tested negative for ketamine. The visual analog scale for craving severity (S.D.) was 56.7 (35.9) at baseline and 31.4 (37.1) at week12.

Conclusion: Our previous open-label experience suggests lamotrigine is potentially effective in managing ketamine dependence. The results of the double-blind, placebo controlled study is to be released after unblinding.

SYMPOSIUM (S7-01)

Depressive symptoms and L-tryptophan-kynurenine pathway metabolism: Focus on neuro-inflammation

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L-Tryptophan is metabolized via serotonin and kynurenine pathways (KP). Several studies have demonstrated that abnormality of both pathways is involved in the pathogenesis of different types of depressive disorder. Indeed, a pivotal enzyme in the KP (i.e. indoleamine 2,3-dioxygenase 1 (IDO1), kynurenine 3-monooxygenase) has also been suggested to play major roles in physiological and pathological events mediated by bioactive KP metabolites. Especially, IDO1 is induced by pro-inflammatory cytokines in the course of an inflammatory response in many human cell types, including neurons, glial cells, macrophages, dendric cells, fibroblasts, and epithelial cells. This enzyme has recently emerged as a modifier of inflammatory states rather than simply as a suppressor of immune function. Here wereport our current findingson the physiological significance of IDO1 and KP enzymes in inflammation-associated neurological diseases.

In this symposium, possible role(s) of KP metabolism and inflammation in CNS diseases especially depressive disorder will discuss.

SYMPOSIUM (S7-02)

An animal model for Tourrette syndrome: Striatal Slitrk-1knocked down mice

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Objectives: The Slit and NTrk-like family 1 (Slitrk-1) gene is one of vulnerable risk genes in Tourette syndrome (TS), a neuropsychiatric disorder with multiple motor and phonic tics regarded as stereotypy behaviors due to hyperdopaminergic reactivity in the corticostriatalthalamic circuit. In the striatum of mammals, Slitrk-1 protein is highly expressed in early childhood but gradually vanish in adulthood except cholinergic interneurons. Postmortem samples from the striatum of adult TS patients, compared to normal subjects, displayed fewer cholinergic interneurons, suggesting Slitrk-1 is important in maintaining cholinergic neuronal functions in the adult striatum. Here we found silencing the Slitrk-1 in the striatum of adult mice, which is only expressed in cholinergic interneurons, can serve as an animal model of TS.
Methods: Adult mice (C57BL/6J, 8-10 weeks) were randomly divided into two groups receiving bilateral microinjection of Slitrk-1siRNA (Slitrk-1-KD mice) and non-targeting scramble siRNA, respectively, into the dorsomedial striatum.
Results: Slitrk-1-KD mice showed normal locomotor activity but had excessive stereotypy behaviors, especially grooming, biting and head sway, which were blocked by haloperidol, an effective anti-tic agent by blocking D2 dopaminergic receptors. These stereotypy behaviors appeared on Day 3, persisted on Day 7 and declined on Day 10 after Slitrk-1siRNA injection. Slitrk-1-KD mice, compared to the scramble group, showed impaired prepulse inhibition (PPI), an endophenotype of TS, and more apomorphine-inducedclimbing behaviors. As compared with the scramble group, Slitrk-1-KD mice display about 30% of the Slitrk-1 protein in the bilateral striatum, and also about 30% of the number of striatal neurons co-expressing Slitrk-1 and choline acetyltransferase in striatal slices.
Conclusions: These results suggest that Slitrk-1 deficit in the adult striatum plays an important role in the pathogenesis of TS and silencing Slitrk-1 in the striatum of adult mice can be a reliable TS animal model.

SYMPOSIUM (S7-03)

PolyIC model of schizophrenia: a role of IFITM3 in the neurodevelopmental impairment

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Epidemiological evidence indicates that perinatal infection with various viral pathogens enhances the risk for several psychiatric disorders, including schizophrenia.Interferons (IFNs) prevent the incursion of viral genomes from the endosomal cascade, and the induction of interferon-induced transmembrane (IFITM) 3 is essential for this function. Thus, mice with IFITM3 deficiency (IFITM3 KO mice) exhibit accelerated progression, and higher mortality as well as systemic viral burdens following influenza A virus exposure.The role of IFITM3 in the CNS has not yet been fully elucidated, although its increased expression was demonstrated in the brains of patients with neuropsychiatric diseases, including schizophrenia.A transient expression of IFITM3 in the brains of mice treated with polyIC, a synthetic analogue of double-stranded RNA that mimics innate immune responses elicited by viral infection, was evident in astrocytes but not in neurons or microglia.PolyIC treatment in neonatal wild-type mice results in deficits of cognitive and social behaviors, activity-dependent glutamate release in the hippocampus, and morphological maturation of dendrites and spines of cortical neurons in adulthood, all of which are preserved in IFITM3 KO mice. The humoral factors derived from astrocytes exposed to polyI:C impair the dendrite elongation and spine formation of cultured neurons in vitro, but this effect of polyIC is abolished when using astrocytes derived from IFITM3 KO mice.Through a quantitative proteomic screen, we found 13 candidate proteins asthe astrocyte-derived humoral factors, including matrix metalloproteinase-3 (Mmp3). We also identified a novel interacting protein of IFITM3 in astrocytes, which could explaine the molecular mechanism underlying the IFITM3-inducedalteration of glial function. These findings suggest that the induction of IFITM3 in astrocytes during neurodevelopment has non-cell autonomous effects that in turn impair neurodevelopment via the disruption of neuron–glia interaction.

SYMPOSIUM (S7-04)

Role of oxidative stress-responsible genes in methamphetamine-induced psychoneurotoxic disorders

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Objectives: To achieve a better understanding on the psychoneurotoxicity induced by methamphetamine (MA), we investigated role of specific genes, which may be responsible for pro-inflammatory and pro-apoptotic, oxidant and antioxidant signaling processes during this psychoneurotoxic scenarios.
Methods: For experimental conditions of cognitive impairments, protein kinase C (PKC)δ-, glutathione peroxidase (GPx)-1-knockout mice and GPx-1 overexpressing transgenic mice were received low doses of MA (1 mg/kg/day, s.c., 7 days) to investigate role of PKCδ and GPx-1 genes in MA-induced memory loss. In addition, PKCδ-, NADPH oxidase (47phox)-, and cannabinoid CB1receptor-knockout mice were treated with four times MA (7 mg/kg, i.p.) or a toxic dose of (35 mg/kg, i.p) to elucidate role of these genes in dopaminergic neurodegeneration induced by MA.
Results: We observed that antipsychotic clozapine exerts anti-inflammatory and anti-oxidant potentials via positive modulation between protein kinase C (PKC) δ and glutathione peroxidase (GPx)-1 genes for restoring cognitive impairment induced by low doses of MA. We then examined whether MA-induced dopaminergic neurotoxicity requires specific signaling process mediated by oxidative stressful proinflammatory genes. We observed that activation of 47phox plays a critical role in mediating dopaminergic neuroinflammation. Neuroprotective mechanism mediated by inhibition of PKCδ, 47phox, and cannabinoid CB1 receptor against MA insult is via inhibiting mitochondrial burdens, microglial activation and pro-apoptotosis.
Conclusion: We suggest that pharmacological targeting of PKCδ with GPx-1, 47phox, or CB1 receptor to alleviate cognitive impairments or dopaminergic neurotoxicity induced by MA is critical for the therapeutic intervention [This study was supported bya grant (14182MFDS979) from the Korea Food and Drug Administration, Republic of Korea. Duy-Khanh Dang, The-Vinh Tran and Hai-Quyen Tran were supported by the BK21 PLUS program, National Research Foundation of Korea, Republic of Korea].

SYMPOSIUM (S8-01)

A Hybrid Setup of Transcranial Magnetic Stimulation - Electroencephalogram (TMS-EEG) and Selective Attention in Schizophrenia: An explorative study

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Transcranial magnetic stimulation (TMS) is a noninvasive method to excite neurons in the brain with weak electric currents by rapidly changing magnetic fields. TMS has been been used in studying the functional relevance of cortical areas in cognitive task performance. Attention deficit is one of the common cognitive impairment observed among patients with schizophrenia specifically in auditory selective attention.Integrating transcranial magnetic stimulation and electroencephalogram (TMS - EEG) may assist in understanding this heterogeneous disorder. In this study, a new stimulation and experiment paradigm combining TMS and EEG has generated a wavelet phase stability (WPS) which is used as a tool to objectively quantify the neural correlates of Auditory Late Response (ALR) in selective auditory attention between control and patients with schizophrenia. A total of 22 subjects – control (mean age: 26.54) and schizophrenia (mean age: 32.18), participated in this study. The subjects underwent two sessions - without TMS and single pulse TMS stimulated at frontal and temporal electrodes. The subjects were also assessed in two different conditions - attention and no attention. In this study, WPS of the controls are larger than schizophrenia patients. The significant differences are also found between control and schizophrenia at both conditions during without TMS and single pulse TMS at temporal electrodes. (ANOVA, $p<0.05$). A bigger phase stability difference between without TMS and single pulse TMS in schizophrenia (frontal and temporal electrodes) at no attention compared to attention. For control subjects, this difference is small at frontal and temporal electrodes at both conditions. Findings suggested that the WPS has the ability to be developed further as an objective measurement for phenotypic heterogeneity in schizophrenia.

SYMPOSIUM (S8-02)

Psychosocial Intervention for Early Psychosis Patients

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Introduction: Psychotic disorder is one condition leads to disability for those having this diagnosis. Many studies showed that the sooner the intervention is given, the better the outcome for the patients. People at risk for psychosis disorder, mostly adolescents-young adults, are often under diagnosed, as they come to seek help for anxiety or depression symptom and academic or social interpersonal dysfunction. Structured Interview for Prodromal Symptoms (SIPS) may be used to detect at risk people among the help-seeking patients. Psychosocial intervention including family involvement is one of the best strategies to manage these patients.
Method: Pilot study with twenty at risk patients, who are randomly assigned to intervention group with additional psychosocial intervention or control group, which get treatment as usual.
Result and discussion: this study describes and summarizes psychosocial intervention approaches that have demonstrated efficacy in treating people at risk for psychosis. We propose intervention that meets the varying needs of individual distress and dysfunction and to help the patients and families become more aware to the trajectory toward psychosis.
Key words: psychosocial, intervention, at risk psychosis

SYMPOSIUM (S8-03)

Schizophrenia: Bridging the Gap between Clinical and Biomedical Researches

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Schizophrenia, a chronic and severe psychotic disorder, is a major cause of disability. Current therapeutic strategies have had limited success on core cognitive impairment and long-term disability. Developments in molecular genetics, genomics, and proteomicshave been advances in the understanding of the neurobiological aspect of schizophrenia and discovery of biomarkers of the disorder. Because of the complexity of pathophysiology of schizophrenia, a variety of biomarkers; biological markers, endophenotypes, neuroimaging-based markers, are the ongoing investigation.

According to the recent finding, researchersdemonstrated that various loci are significantly associated with schizophrenia, and the risk is influenced by a much greater number of genes of smaller effect. The recent studies pointed to genes involved in neurodevelopment, genes involved in the immune and stress response, genes involved in the neurotransmitter systems; dopamine D2 receptor gene, glutamate gene. Many of the susceptibility genes were also reported toincrease the risk of other psychiatric disorders, i.e., bipolar disorder, major depressive disorder. In addition to thepolygenes, some of the schizophreniashave been found to be associated with the occurrence of copy number variants (CNVs), affecting mainly neurodevelopment genes. Some of these CNVs have also been implicated in the etiology of developmental disorder and learning disability.

To translate and bridge these finding of biomedical researches to clinical practice is beneficial, but quite complicate. The key areas for bridging are enhancing researcher and practitioner dialogue, making ongoing outcome assessment feasible for practitioners, and translating efficacy research into clinical practice.

SYMPOSIUM (S8-04)

Tobacco Dependence in Schizophrenia: Where Is the Problem?

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Smoking rates are high in people with schizophrenia compared to general population and other psychiatric disorders. Tobacco dependence has some biological aspects that might be different in people with schizophrenia. Some studies suggest a dissociation in cortical-subocortical dopaminergic pathways implicated in the pathophysiology of schizophrenia. Nicotinic receptors have a hypothesized role in modulating and potentially normalizing this disturbance. Nicotine, through increased glutamatergic transmission has a role in affecting striatal dopamine levels. Studies found that people with schizophrenia have a reduced number and function of low affinity alpha-7 nicotinic receptors. High nicotine levels may be needed for the activation of these receptors, which in turn leads to greater severity of tobacco dependence and more difficulty quitting. Studies indicate a 20% reduction in life expectancy and increased rates of smoking-related respiratory and cardiovascular diseases in people with schizophrenia compared to the general population. Furthermore, not only is schizophrenia associated with health-related issues, but also tobacco use in schizophrenia is known to cause financial and social suffering. Smokers spend around one third of their income on smoking. Moreover, smoking affects community integration as smokers have less money to spend on clothing and housing. Besides the stigma of mental illness, smokers with schizophrenia also acquire the added stigma of being smokers. Thus, there is no doubt that smoking has a biopsychosocial impact on people with schizophrenia. Therefore, tobacco dependence is an important issue to be addressed as part of recovery based treatment for people with schizophrenia.

SYMPOSIUM (S09-1)

Treatment of internet Addiction in Korea –Biological Aspect

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Internet gaming disorder (IGD) has recently been considered as a “behavioral addiction” based on the neurobiological features which resemble that of known substance use disorders. The findings of previous research indicate that the IGD is closely related to brain dysfunctional connectivity in the frontolimbic area and the posterior cingulated cortical region as well as structural brain alteration in the dorsolateral prefrontal cortex (DLPFC). These results may serve as feasible biological therapeutic target when dealing with IGD. This session will provide state-of-the-art information on the development of IGD treatment strategies in South Korea: 1) Pharmacological and psychosocial treatments, 2) MRI-base image-guided brain neuromodulation system for treatment, 3) IGD prevention and treatment program using virtual reality (VR) software.

Keywords: Internet gaming disorder, behavioral addiction, treatment, neuromodulation, virtual reality

SYMPOSIUM (S09-2)

Nicotine Dependence and its Treatment in Japan

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The aim of this session is to analyze and compare the structure of craving among nicotine, other substances, and behavioral addiction. Craving is hypothesized to be composed of three determinants. The first is the primary reinforcing property of a substance. The potential of nicotine as a primary reinforcer is weaker than that of other substances. On the other hand, it is difficult to define the primary reinforcing property in behavioral addiction. With regard to induction of craving, compensatory desensitization of the reward system that mediates the positive reinforcing property is considered to form a basic component of craving, and can be commonly observed both in substance addiction and in behavioral addiction. The second determinant is the secondary reinforcing property of a substance (conditioned aspects of the environment, such as contextual or specific cues associated with substance taking). Nicotine shows a robust conditioning property. The third determinant to elicit craving is the negative affective motivational property during withdrawal. Nicotine produces negative affective symptoms with a lesser degree of somatic withdrawal signs. As for the secondary conditioning processes and the negative motivational aspects of withdrawal, both substance and behavioral addiction have similar characteristics in nature. Treatment strategy is discussed using this hypothesis.

SYMPOSIUM (S09-3)

Treatment-Resisted Alcoholics-Psychiatric Complications

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Background: It is well known that comorbidity exists between psychiatric disorder and alcohol use disorders(AUD). Especially, Alcoholism patients have a high prevalence rate of depression. We have been studying about the treatment response and effectiveness of antidepressant to depression of patients with comorbid AUD. As a result, it was observed that the treatment response and the therapeutic effect of AUD patients (AUDIT=>12) were lower than without AUD patients (AUDIT<12). In addition, it was found that the effect of anti-depressant was decreased in AUD patients and there were negative correlation between the improvement of depressive symptom and the alcohol consumption. Therefore in this study, we investigated about effectiveness of acamprosate for depressive patient comorbid with AUD.
Subject & Method: The participants were depression patients with(without) AUD who diagnosed by ICD-10. The patients were assessed the depressive symptoms and the alcohol problems by using 17-items HAM-D and AUDIT. Those whose the HAM-D score was less than 14 were excluded. They were divided into 3 groups: Depression group (AUDIT score<12, without Acamprosate), Non-Acamprosate group (AUDIT score =>20,without Acamprosate) and Acamprosate group (AUDIT score<=20,with Acamprosate).The effect of medication on depressive symptoms was monitored over 12 weeks using HAM-D.
Result: There was no significant difference of HAM-D score at the baseline. However, significant difference was observed at 8 and 12 week between Acamprosate group and Non-Acamprosate group. Depression group and Acamprosate group showed significant improvement in HAM-D score through the study period. There was not difference of the dose of antidepressant between Acamprosate group and Non-Acamprosate group.
Conclusion: Acamprosate is considered to affect on modulation of glutamate system via NMDA receptors and mGlu5 receptors. The results suggest acamprosate may effective not only as an anti-craving agent but also depressive symptom of alcoholics due to its NMDA and mGlu5 receptor antagonist like action.

SYMPOSIUM (S09-4)

Efficacy of Electropressure as Adjunctive Therapy Among Methadone Maintanance Treatment (MMT) Patient : RCT Study-Preliminary Result

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Opiate dependence causes a significant burden to the global community. Methadone maintenance therapy (MMT) was supported by Malaysia government in late 2005 after the escalation of the HIV epidemic and the desire for locally driven evidence-based harm reduction strategies. MMT was able to stop the spreading of HIV among Intravenous drug user. However, patients were suffering from opiate withdrawal symptoms while waiting for the desire and optimal dosage of methadone. Therefore, we use electro-acupuncture in this randomized controlled with the aim of reducing opiate withdrawal symptoms during the induction phase. 40 eligible patients were randomized into 1:1 true electro acupuncture (EA) and sham acupuncture 30 minutes per session for 7 days then weekly for 11 weeks. By the end of this study, participants who received true EA reported that the daily consumption of methadone dosage was decreased by 15.5 mg/day. EA treatment is effective as adjunctive treatment among MMT patients.

SYMPOSIUM (S10-1)

Complementary and alternative medicine for insomnia in Japan

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Frequency of insomnia is increasing with age. Benzodiazepine receptor agonist has been prescribed for insomnia in the elderly, but there are some patients who complain the effect is not sufficient. Adherence for sleeping pills is very low in elderly Japanese, because there has been strong stigma against sleeping pills. Complementary and alternative medicine for insomnia is widely used in elderly Japanese.
Sedative antidepressants, novel antipsychotics, anti-histamine drugs, and supplements are used for insomnia as complementary and alternative medicine. But evidence of these drugs for insomnia is insufficient.
In this presentation, I outline the previous reports such as the advantages and disadvantages of these drugs for the treatment of insomnia in the elderly.

SYMPOSIUM (S10-2)

Dual Orexin Receptor Antagonist for treatment of insomnia

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The International Classification of Sleep Disorders was revised in 2014, resulting in marked changes in the diagnosis of insomnia. Insomnia used to be classified into primary disease and secondary disease, whereas it is currently diagnosed as comorbid disorder of other diseases, and classified into three categories: chronic insomnia (at least 3 times per week for more than 3 months), short-term insomnia (less than 3 months), and others.

Orexin receptor antagonist, suvorexant, which has different mechanisms of action from those of conventional drugs frequently used for insomnia, GABA-receptor agonists, was marketed in Japan first in the world in 2014. Although this new drug raises high expectations as an effective insomnia treatment option, it is required to accumulate its clinical experiences particularly by sleep experts in daily practice.

So far, suvorexant was administrated to 107 insomnia patients from December 2014 to November 2015 in our hospital. In this lecture, I would like to report efficacy of suvorexant for 37 naïve patients as well as their therapeutic courses.

SYMPOSIUM (S10-3)

Efficacy and Safety of Sansoninto in Insomnia with Psychiatric Disorder

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Background: Prior research confirms the relationship between insomnia and psychiatric disorders. Benzodiazepine hypnotics have been widely used in psychiatry for a long time.
Objective: The efficacy and safety of sansoninto (SNT), an herbal medicine, was examined in adult psychiatric disorder patients with insomnia symptoms.
Methods: Adult, child and adolescent patients with sleep disturbance meeting DSM-IV-TR diagnostic criteria for psychiatric disorders were treated openly with SNT (2.5–7.5 g) at bedtime. Patients maintained sleep diaries throughout the study. Efficacy was analyzed using a repeated measures methodology. The primary outcome was the Pittsburgh Sleep Quality Index (PSQI). The secondary outcomes were the Insomnia Severity Index (ISI), Athens Insomnia Scale (AIS), Clinical Global Impression-Improvement (CGI-I), and change of dosage of benzodiazepine hypnotics (diazepam equivalent).
Results: Significant symptom reduction was observed on all parameters (PSQI, ISI, AIS, CGI-I, and dosage of benzodiazepine hypnotics). No withdrawal involved treatment-related adverse events.
Conclusion: Data from this study suggests SNT was an effective and generally well tolerated treatment for insomnia symptoms in this sample of Adult, child and adolescent patients with psychiatric disorders.

SYMPOSIUM (S11-1)

Potential role of muscarinic receptors in the pathophysiology of schizophrenia

Brian Dean
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Neuropsychopharmacological evidence from humans and rodents, as well as data from postmortem CNS and neuroimaging studies, support a role for muscarinic receptors in the pathophysiology and treatment of schizophrenia. In this presentation data from a neuroimaging study and postmortem CNS studies will be presented to argue there are widespread decreases in muscarinic receptors in the CNS from subjects with schizophrenia. Available evidence to suggest cortical muscarinic M1 receptors and sub-cortical muscarinic M4 receptors are selectively decreased in schizophrenia will be reviewed. It will also be argued that cortical muscarinic M1 receptors are decreased in a sub-group of subjects with schizophrenia and these may represent a distinct disorder within the syndrome of schizophrenia. Data from studies in rodents and humans that suggests activating muscarinic M1 and M4 receptors will be beneficial in the treatment of schizophrenia will be summarised. Concluding, the possibility that such treatments may not be universally successful in subjects with schizophrenia will be discussed.

SYMPOSIUM (S11-2)

The involvement of acetylcholine system in hyperactivity in dopamine-deficient (DD) mice

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Dopaminergic systems have been known to be involved in the regulation of locomotor activity and development of psychosis. However, the observations that some Parkinson's disease patients can move effectively under appropriate conditions despite low dopamine levels (eg, kinesia paradoxia) and that several psychotic symptoms are typical antipsychotic resistant and atypical antipsychotic sensitive indicate that other systems beyond the dopaminergic system may also affect locomotor activity and psychosis. The present study showed that dopamine-deficient (DD) mice, which had received daily L-DOPA injections, could move effectively and even be hyperactive 72 h after the last L-DOPA injection when dopamine was almost completely depleted. Such hyperactivity was ameliorated by clozapine but not haloperidol or ziprasidone. Among multiple actions of clozapine, muscarinic acetylcholine (ACh) activation markedly reduced locomotor activity in DD mice. Furthermore, the expression of choline acetyltransferase, an ACh synthase, was reduced and extracellular ACh levels were significantly reduced in DD mice. These results suggest that the cholinergic system, in addition to the dopaminergic system, may be involved in motor control, including hyperactivity and psychosis. The present findings provide additional evidence that the cholinergic system may be targeted for the treatment of Parkinson's disease and psychosis.

SYMPOSIUM (S11-3)

The neurobiology of treatment resistant and responsive schizophrenia with respect of dopaminergic systems in the CNS

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Some patients with schizophrenia show poor response to first-line antipsychotic treatments and this is termed treatment resistant schizophrenia. The differential response to first-line antipsychotic drugs may reflect a different underlying neurobiology. Indeed, a previous study found dopamine synthesis capacity was significantly lower in patients with treatment resistant schizophrenia. However, in this study, the treatment resistant patients were highly symptomatic whilst the responsive patients showed no or minimal symptoms.
We will review all the molecular imaging studies regarding treatment response and show how dopaminegic fucntion is linked to treatment response.

SYMPOSIUM (S11-4)

Understanding the Potential Mechanism of Action of the Atypical Antipsychotic Drug Clozapine

Suresh Sundram
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Clozapine appears to be a clinically singular treatment for schizophrenia. It is effective in treatment resistant schizophrenia (TRS) where conventional antipsychotic drugs (APD) are ineffective and it appears to be protective against suicide in both observational and clinical trial studies. It is unlikely that canonical receptor signalling pathways such as the dopamine D2 or serotonin 5-HT2A receptors mediate these particular clinical effects given their general targeting by most APD. We investigated using primary neurons a range of canonical and non-canonical signalling systems and identified a critical role for epidermal growth factor receptor (EGFR) phosphorylation. This transactivation of EGFR by clozapine was the first demonstration that an APD could transactivate a receptor tyrosine kinase. We corroborated this in animal in vivo studies and prompted post-mortem human brain and clinical investigation of the EGF system. Our data support the hypothesis that components of the EGF system may be attenuated in their signalling and that clozapine may act to augment this. Identifying a mechanism of action of clozapine involving alternative signalling systems may provide new insights into the pathology of TRS and suicidality in schizophrenia and may in turn point toward novel therapeutics.

SYMPOSIUM (12-1)

Role of synaptic vesicle glycoprotein 2A (SV2A) in modulating epileptogenesis

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Dysfunction of synaptic neurotransmitter release is closely linked to the etiology of various CNS diseases including epilepsy. Synaptic vesicle glycoprotein 2A (SV2A) is a prototype synaptic vesicle protein modulating action potential-dependent neurotransmitter release and highly expressed in the brain. Previous studies suggest that SV2A is involved in the pathogenesis and treatment of epileptic disorders. This is based on the following evidences, 1) SV2A-knockout mice exhibited severe seizures, 2) SV2A acts as a binding site for antiepileptics (e.g., levetiracetam and its analogues), 3) SV2A expression is altered in various epileptic conditions both in animals (e.g., kindling and genetic model) and humans (e.g., intractable temporal lobe epilepsy and focal cortical dysplasia). In addition, a recent clinical study showed that a missense mutation in the SV2A gene resulted in intractable epilepsy, involuntary movement abnormalities and developmental retardation in humans. Although the mechanism of SV2A in modulating development of epileptic disorders (epileptogenesis) remains unknown, our recently developed a novel rat model ($Sv2a^{L174Q}$ rat) carrying a missense mutation (L174Q) in the Sv2a gene and demonstrated that SV2A specifically expressed in GABAergic neurons both in the hippocampus and amygdala, and that the SV2A dysfunction preferentially disrupts depolarization-induced GABA, but not glutamate, release with lowering the synaptotagmin1 (Syt1) expression. These evidences illustrate the crucial role of SV2A-GABAergic system in modulating epileptogenesis, which encourages drug discovery research of novel therapeutic agents.

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SYMPOSIUM (12-2)

Review of Traditional Chinese Medicine for Treatment of Epilepsy

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Epilepsy is a brain disorder which affects about 50 million people worldwide. Over 30% of people with epilepsy have uncontrolled seizures even with the best available drugs, and the serious side effects and chronic toxicity of the antiepileptic drugs, which lead to use of herbal medicine as a form of complementary and alternative medicine. There are many herbs have been confirmed for the treatment of epilepsy, such as Panchagavya ghrita, Convolvulus pluricaulis, Rhizoma acori graminei, Gastrodia elata in Ayurvedic and Traditional Chinese Medicine(TCM). This review highlights the use of TCM therapies for epilepsy. TCM follow a general principle of 'Bian Zheng Lun Zhi' that means timely use different prescription according to the specific symptoms of patients and different stages of epilepsy, such as phlegm and blood stasis resistance type epilepsy using pinellia tuber, poria cocos, dried tangerine, stone calamus, polygala, scorpion, etc; phlegm and fire disturbance type epilepsy apply pinellia, tangerine, acid-insoluble ash, bamboo shavings, liver and kidney deficiency type apply radix paeoniae alba, donkey-hide gelatin, tortoise plastron, radix rehmanniae, ginseng, gastrodia elata, uncaria, batryticated silkworm, etc. We analyze ancient and modern prescriptions and summarize the use of drugs with a higher frequency, such as Acorus calamus, Gastrodia elata, Batryticated silkworm, Buthus martensii, Pinellia ternata,Wolfiporia extensa, etc. and show some experimental results of these herbs that provide support for the efficacy of TCM in theory.

SYMPOSIUM (12-3)

Glia-Mediated Eplileptogenicity

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Temporal lobe epilepsy (TLE) is the most common type of drug-resistant epilepsy, partly characterized by hippocampus sclerosis. Recent accumulating evidence show that characteristic feagures of glial cells in the hippocampus are dramatically changed in the TEL, but an involvement of such glial changes in the pathogenesis of TLE is still a matter of debate. Here, we show that excess Ca^{2+} excitability in reactive astrocytes (here we termed as “epileptogenic astrocytes”) induced by status epilepticus (SE) is required for induction of epileptogenicity. Pilocarpine (Pilo) was used to induce SE in male adult B6 mice. Morphological changes in glia were assessed by immunohistochemical analysis. Functional analysis of glia was performed by Ca^{2+} imaging in the hippocampal slices. Pilo increased Iba1-positive signals in the hippocampus (1-3 days after SE), suggesting that microglial activation is quick and transient. On the contrally, GFAP-positive signals were increased there from 7 to 28 days after SE, suggesting that activation of astrocytes was slow-onset and sustained.. The activation of astrocytes was dependent on microglial activation because inhibition of microglia by minocycline abolisehd such Pilo-evoked activation in astrocytes. Twenty-eight days after SE, the mice showed susceptibility to Pilo, suggesting induction of epileptogenicity at this timepoint. The temporal profile of epileptogenicity was well associated with that of astrocytic activation but not microglial one. The reactive astrocytes displayed higher excitability of Ca^{2+} signals from 25 to 32 days after SE. Importantly, reduction of such an aberrant Ca^{2+} in astrocytes resulted in inhibition of epileptogenicity, suggesting that there should be a causal relationship between the aberrant Ca^{2+} excitability in astrocytes and eplilepcy. Taken together, we demonstrated that reactive astrocytes induced by microglia should be “epileptogenic astrocytes”, whose aberrant Ca^{2+} excitation is required for induction of epileptogenesis.

SYMPOSIUM (S12-4)

Discovery and Development of Perampanel

Takahisa Hanada
Japan

SYMPOSIUM (12-5)

New Classification of Seizure Types, ILAE 2017

Kurnia Kusumawati (Indonesia)

SYMPOSIUM (13-1)

Microglia and the future treatment of Autism Spectrum Disorder(ASD)

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INTRODUCTION: Autism Spectrum Disorder(ASD) is a neurodevelopmental disorder. Although widespread symptoms degrade patient's and guardian's quality of life, the neurobiological basis remains poorly understood, and specific treatment is yet to be found. Recently, microglia is known to play an important role in neurodevelopment, psychiatric and neurodegenerative disorder such as schizophrenia, Alzheimer's disease and ASD. In this review, pathophysiological roles of micoglia in the ASD and the possible therapeutic interventions related with its functions are discussed. METHODS: Literature searches for major electronic databases including Medline, Cochrane Library of Systemic Reviews, and PsycINFO, were conducted. RESULTS: Growing evidences from animal and human researches indicate that microglial activation of dysfunction can profoundly affect neural development, resulting in neurodevelopmental disorders like ASD. In many researches, microglial abnormal activation occurred not only in the developing brain but also in that of adult patients. While various therapies are being tested from this result, potential use of natural flavonoids, luteolin and possible inhibitor of microglia activation in minocyline was studied. Luteolin had an effect of anti-oxidant, anti-inflammatory, microglia inhibition, neuroprotection, and showed a cognitive improvement in an animal studies and children with ASD. According to latest research, increase of luteolin-containing dietary formulation in a children with ASD, shows reduced serum levels of tumor necrosis factor(TNF) and interleukin-6(IL-6). Also in rodents, minocyline has shown to have protection effect against apoptosis along with inflammation associated brain edema and blood brain barrier dysfunction. In other two studies, minocyline also ameliorated prenatal valproic acid induced autistic behavior in rats and prenatal minocyline treatment improved mother-infant communication in oxytocin receptor-defiant mice. CONCLUSIONS: Understanding the role of microglia is important not only in developing ASD but also in treating this inexpugnable disease. For the finding of promising therapeutic intervention in individuals with ASD, more larger-scale and a clinically applied research should be followed.

SYMPOSIUM (13-2)

Psychiatric Translational Research Using Human Blood-induced Microglial (iMG) Cells

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The role of microglia in stress responses has recently been highlighted, yet the underlying mechanisms of action remain unresolved. The present study examined disruption in working memory due to acute stress using the water-immersion resistant stress (WIRS) test in mice. Mice were subjected to acute WIRS, and biochemical, immunohistochemical, and behavioral assessments were conducted. Spontaneous alternations (working memory) significantly decreased after exposure to acute WIRS for 2 h. We employed a 3D morphological analysis and site- and microglia-specific gene analysis techniques to detect microglial activity. Morphological changes in hippocampal microglia were not observed after acute stress, even when assessing ramification ratios and cell somata volumes. Interestingly, hippocampal tumor necrosis factor (TNF)-α levels were significantly elevated after acute stress, and acute stress-induced TNF-α was produced by hippocampal-ramified microglia. Conversely, plasma concentrations of TNF-α were not elevated after acute stress. Etanercept (TNF-α inhibitor) recovered working memory deficits in accordance with hippocampal TNF-α reductions. Overall, results suggest that TNF-α from hippocampal microglia is a key contributor to early-stage stress-to-mental responses.

SYMPOSIUM (13-3)

Digging Up the Unconscious Roles of Microglia Using Minocycline-Pharmacological Trials

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Microglia has been highlighted to understand the underlying pathophysiology of various psychiatric disorders such as schizophrenia, depression, and autism, thus researchers all around the world have been conducting experimental studies focusing on microglia in psychiatric disorders. On the other hand, the actual roles of microglia in normal mental activities, especially for healthy humans, have not been investigated. As the first step to clarify this unexplored field, we have been conducting an economic game – trust game – in order to assess the tendency of social decision-makings among healthy Japanese young males with or without 4-day-treatment of minocycline, an antibiotic with microglial inhibitory effects. Interestingly, minocycline significantly modulated personality-oriented and/or drive-oriented social behaviors (Kato et al., 2012; Watabe et al., 2012; Watabe et al., 2013). These results have proposed novel psychosocial and/or unconscious roles of human microglia in healthy persons.

We believe that the pharmacological trials with minocycline promise to elucidate unresolved aspects of human microglia in various unconscious roles and psychiatric disorders. Further translational research should be conducted to validate our pilot findings.

SYMPOSIUM (13-4)

Electroconvulsive shock attenuated microgliosis and astrogliosis in the hippocampus and improved prepulse inhibition deficit of Gunn rat

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Background: Electroconvulsive therapy (ECT) is regarded as one of the efficient treatments for intractable psychiatric disorders, but the mechanism of therapeutic action remains unclear. Recently, many studies indicate that ECT affects the immune-related cells, such as microglia, astrocytes, and lymphocytes. Moreover, microglial activation and astrocytic activation have been implicated in the postmortem brains of schizophrenia patients. We previously demonstrated that Gunn rats showed schizophrenia-like behavior and microglial activation in their brains. The present study examined the effects of electroconvulsive shock (ECS), an animal counterpart of ECT, on schizophrenia-like behavior, microgliosis, and astrogliosis in the hippocampi of Gunn rats.

Methods: The rats were divided into four groups, i.e., Wistar sham, Wistar ECS, Gunn sham, and Gunn ECS. ECS groups received ECS once daily for six consecutive days. Subsequently, prepulse inhibition (PPI) test was performed, and immunohistochemistry analysis was carried out to determine the activation degree of microglia and astrocytes in the hippocampus by using anti-CD11b and anti- GFAP antibody, respectively.

Results: We found PPI deficit in Gunn rats compared to Wistar rats, and it was significantly improved by ECS. Immunohistochemistry analysis revealed that immunoreactivity of CD11b and GFAP was significantly increased in Gunn rats compared to Wistar rats. ECS significantly attenuated the immunoreactivity of both CD11b and GFAP in Gunn rats.

Conclusions: ECS ameliorated schizophrenia-like behavior of Gunn rats and attenuated microgliosis and astrogliosis in the hippocampi of Gunn rats. Accordingly, therapeutic effects of ECT may be exerted, at least in part, by inhibition of glial activation. These results may provide crucial information to elucidate the role of activated glia in the pathogenesis of schizophrenia and to determine whether future therapeutic interventions should attempt to up-regulate or down-regulate glial functions

SYMPOSIUM (14-1)

Difference in recognition of metabolic adverse events between psychiatrists and patients with schizophrenia in Japan

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Metabolic syndrome is a growing concern among patients with schizophrenia. The current study assessed attitudes toward metabolic adverse events among patients with schizophrenia.
A brief questionnaire was constructed to investigate patient recognition of the following broad areas: dietary habits, lifestyle, self-monitoring, knowledge, and medical practice among 22,072 patients and the psychiatrists' recognition of the metabolic risk of antipsychotic therapy, pattern of monitoring patients for physical risks, practice pattern for physical risks, and knowledge of metabolic disturbance among 8,482 psychiatrists in Japan.
85.2% reported that psychiatrists were concerned about prescribing antipsychotics that have a risk of elevating blood sugar; 47.6% stated that their frequency of monitoring patients under antipsychotic treatment was based on their own experiences; and only 20.6% of respondents answered that the frequency with which they monitored their patients was sufficient to reduce the metabolic risks. Approximately 55.0% of inpatients and 44.8% of outpatients reported that they did not exercise at all. More than half of the inpatients and outpatients hoped to receive regular blood tests to prevent weight gain and diseases such as diabetes.
Educational efforts and the promotion of the best pharmacotherapy and monitoring practices are needed for not only patients with schizophrenia but also psychiatrists.

SYMPOSIUM (14-2)

The impact of megadose polypharmacy in antipsychotic pharmacotherapy on electrocardiograms for Japanese patients with schizophrenia

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Close attention is paid to the prolongation of electrocardiogram QT caused by the oral administration of antipsychotic drugs and the possible consequent incidence of fatal arrhythmia. We examined the effects of prolongation of QT in antipsychotic drugs and showed that age, sex, the dosage and blood concentration of antipsychotic drugs along with the differences between drugs affect the QT interval. In addition, it has been revealed that the resting heart rate (RHR) among the general population increases the relative risk of overall mortality and sudden death. While it is known that the administration of antipsychotic drugs increases RHR, the details are obscure. On the other hand, although various problems have been pointed out in the medical practice of Japanese psychiatry, megadose polypharmacy ranging from three to four drugs is more common in Japan than in Western countries, indicating that the situation has not yet improved. In this project, we analyze the electrocardiogram data of approximately ten thousand ambulatory patients as well as hospitalized patients and examine the impact of megadose polypharmacy in antipsychotic pharmacotherapy on QT interval and RHR. As there have been few reports to date on the kinds of physical side effects megadose polypharmacy directly causes in patients, we will examine megadose polypharmacy again based on the analysis results of this project in this study.

SYMPOSIUM (14-3)

Can nutritional education improve obesity weight among patients with schizophrenia?

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Obesity among patients with schizophrenia is a growing concern because being overweight is widely regarded as a major risk factor for cardiovascular disease and premature mortality. Minimizing weight gain in a population with an already high prevalence of obesity is of clinical and social importance. Dietary patterns have been suggested as one modifiable factor that may play a role in development of obesity. Firstly, we identified three dietary patterns (the healthy dietary pattern, the processed food dietary pattern, and the alcohol and accompanying dietary patterns) among patients with schizophrenia. After adjusting for covariates, patients within the high tertile of each healthy dietary pattern and processed food dietary pattern had a significantly lower prevalence of obesity compared with low tertile of dietary pattern. Second, we conducted a randomized controlled trial to investigate the effect of monthly nutritional education on weight change among patients with schizophrenia in Japan. Two hundred and sixty-five obese pateints who had a DSM-IV diagnosis of schizophrenia or schizoaffective disorder and had been stabilized and treated with an antipsychotic drug for at least three months, were recruited. Participants were randomly assigned to a standard care (A), doctor's weight loss advice (B), or an individual nutritional education group (C) for 12 months. After the 12-month treatment, one hundred and eighty-nine patients were evaluated for the prevalence of metabolic syndrome based on the ATP III-A definition and weight changes. Group C showed increased weight loss over the 12-month study period, and the change in weight differed significantly from that of group A. Individual nutrition education provided by a dietitian was highly successful in reducing obesity in patients with schizophrenia and could be the first choice to address both weight gain and metabolic abnormalities induced by antipsychotic medications.

SYMPOSIUM (14-4)

Physical risks in Japanese patients with schizophrenia: From a nationwide survey

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Patients with schizophrenia have a higher risk of metabolic syndrome (MetS). MetS prevalence varies with ethnicity. Although environmental factors, such as lack of physical activity and unbalanced diet, can lead to MetS, these may differ between outpatients and inpatients with schizophrenia. Moreover, several studies have reported that being underweight is a recognised health risk, and some studies have reported increased mortality with weight loss. Therefore, Japanese inpatients with schizophrenia may have higher mortality risk due to underweight compared with the general population. The Japanese mental health care system differs from that in other countries. Therefore, we conducted a nationwide survey to clarify the prevalence of MetS and underweight and under-nutrition in Japanese outpatients and inpatients with schizophrenia.

We investigated the risk of MetS and underweight and under-nutrition by questionnaire in 520 facilities for outpatients and 247 facilities for inpatients. There were 7655 outpatients and 15461 inpatients with schizophrenia. The result revealed that MetS prevalence in Japanese outpatients was approximately 3-fold higher than in inpatients. On the other hand, the prevalence of underweight and under-nutrition in Japanese inpatients with schizophrenia was higher than in outpatients and the general population. The results also suggest that the difference in physical health between outpatients and inpatients with schizophrenia may be related to the mental health system in Japan. We should pay more attention to the risk of physical disease in Japanese patients with schizophrenia, considering the difference in health characteristics between outpatients and inpatients in clinical practice.

SYMPOSIUM (S15-1)

Reviewing Japanese Clozapine Patients Monitoring System (CPMS) Data since 2009

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This symposium will review evidences regarding clozapine treatment for treatment-refractory schizophrenia (TRS) to discuss safer and more efficient treatment strategy of clozapine for the patients with TRS. We will show a dataset of clozapine patients monitoring system (CPMS) in Japan, which has demographic information of all clozapine users in Japan. The data could show accurate incidence of clozapine-induced adverse effects.

SYMPOSIUM (S15-2)

Revisiting clozapine administration: dosing regimen and switching strategy

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There still remain some clinically important questions about how to administer clozapine, including (1) how to introduce clozapine, (2) clozapine dosing frequency, and (3) how to switch to clozapine. It is believed that clozapine needs to be introduced through a slow dose titration schedule and administered with a divided dosing regimen to minimize risks of side effects such as seizures, sedation, hypotension, bradycardia, and syncope. However, recent studies have challenged these notions: Ifteni et al. analyzed the data on 111 patients with schizophrenia who received rapid clozapine dose titration (i.e., mean of 372 mg/day at day 5.1), and found that no patients had seizures, severe hypotension, or other major side effects; Takeuchi et al. cross-sectionally collected data on 676 and 308 patients at institutes in Canada and United States, respectively, and showed that approximately 75% of patients in both institutes received once-daily clozapine dosing. Moreover, rates of positive symptom remission and diagnosis of seizures did not significantly differ between once-daily and divided dosing. In contrast to investigations evaluating clozapine titration, there has been only one study examining immediate vs. gradual antipsychotic discontinuation when switching to clozapine; Takeuchi et al. conducted a double-blind, randomized controlled trial in 33 patients with schizophrenia who underwent a switch to clozapine, and observed no significant differences in terms of efficacy and tolerability between immediate and gradual antipsychotic discontinuation in the context of relatively slow clozapine dose titration (i.e., 300 mg/day at day 12). These findings suggest that clozapine can be introduced rapidly and administered with a once-daily dosing regimen; in addition, the current antipsychotic can be discontinued immediately when switching to clozapine, although further evidence is warranted.

SYMPOSIUM (S15-3)

Haematological aberrations from clozapine – what lessons might be learnt?

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In most clinical guidelines, clozapine has been listed as the antipsychotic of choice for treatment resistant schizophrenia (TRS). Clozapine has had a stormy history because of its association with agranulocytosis which was first reported in the 1970s. When it was eventually reintroduced in the early 1990s, haematological monitoring became mandatory. The exact aetiopathogenesis of clozapine induced agranulocytosis (CIA) is as yet unknown, though there has been speculation of immune mediated mechanisms. As a result of mandatory monitoring, studies have found a series of other haematological aberrations such as eosinophilia, thrombocytopenia, thrombocytosis and neutrophilia, which were observed in people exposed to clozapine. These findings might worry clinicians and lead to discontinuation of clozapine. In the present analysis, we investigated the 1-year trajectories of all major cell lines and the differential white cell counts in a naturalistic sample. Haematological indices were extracted from the clozapine registry of a single tertiary hospital. Individuals with a pre-clozapine and at least 1 post-clozapine haematological observation were included. A total of 101 individuals were included in this study and 66 were still prescribed with clozapine at the end of 1 year. There were no cases of agranulocytosis but 5 individuals developed neutropenia. Cumulative incidence rates of neutrophilia were 48.9%, 5.9% for eosinophilia, and 3% each for thrombocytosis and thrombocytopenia. There was a synchronized but transient increase in neutrophils, monocytes, eosinophils, basophils and platelets as early as the first week of clozapine exposure. This spike seems transient for most cell lines and reverted to normal at week 9 of clozapine treatment. The study suggests that hematological aberrations are not only observed in neutrophils, but across a spectrum of different cells lines. More importantly, these aberrations are transient; therefore, we do not recommend discontinuation of clozapine as a result of these observations.

SYMPOSIUM (S15-4)

Long term follow up on the development of treatment resistance in first-episode schizophrenia spectrum disorders

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This is a retrospective case-control study to explore the pattern and predictors of treatment resistant schizophrenia with a large cohort of first-episode psychosis patients with more than 10 years of illness duration.
Clozapine prescription was considered as proxy indication of treatment resistance in the current study for screening purpose. A detail screening of clozapine prescription history of all 1400 patients, who were presented to mental health service from 1-Jan-1998 to 31-Aug-2003, was conducted. Treatment resistant status of patients was further verified with clinical and medication information collected from the medical records based on the existing operational criteria. Patients in the control group were identified randomly from those who were not prescribed with clozapine, matched with the diagnosis of patients with clozapine in a 1:2 ratios. Operational criteria were used to identify those who were treatment resistant without prescribing clozapine within this group. The rest was considered the non-treatment-resistant (Non TR) group. The total sample for analysis was 469, with 160 clozapine patients and 309 control patients. Face-to-face interview and detail medical record review were conducted for all patients.
Treatment resistant schizophrenia (TRS) was found to be 11.79% with an average of 7.56-month delay in clozapine prescription. Binary logistic regression was performed and the model of age of onset, years of education, number of relapse in the first three years, duration of first episode, Clinical Global Impression (Severity) Scale positive symptoms (CGIp) at the end of first month, substance abuse history and premorbid adjust scale (adult) significantly predicted treatment resistance status (Omnibus chi-square = 47.86, df=7, $p<0.0001$). The model accounted for between 15.9% and 21.4% of the variance in treatment resistance status.
The results supported that both neurodevelopmental and early treatment outcomes might be related to the development of treatment resistance, thus may be used as indicators in the future.

SYMPOSIUM (S16-1)

Memory as a New Therapeutic Target

Karim Nader (Canada)

SYMPOSIUM (S16-2)

Distinct noradrenaline cell populations coordinate the balance between fear and extinction learning

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Aversive experiences produce powerful emotional memories which trigger stereotyped defensive responses. However, these emotional responses need to be extinguished when they are no longer appropriate to enable normal, flexible behavior. Noradrenaline is important for both fear and extinction learning and an important drug target for the treatment of anxiety and mood disorders. Traditional views of noradrenaline function suggest that it modulates global brain states and diverse behaviors through what is believed to be a homogeneous cell population in the brainstem locus coeruleus (LC). However, it is unclear how the LC coordinates disparate behavioral functions. In direct contrast to traditional models of LC function, we've found that distinct populations of LC-noradrenaline neurons projecting to the amygdala or medial prefrontal cortex (mPFC) differentially regulate fear or extinction learning, respectively. Brain-wide efferent mapping of these cell populations revealed unique and specific connectivity with amygdala and mPFC targets. Coupled with this functional and anatomical modularity, LC neurons multiplex distinct signals during fear and extinction learning. In response to strong aversive stimuli occurring during fear learning most LC neurons are strongly activated. By contrast, distinct populations of LC neurons are selectively and mildly engaged in response to fear or safety cues. This is reflected as a shift in the balance of activity across amygdala and mPFC projecting cell modules during early and late extinction. These results suggest a revised view of LC-noradrenaline function in which a mosaic of projection- and behavior-specific modules is coupled with combinatorial activation modes to enable the adaptive tuning of emotional responding and behavioral flexibility.

SYMPOSIUM (S16-3)

Disrupting the Process of Fear Memory Reconsolidation: Towards a New Intervention for PTSD

Merel Kindt (Holland)

SYMPOSIUM (S16-4)

Forgetting of Remote Fear Memory after Long-time Memory Recall by Hippocampal Neurogenesis Enhancers

Satoshi Kida (Japan)

SYMPOSIUM (S17-1)

Korean Medication Algorithm Project for Depressive Disorder 2017 (KMAP-DD 2017) to make sure of the); 3rd revision

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Aim: This study isconstitutes a third revision of the guidelines for the treatment of major depressive disorder (MDD) issued by the Korean Medication Algorithm Project for Depressive Disorder 2017 (KMAP-DD 2017) to make sure of the). It incorporates changes of experts'in the expert consensus that occurred between 2012 and 2016 in company with the development of new drugsas well as information regarding newly developed and publication of recentrecently published clinical trials.
Methods: Using a 44-item questionnaire, an expert consensus was obtained on pharmacological treatment strategies for 1) nonpsychotic MDD, 2) psychotic MDD, 3) persistent depressive disorder (dysthymia) and depression subtypes, 4) continuous and maintenance treatment, and 5) special populations; consensus was also obtained regarding 6) the choice of an antidepressant (AD) according toin the context of safety and adverse effects, and 7) non-pharmacological biological therapies.
Results: AD monotherapy was recommended as treatment of choice (TOC) for nonpsychotic depression in adults, children and adolescents, elderly adults, and patients with postpartum depression or premenstrual dysphoric disorder. The combination of AD and atypical antipsychotics (AAP) was recommended for psychotic depression. The duration of the initial AD treatment for psychotic depression depends on the number of depressive episodes. Most experts recommended stopping the initial AD and AAP therapy after a certain period in patients with one or two depressive episodes. However, for those with three or more episodes, maintenance of the initial treatment was recommended for as long as possible. Monotherapy with various selective serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs) was recommended for dysthymic disorder and melancholic type MDD.
Conclusion: The pharmacological treatment strategy of KMAP-DD 2017 is similar to that of KMAP-DD 2012; however, the preference for the first-line use of AAPs was greaterstronger in 2016 than in 2012.

SYMPOSIUM (S17-2)

Constant Evolution: New 2016 edition of the CANMAT guidelines for treatment of Major Depressive Disorder

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Major Depressive Disorder is a highly prevalent mental disorder, associated with significant personal and social burden. Numerous treatments are available, although the overall outcomes are less than ideal. Clinical practice guidelines have been useful to guide practicing clinicians in choosing treatment options and algorithms. Most recent guidelines have followed the principles of evidence-based medicine and their recommendations are based on that. Canadian Network for Mood and Anxiety Treatments (CANMAT) is an academic not for profit organization, with long tradition in developing and implementing clinical practice guidelines. This presentation will review the history of CANMAT guidelines for MDD, and present larger picture of newly published 2016 edition. General principles of management and evidence-based levels of evidence and treatment recommendations will be presented for different treatment modalities: psychotherapy, psychopharmacology, neurostimulation and complementary and alternative medicine. Some considerations for special populations will be also discussed. There will be enough time allocated to questions and answers and general discussion.

SYMPOSIUM (S17-3)

Guidelines for the management of patients with bipolar disorder: A joint CANMAT-ISBD viewpoint

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Canadian Network for Mood and Anxiety Treatments (CANMAT) has published its first treatment guidelines for bipolar disorder in 2005 with international commentaries. Since then, the guidelines have been updated in 2007, 2009 and 2013.

The CANMAT Bipolar group is currently in the process of developing a complete revision of the guidelines in collaboration with the International Society for Bipolar Disorders, and these are expected to be published in 2017. The objective of this symposium is to provide a brief overview of these guidelines and focus on new advances in management of bipolar disorder.

SYMPOSIUM (S17-4)

Clinical practice guidelines for the management of bipolar disorder in adults: Malaysia's perspective

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Bipolar Disorder (BD) is a challenging disorder, not just due to the masquerading nature of the illness itself, our understanding on this disorder are still evolving. The variety in its clinical manifestations leads to the difficulties in diagnosing the condition accurately. BD rarely presents alone without other co-morbidities which further hinder the early accurate diagnosis which later affecting the prognosis. Unlike unipolar depression which could be managed effectively at the primary care setting, in Malaysia, majority of people with BD are treated in the hospitals with psychiatrists. Delay in seeking treatment, recurrent relapses or admissions, concurrent substance misuse and limited availability of psychosocial interventions further complicate the management of BD. Another challenge would be the continuity of the services especially when the patients are back in the community once they are stable. Treatment compliance, blood monitoring and regular supervision are lacking due to various limitations. In view of BD is a complex illness, various possible manifestations and unavailability of local clinical practice guidelines, patients are managed in various ways. Hence an evidence-based CPG on BD applicable to local context is timely required. The objectives of this CPG are to provide evidence-based guidance in all phases of BD, improve recognition and early intervention of BD and to promote and enhance evidence-based pharmacology and psychosocial interventions. This CPG is aimed to be used at primary, secondary, tertiary health care and those involved in psychiatric training. It focuses on the management of BD in adults with special consideration on dual diagnosis, women with child bearing age and elderly. This presentation will highlight the local needs, recommendations which are different from other international CPG and also the challenges in the implementation phase in Malaysia health care setting.

SYMPOSIUM (S18-1)

A Novel Pain Control System via Brain GPR40/FFAR1 Signaling

Kazuo Nakamoto
Japan

SYMPOSIUM (S18-2)

A novel non-opioid mechanism for acupuncture analgesia: Involvement of orexin and endocannabinoid systems

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Objectives: Acupuncture has been used to relieve pain for thousands of years through poorly understood. We previously revealed a novel analgesic mechanism elicited by orexin-induced disinhibition in the ventrolateral periaqueductal gray (vlPAG), which is mediated by 2-arachidonoylglycerol (2-AG), an endocannabinoid, generated after OX1R activation (Ho et al., J Neurosci 31:14600, 2011). Here, we validated a hypothesis that acupuncture can induce analgesia through this mechanism based on a report that electroacupuncture reduced GABA levels in the vlPAG in a manner blocked by a CB1R antagonist (Fu and Longhurst 106:1800, 2009).

Methods: EA-induced analgesia was accessed by the hot-plate response in mice receiving bilateral electrical stimulation (2 Hz, 2 mA, 0.15 ms) at the PC6 acupoint (EA-PC6) for 20 min under isofluorane anesthesia. Orexin A and GABA levels in the vlPAG were measured by ELISA and HPLC, resepctively.

Results: EA-PC6, but not at a non-acupoint location or in the shame group of mice that received acupuncture needle insertion but no electrical stimulation, increased the number of c-Fos expressing-orexin neurons in the lateral hypothalamus, increased orexin A levels and lowered GABA levels in vlPAG, and reduced nociceptive responses in the mouse hot-plate test. Systemic injection of an OX1R or CB1R antagonist significantly attenuated EA-PC6-induced antinociception and restored GABA levels in the vlPAG. Intra-vlPAG inhibition of 2-AG synthesis or blockade of OX1Rs or CB1Rs, but not opioid receptors, attenuated EA-PC6-induced antinociception. In $Cnr1^{-/-}$ mice, which lack CB1 receptors, EA-PC6 elicited a much smaller antinociceptive effect than in wild type mice.

Conclusions: These findings suggest that EA-PC6 activates hypothalamic orexin neurons, releasing orexins that induce analgesia by inhibiting GABA release in the vlPAG through a cascade that is sequentially mediated by OX1Rs, 2-AG and CB1Rs, and is opioid-independent. The latter characteristic of EA-PC6-induced analgesia may provide a novel strategy for pain management in opioid-tolerant patients.

SYMPOSIUM (S18-3)

Neuropathic pain generator visualization study on rodent model with metalloproteinase-12 activatable MRI probe

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Neuropathic pain from nerve root compression has high co-occurrence rate with depression. Little work has been done on developing a molecular probe for compressive neuropathy. Radiological investigation may offer anatomical clues but cannot accurately localize pain generators. Hence, the development of a molecular probe, metalloproteinase-12 (MMP-12) to visualize pain and depression generator can play a significant role in the improving the treatment efficiency.

MMP-12 activatable cell penetrating peptide sequence is coupled to a MRI contrast iron-oxide nanoparticle. After excision by the MMP-12, the cell penetrating peptide will be exposed and taken up by tissue. Enhancing probe uptake will be shown in MRI image as a signal void.

For MRI probe evaluation, L5, L6 rat ligation model will be used. Sixty rats will be divided into three groups; ligation, sham operation and naïve group. For the ligation group, the animals will be anesthetized and the right paravertebral region exposed. After removal of the L6 transverse process, the L5 and L6 spinal nerves will be ligated with 6-0 silk suture and transected distal to the ligature. Sham operation group will follow the same procedure without ligation. Naïve group will not receive any intervention.

4 rats per group will be used for metalloproteinase quantification with ELISA method, and 2 rats will be used for immunohistochemical study. Pain response will be assessed with thermal and mechanical withdrawal latency. Severity of depression will be assessed by forced swim test and sucrose preference test. After either 1 or 2 weeks, 2μl of 10μg/ml MMP-12 probe will be injected into L5, L6 DRG of remaining animals.

This study will use our molecular knowledge of pain generators for developing an MR imaging probe to aid in diagnosis and management of the patient with neuropathy.

SYMPOSIUM (S18-4)

Molecular mechanisms underlying individual differences in pain and analgesic sensitivity

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Considerable variability exists in the sensitivity to analgesic opioids across individuals, which has been an unresolved clinical issue in pain management. CXBH mice, known as an “opioid receptor-rich” strain, are a recombinant inbred mouse strain established by crossing the C57BL/6By and BALB/cBy strains. In the present study, we investigated nociceptive and antinociceptive sensitivity in CXBH mice and elucidated the underlying molecular mechanisms.

The behavioral responses to nociceptive stimuli were examined in the tail-flick test hot-plate test, Randall-Selitto test, and a bdominal constriction test. Whole-genome gene expression profiles in the brains of each mouse strain were analyzed with illumina Expression BeadChips. Northern blot analysis was performed to estimate the expression levels of the μ, δ and κ opioid receptors.

CXBH mice exhibited slightly higher morphine-induced antinociception compared with C57BL/6J and BALB/cBy mice in the hot-plate test but not tail-flick test. CXBH mice exhibited a marked reduction of nociceptive sensitivity, regardless of the type of nociceptive stimulus, with the exception of tail stimulation. Changes in gene expression that corresponded to reduced nociceptive sensitivity in the brains of CXBH mice were observed in 62 transcripts, including pain- and analgesia-related transcripts, in a whole-genome expression assay. The total mRNA expression of opioid receptors was higher in CXBH mice than in C57BL/6J and BALB/cBy mice. However, the expression levels of MOR-1 mRNA, a major transcript of the μ opioid receptor gene, were not different among the C57BL/6J, BALB/cBy, and CXBH mice. Supraspinal nociceptive responses but not antinociceptive responses were reduced in the CXBH mice, and the expression levels of transcripts were altered in the brain of this strain.

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SYMPOSIUM (S19-1)

Model-Guided Antipsychotic Dose Reduction: A Series of Clinical, Pharmacokinetic, and Brain Imaging Studies

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Background: Positron emission tomography (PET) studies have demonstrated that a therapeutic window of striatal $D_{2/3}$ receptor occupancy (65-80%) is associated with clinical response in the acute phase of the schizophrenia while $D_{2/3}$ receptor occupancy required for the maintenance of remission can be lower. We recently developed a model to predict central $D_{2/3}$ receptor occupancy levels from plasma antipsychotic concentrations collected prior to dosage change. This model could be utilized to select oral antipsychotic doses aimed at achieving optimal $D_{2/3}$ receptor occupancy on an individual basis.
Methods: We have currently been conducting a single-blind randomized controlled trial to test the feasibility of the model-guided antipsychotic dose reduction in patients with schizophrenia receiving relatively high doses of risperidone or olanzapine. Clinically stable patients with schizophrenia are randomly assigned to either model-guided treatment group or dose continuation group, and observed for one year. In the dose reduction group, oral doses that achieve 65% dopamine $D_{2/3}$ receptor occupancy at trough are predicted for each individual subject, and antipsychotic doses are reduced in 4 weeks accordingly.
Results: Twenty-six subjects have been included so far, and a total of 50 subjects are targeted. No serious adverse event occurred. Other preliminary results will be presented. In addition, the evidence on the model as well as clinical implications and limitations will be shown.
Conclusion: Although these findings require replication, they have important clinical implications for individualized maintenance treatment strategies to optimize dopamine $D_{2/3}$ receptor blockade with antipsychotics in schizophrenia.

SYMPOSIUM (S19-2)

Antipsychotic Discontinuation in First Episode Psychosis: What Would Happen to Presynaptic Dopamine Capacity?

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Recent meta-analysis revealed that elevated presynaptic striatal dopaminergic function is a robust feature of psychosis like schizophrenia. Considering increased dopaminergic capacity in psychotic disorders, it is not surprising that antipsychotic drugs, which primarily block dopaminergic neurotransmission, are mostly effective in the treatment of psychosis.

However, it remains obscure what would happen to presynaptic dopaminergic function with antipsychotic treatment. This is an important issue addressing whether the current antipsychotic drugs are correcting the primary dopaminergic abnormality or not. In addition, the issue can give a clue regarding the mechanism of relapse in psychotic disorders.

We reviewed the dopaminergic dysfunction in schizophrenia and will introduce preliminary result regarding the effect of antipsychotic discontinuation on the presynaptic dopamine capacity in clinically stable first-episode psychosis which is measured by using [18F]DOPA PET.

SYMPOSIUM (S19-3)

Neurometabolite Levels in Antipsychotic Naïve/Free Patients with Schizophrenia: A Meta-Analysis of 1H-MRS Studies

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Background: Studies using proton magnetic resonance spectroscopy (1H-MRS) have reported altered neurometabolite levels in patients with schizophrenia. However, results are inconsistent and confounded by the influence of antipsychotic (AP) administration. Thus, the aim of the present study was to examine neurometabolite levels in AP-naïve/free patients with schizophrenia through a meta-analysis.
Methods: A literature search was conducted using Embase, Medline, and PsycINFO to identify studies that compared neurometabolite levels in AP-naïve/free patients with schizophrenia to healthy controls (last search: August 2016). Eight neurometabolites (glutamate, glutamine, glutamate + glutamine, N-acetylaspartate [NAA], choline, creatine, myo-inositol, and γ-Aminobutyric acid) and 7 regions of interest (ROI; medial prefrontal cortex, dorsolateral prefrontal cortex, frontal white matter, occipital lobe, basal ganglia, hippocampus/medial temporal lobe, and thalamus) were examined. Standardized mean differences (SMDs) were calculated to assess neurometabolite level differences between groups.
Results: Twenty-two studies (N=1142) were included in the analysis. The results showed lower thalamic NAA levels in the patient group (SMD=-0.56, P=0.0005). No differences were identified for other neurometabolites. This study extends previously reported findings demonstrating a decrease of NAA levels in patients with chronic schizophrenia. On the other hand, previously reported alterations of glutamatergic neurometabolite levels were not replicated. No relationships were found between neurometabolite levels and subjects' characteristics (i.e., age, gender, and duration of untreated psychosis).
Conclusion: Future studies should continue to investigate neurometabolite levels in AP-naïve patients with schizophrenia to help elucidate the underlying pathophysiology of the disease and facilitate novel treatment development.

SYMPOSIUM (S19-4)

A study of tryptophan, kynurenine and serotonin transporter in first-episode drug-naïve patients with major depressive disorder

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Background: Balance between serotonin and kynurenine (KYN) pathway of the tryptophan (TRP) metabolism is associated with the pathophysiology of major depressive disorder (MDD). Serotonin functioning depends on the serotonin transporter (SERT), which terminates neurotransmitter action. This study aimed to examine the association between TRP metabolism and SERT availability in first-episode drug-naïve MDD patients.
Methods: Thirty-three MDD patients and 33 age- and sex- matched healthy controls (HC) were recruited. SERT availability was measured using the radiotracer 123I-ADAM with single photon emission computed tomography in the midbrain, thalamus, caudate and putamen. Serum TRP and KYN concentrations were measured using enzyme-linked immunosorbent assay. Tryptophan breakdown index (TBI) was calculated from the KYN/TRP ratio. Mann-Whitney U Test and Spearman's rank correlation were performed for statistical tests.
Results: There was a borderline significance between MDD and HC in TRP, but lack of a difference in KYN. TBI was lower in MDD than HC. No differences in SERT availability between MDD and HC in the four brain regions. When correlating TRP, KYN, and TBI with SERT in four brain regions in both groups, only KYN correlated with SERT in the midbrain in HC. A further analysis showed that, at TBI > 0.06, midbrain SERT correlated with TRP, KYN, and TBI in HC. However, this could not be found in MDD.
Conclusions: Our results demonstrate complicated interactions between TRP metabolism and SERT in different brain regions. The significance of the association between TRP metabolism and SERT in HC, in particular at different levels of TBI, is warrant for further study.
Key words: tryptophan, kynurenine, serotonin transporter, major depressive disorder, 123I-ADAM, SPECT

SYMPOSIUM (S20-1)

R-Ketamine as a rapid onset and sustained antidepressant

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The *N*-methyl-D-aspartate receptor (NMDA-R) antagonist ketamine is one of the most attractive antidepressants since this drug can produce rapid-onset and sustained antidepressant effects in treatment-resistant patients with major depression and bipolar depression. Recent meta-analyses show that the antidepressant effect of ketamine is greater potent than other NMDA-R antagonists (e.g., memantine, traxoprodil, lanicemine, rapastinel) in patients with depression. Ketamine (Ki = 0.5 M for NMDA-R) is a racemic mixture containing equal parts of S-ketamine (esketamine: Ki = 0.30 M) and R-ketamine (Ki = 1.4 M). Janssen Pharmaceutical Co. Ltd has been developing intranasal administration of esketamine in the treatment of depression. In the animal models of depression, we reported that R-ketamine showed greater potency and longer lasting antidepressant effects than esketamine. Furthermore, esketamine, but not R-ketamine, caused behavioral abnormalities such as hyperlocomotion, prepulse inhibition (PPI) deficits, and abuse potential. Furthermore, repeated intermittent administrations of esketamine, but not R-ketamine, caused loss of parvalubumin (PV)-immunoreactivity in the medial prefrontal cortex and hippocampus of mice. A positrom emission tomography study showed that s single infusion of esketamine (0.5 mg/kg, 40-min), but not R-ketamine (0.5 mg/kg, 40-min), significantly caused reduction of dopamine $D_{2/3}$ receptor binding in the striatum of conscious monkey, suggesting that esketamine, but not R-ketamine, can cause marked dopamine release in the monkey striatum. These all findings suggest that R-ketamine shows greater potency and longer lasting antidepressant effects than esketamine, and that, unlike to esketamine, R-ketamine does not cause behavioral side effects. Therefore, R-ketamine would be a rapid onset and sustained antidepressant without psychotomimetic side effects in humans.

SYMPOSIUM (S20-2)

Ketamine-like antidepressant effects of sarcosine

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Modulation of glutamatergic neurotransmission has become an attractive approach for discovering novel antidepressants. Ketamine, an antagonists of the NMDA subtype glutamate receptor (NMDAR) exhibits antidepressant-like effects in animal models and in patients with major depression and bipolar depression. On the other hand, decades ago, D-cycloserine, a partial agonist of the NMDAR, was incidentally found to have antidepressant activity. In rodent models., a reversible glycine transporter inhibitor, SSR504734, showed antidepressant effects. In postmortem study, expression of NMDAR 1 and 2A subunit was decreased in brains of depressive patients. Recently, NMDA-enhancing treatments, such as sodium benzoate, also decreased depressive symptoms in patients with schizophrenia in clinical trials. Therefore, hypofunction at the NMDAR may also play a role in major depression. However, it remains unclear whether enhancement of the NMDAR can be a treatment for depression. We examined the effects of sarcosine in various rodent models and conducted a 6-week randomized, double-blinded, citalopram-controlled trial in patients with major depressive disorder. Clinical efficacy and safety were assessed biweekly. Sarcosine decreased immobility in the forced swim test and tail suspension test, and other depression-like behaviors in rats. In patients with major depressive disorder, sarcosine significantly ameliorated severity of depression and improved general function than citalopram treatment. Sarcosine-receivers were more likely to remit and stay at the study. Sarcosine had excellent safety profile. Our findings suggest that sarcosine can improve depression-like behaviors in rodent models and treat depression in humans. We also found that sarcosine and ketamine may share similar mechanisms; a single dose of sarcosine exerted antidepressant-like effects with rapid concomitant increases in the mammalian target of rapamycin (mTOR) signaling pathway activation and enhancement of AMPA receptor membrane insertion.

SYMPOSIUM (S20-3)

Ketamine: From an abused drug to a rapid-onset antidepressant

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Recent studies have confirmed that ketamine, a general anesthetic, exerts rapid and robust antidepressant effects. Our studies showed that parvalbumin (PV) interneurons, which mainly provide inhibitory signals to pyramidal cells might be an important mechanism underlying antidepressant effects of ketamine. Ketamine reduces the expression of PV and glutamate decarboxylase 67 (GAD67) in PV interneurons rapidly and increases the level of glutamate in prefrontal cortex. Moreover, inhibition of ketamine-induced loss of PV and GAD67 blocks ketamine induction of antidepressant effects. PV interneurons also receive excitatory signals from pyramidal cells, and the interaction between these two kinds of cells plays an important role in the formation and regulation of the γ oscillation in neural microcircuit. Our future work is to apply electrophysiologic techniques to study the role of γ oscillation mediated by PV interneurons in the antidepressant effects of ketamine and the underlying mechanisms.

Key words: ketamine; parvalbumin interneuron; gamma oscillation

SYMPOSIUM (S21-1)

Is 20 mg long-acting methylphenidate affecting the cardiovascular system in children with ADHD?

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Introduction: ADHD is categorized as neurodevelopmental disorder in the DSM 5; the symptoms include inattentiveness, hyperactivity and impulsivity behavior. Children with ADHD are showing learning difficulties and also relational problems with their peers and surrounding. The gold standard of treatment is using the multimodal approach, by mean of combining pharmacotherapy and behavior modification. The first line medication is methylphenidate hydrochoride. Instead of it's effectiveness, some studies also mentioned the cardiovascular side effects such as increasing heart rate and blood pressure although it was not consistently proven. Therefore, this study tried to identify the effect of 20mg-long acting methylphenidate towards cardio-vascular system in children with ADHD.
Method: This was a one group pre- and posttest design. Twenty-one children aged 7 – 10 years old with drug naïve ADHD participated in this study. They took 20 mg-long acting methylphenidate for 14 weeks and blood pressure and heart rate were examined every two weeks (included 4 weeks of drug free period). We also asked the mother to fill in the Indonesian Hyperactive Behavior Checklist for Children (SPPAHI) every two weeks. In addition, every complaint that came from the research subjects during the study was also counted. We used the time series statistical analysis with $p<0.05$ for testing the hypothesis.
Results: The systolic and diastolic blood pressure fluctuated insignificantly during the 18 weeks of study ($p=0.115$ and $p=0.059$). Nevertheless, the heart rate also altered insignificantly ($p=0.091$). Interestingly the fluctuations (blood pressure and heart rate) were stated in the normal ranged even though the medication has already been stop. The most frequent of complaints that related with the methylphenidate using were dizziness, nausea, and gastrointestinal upset, but it was mild and lasted for not more than 2 weeks.
Conclusion: 20-mg long-acting methylphenidate in children with ADHD did not have any negative effect towards blood pressure and heart rate during the study. However, it is still needed to observe the cardiovascular system especially for long-term used.

SYMPOSIUM (S21-2)

Successful Clozapine Treatment for Schizophenia with Childhood Onset in Korea

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SYMPOSIUM (S22-1)

Overview of development of Korean treatment guideline for bipolar disorders

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Objective: The Korean Medication Algorithm for Bipolar Disorder (KMAP-BP) was firstly published in 2002, with updates in 2006 and 2010. This third update reviewed the experts' consensus of opinion on the pharmacological treatments of bipolar disorder**.**
Methods: The newly revised questionnaire composed of 55 key questions about clinical situations including 223 sub-items was sent to the experts. Sixty-four of 110 experts replied. For the newly added section (treatment guideline for child and adolescent bipolar disorders) in KMAP-BP 2014, 23 of 38 experts replied to this special section. Data were analyzed according
to the same methods to be used in conjunction with the previous publications.
Results: The recommendations for the management of acute mania remained largely unchanged. Combination of mood stabilizer (MS) and atypical antipsychotic (AAP) was the first-line treatment option in acute mania. Valproic acid (VP), lithium (Li), and several AAPs continued to be first-line treatments. MS or AAP monotherapy was the first-line treatment in hypomania. More frequent use of AAP as a first-line agent was noted in KMAP-BP 2014. For management of mild to moderate bipolar depression, MS monotherapy, combination of MS and AAP, combination of AAP and lamotrigine (LTG) was the first-line treatments. In severe non-psychotic depression, combination of MS and AAP, combination of AAP and LTG, and
combination of MS and antidepressant (AD) was the first-line treatments. For the management of severe psychotic bipolar depression, combination of MS and AAP, combination of AAP and LTG, combination of MS, AAP and AD or LTG, combination of AAP and AD, and combination of AAP, AD and LTG was the first-line treatments. Li, VP, LTG, aripiprazole (ARP), olanzapine (OLZ) and quetiapine (QT) were the first-line treatment for bipolar depression. Although many treatment options were recommended, there were few consensus of opinion in bipolar depression. Treatment of mixed features was firstly added in KMAP-BP 2014. Combination of MS and AAP was the treatment of choice for management of mixed features. AAP monotherapy was also the first-line treatment. VP, Li, ARP, OLZ and QT were the first-line treatment for management of all phases of mixed features. Risperidone was added in mixed mania and LTG in mixed depressive features. There have been many treatment options for management of rapid cycling in bipolar disorder, when considered the combination of MS and AAP was only first-line treatment in KMAP-BP 2014. Combination of MS and AAP, MS or AAP monotherapy was
the first-line options for management of maintenance phase after manic episode. For maintenance treatment after bipolar I depression, combination of MS and AAP, combination of MS and LTG, combination of AAP and LTG, MS or LTG monotherapy, and combination of MS, AAP and LTG were the first-line options. For management of maintenance phase of bipolar
II depression, combination of AAP and LTG, combination of MS and LTG, combination of MS and AAP, AAP or LTG monotherapy were recommended as the first-line options.
Conclusion: The experts' opinion of consensus was markedly changed in KMAP-BP 2014 than in previous publications. Preferred treatment with AAP and LTG was especially noted for management of bipolar disorder. We confirmed the treatment options recommended in KMAP-BP 2014 were much in concordance with current updated treatment guidelines for bipolar
disorder. Despite the limitations of expert consensus guideline, KMAP-BP 2014 may reflect the current patterns of clinical practice and recent researches.

SYMPOSIUM (S21-3)

Treating acute agitation in children and adolescent in clinical setting

Benjaporn Panyayong

Pediatric agitation is often a complex clinical challenge for any Emergency Department staff, which requires appropriate identification of the underlying etiology,and clinical management (utilizing behavioral techniques, and psychopharmacol-ogy). Acute aggression is a behavioral emergency that requires urgent and immediate intervention to reduce the danger to the patient and the caregiver. Agitation is a nonspecific cluster of behavior that occurs in a diverse number of psychiatric disorders such as delirium, and substance-induced psychosis (includi-ng prescribed mediations). The triad of pediatric aggression of anger, agitation, and outbursts(AAO), can readily escalate as a frequent precipitant leading to a psychiatric hospitalization of the child, or adolescent. The AAO of children with anxiety, or pervasive development disorder showed significantly more distress relative to anger alone, and agitation from substance-induced psychosis in adoles-cents (methamphetamine), is a major problem in Thailand. Research has showed that agitation from methamphetamine intoxication is frequent, and its severity appears to correlate directly with methylphenidate blood level. The management of behavioral symptoms includes environment management in order to ensure the safety for the patient and hospital staff. Medication for agitation is often necessary, and will be discussed in the session

SYMPOSIUM (S21-4)

Evidence Based Case Report: Omega-3 for Children to Improve Social Behavior in Autism Spectrum Disorder

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Background: Families of children with Autism Spectrum Disorder (ASD) often require information regarding the use of supplements. Omega-3 is often inquired due to its antioxidant properties to protect nervous tissue and modify gene expression and neuronal function.

Aim: To review the evidence regarding the efficacy of omega-3 supplement in improving clinical symptoms in children with ASD.

Methods: Five search engines were used to review the evidence, namely Pubmed, SpringerLink, Cochrane Library, ScienceDirect, and Scopus. The keywords were (child* with autism) (omega-3 OR poly unsaturated fatty acid) (placebo) (aberrant behavior checklist OR social responsiveness scale). Articles were limited to those published in 2012 or later, written in English, available in full text, and research on humans. Articles were then selected based on relevance.

Results: The evidence search resulted in two clinical trials. The first study used 240 mg arachidonic acid (ARA), 240 mg docosahexaenoic acid (DHA), and 0.96 mg astaxanthin. The second study used 350 mg eicosapentaenoic (EPA), and 230 mg DHA. The studies demonstrated statistically significant change in social withdrawal based on Aberrant Behavior Checklist-Lethargy subscale (3.5, p-value 0.04; and 2.2, p-value 0.05, respectively). The studies did not report any severe adverse effects.

Conclusion: Omega-3 supplementation is relatively safe and may be beneficial in improving social interaction in children with ASD. Further studies with larger samples and specific types of Omega-3 are required.

SYMPOSIUM (S22-2)

Third revision of Korean medication algorithm for manic, mixed and depressive episodes

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Objective: To constitute the third revision of the guidelines for the treatment of bipolar disorder issued by the Korean Medication Algorithm Project for Bipolar Disorder (KMAP-BP 2014).
Methods: A 56-item questionnaire was used to obtain the consensus of experts regarding pharmacological treatment strategies for the various phases of bipolar disorder and for special populations.
Results: The first-line pharmacotherapeutic strategy for acute manic episode is combination of mood stabilizer and an atypical antipsychotic (AAP), and it is the treatment of choice for euphoric, psychotic and dysphoric/mixed mania. The preference for monotherapy with AAP (for all three types of mania) or mood stabilizer (for euphoric mania) was increased in KMAP-BP 2014. Valproic acid and lithium are chosen as the preferred mood stabilizer of the first-line treatment of acute manic episode and valproic acid was the treatment of choice for all types of mania. AAP is more widely accepted than before in manic and hypomanic episode. Moreover, the preference for combination treatment in manic patients who failed to respond in early stage treatment was increased. For acute depressive episode, the first-line pharmacotherapeutic strategy for acute bipolar depressive episode with moderate, non-psychotic severe and psychotic severe episode was mood stabilizer combined with AAP or AAP with lamotrigine. Among AAPs, olanzapine, quetiapine and aripiprazole were preferred. When considering the efficacy and safety simultaneously, (es)citalopram, bupropion, and sertraline were recommended among antidepressants for bipolar depression.
Conclusion: In KMAP-BP 2014, the preference for AAP was increased in the treatment of acute mania, and depression. There was increased expert preference for the use of AAP and LTG. The major limitation of the present study is that it was based on the consensus of Korean experts rather than on experimental evidence.

SYMPOSIUM (S22-3)

Third revision of Korean medication algorithm for maintenance phase of bipolar disorders

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Objectives : In this study, we aimed to deal with the recommendations for the maintenance treatment for bipolar disorder in Korean Medication Algorithm Project for Bipolar Disorder (KMAP-BP) 3rd revised.
Method : The questionnaire regarding strategies for maintenance treatment was composed of overall treatment strategies after acute mood episodes, choice of antipsychotics and antidepressants, treatment duration and treatment strategies for breakthrough symptoms.
Results : Regarding the maintenance treatment after acute hypomanic or manic episode in bipolar I or II disorder, combination therapy of mood stabilizer and an atypical antipsychotic agent, monotherapy of mood stabilizer and monotherapy of an atypical antipsychotic agent were chosen as 1st-line treatment. Regarding the maintenance treatment after depressive episode in bipolar I or II disorder, combination therapy of mood stabilizer and an atypical antipsychotic agent, combination of mood stabilizer and lamotrigine, combination of an atypical antipsychotic agent and lamotrigine, mood stabilizer monotherapy, lamotrigine monotherapy, and atypical antipsychotic agent monotherapy were chosen as 1st-line treatment. Preference for atypical antipsychotics and antide-pressants became increased in KMAP-BP 3rd revised compared to KMAP-BP 2nd revised. **Conclusion :** The recommendations for the maintenance treatment in KMAP-BP 3rd revised seem to reflect current changes in prescription pattern for bipolar disorder.

SYMPOSIUM (S22-4)

Comparison with other international treatment guidelines

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Our goal was to compare the recommendations of the Korean Medication Algorithm Project for Bipolar Disorder 2014 (KMAP-BP 2014) with other recently published guidelines for the treatment of bipolar disorder. We reviewed a total of four recently published global treatment guidelines and compared each treatment recommendation of the KMAP-BP 2014 with those in other guidelines. For the initial treatment of mania, there were no significant differences across treatment guidelines. All recommended mood stabilizer (MS) or atypical antipsychotic (AAP) monotherapy or the combination of an MS with an AAP as a first-line treatment strategy for mania. However, the KMAP-BP 2014 did not prefer monotherapy with MS or AAP for dysphoric/psychotic mania. Aripiprazole, olanzapine, quetiapine, and risperidone were the first-line AAPs in nearly all of the phases of bipolar disorder across the guidelines. Most guidelines advocated newer AAPs as first-line treatment options in all phases, and lamotrigine in depressive and maintenance phases. Lithium and valproic acid were commonly used as MSs in all phases of bipolar disorder. As research evidence accumulated over time, recommendations of newer AAPs – such as asenapine, paliperidone, lurasidone, and long-acting injectable risperidone – became prominent. This comparison identifies that the treatment recommendations of the KMAP-BP 2014 are similar to those of other treatment guidelines and reflect current changes in prescription patterns for bipolar disorder based on accumulated research data. Further studies are needed to address several issues identified in our review.

SYMPOSIUM (S23-1)

A novel mechanism for stress-induced cocaine relapse: Orexin-initiated and endocannabinoid-mediated dopaminergic disinhibition in the ventral tagmental area

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Objectives: Drug relapse can be initiated by environmental cues, re-exposure, or stress and limits the success of rehabilitation programs. The orexin system has been reported to be associated with drug relapse while the mechanism, especially stress-induced drug relapse, is unclear. Here, we revealed a novel mechanism for stress-induced cocaine relapse using electrophysiological, anatomical, immunohistochemical and neurochemical approaches.
Methods: Whole cell patch clamp recordings were preformed in dopaminergic neurons in brain slices containing the ventral tegmental area (VTA). The orexin A level in the VTA homogenate was measured by ELISA. 2-arachidonoylglycerol (2-AG), an endocannabinoid, was measured by LC/MS/MS. In mice, the cocaine-conditioned place preference (CPP) training was established by a bias CPP training program, followed by an extinction day and then a restraint stress-induced reinstatement of extinguished cocaine CPP. Restraint stress was given to the mouse by putting it in a centrifuge tube for 30 min.
Results: A 30 min- restraint stress in mice activates lateral hypothalamic (LH) orexin neurons, increases levels of orexin A and 2-AG in the VTA, and reinstates extinguished cocaine-CPP. This stress-induced reinstatement of cocaine CPP depends on type 1 orexin receptors (OX1Rs), type 1 cannabinoid receptors (CB1Rs) and diacylglycerol lipase (DAGL) in the VTA. In dopaminergic neurons of VTA slices, orexin A presynaptically inhibits GABAergic transmission. This effect is prevented by internal GDP-b-S or inhibiting OX1Rs, CB1Rs, phospholipase C or DAGL, and potentiated by inhibiting 2-AG degradation.
Conclusions: These results suggest that restraint stress activates LH orexin neurons, releasing orexins into the VTA to activate postsynaptic OX1Rs of dopaminergic neurons and generate 2-AG through a G_q-protein-phospholipase C-DAGL cascade. 2-AG retrogradely inhibits GABA release through presynaptic CB1Rs, leading to VTA dopaminergic disinhibition and reinstatement of cocaine CPP.

SYMPOSIUM (S23-2)

The associations between Plasma Orexin-A Levels and metabolic abnormalities in Patients with Schizophrenia taking Clozapine or Other Less Obesogenic Antipsychotics

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Background: The role of orexin-A in antipsychotic-induced metabolic abnormalities remains unclear.
Aims: To investigate the association between orexin-A levels and metabolic abnormalities in patients with schizophrenia treated with clozapine or less obesogenic antipsychotics.
Methods: Plasma orexin-A levels and metabolic parameters were determined in 160 patients with schizophrenia including 109 taking clozapine and 51 taking aripiprazole, amisulpride, ziprasidone, or haloperidol, and 60 controls.
Results: Orexin-A levels were significantly higher in the less obesogenic antipsychotic group, followed by the clozapine group and then controls. Higher orexin-A levels were associated with better metabolic profiles in the patient group but not in controls. Regression analysis showed orexin-A had a counteractive role in the risk of metabolic syndrome (OR = 0.10, $P < 0.05$).
Conclusions: Orexin-A is up-regulated in antipsychotic-treated patients with schizophrenia. The less obesogenic antipsychotic group had higher orexin-A levels than the clozapine group. Higher orexin-A levels may have protective effects against the development of metabolic abnormalities.
Keywords: orexin-A; schizophrenia; antipsychotics; metabolic abnormalities; metabolic syndrome

SYMPOSIUM (S23-3)

Genetic polymorphisms in the orexin system (focusing on a polymorphism associated with nicotine dependence)

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Background/Objective: The orexin system is well known to regulate feeding behavior and states of sleep/wakfulness. Despite lack of studies that reportedly investigated genetic variations in the orexin system affecting feeding behavior in humans, a growing number of human genetic studies have been accumulated targeting headache and some psychiatric diseases including those related to sleep, such as nalcorepsy. However, few such studies have focused on variations associated with reward-related traits, although the orexin system has been suggested to be involved in the rewarding effects. In this symposium, we present a study that comprehensively explored genetic contributors to nicotine dependence by using whole-genome genotyping arrays in Japanese subjects.
Method: A two-stage genome-wide association study (GWAS) was conducted for 148 subjects using the Fagerström Test for Nicotine Dependence (FTND), Tobacco Dependence Screener (TDS), and number of cigarettes smoked per day (CPD) as indices of nicotine dependence. For the additional association analyses, patients who underwent major abdominal surgery, patients with methamphetamine dependence/psychosis, and healthy subjects with schizotypal personality trait data were recruited. Autopsy specimens with various diseases were also evaluated.
Result/Discussion: After the GWAS between more than 200,000 marker single-nucleotide polymorphisms (SNPs) and the FTND, TDS, and CPD, the nonsynonymous rs2653349 SNP (located on the gene that encodes orexin [hypocretin] receptor 2) was selected as the most notable SNP associated with FTND in the two-stage GWAS. This possible association was replicated for independent 374 samples. This SNP was also associated with postoperative pain, the initiation of methamphetamine use, schizotypal personality traits, and susceptibility to goiter.
Conclusion: We obtained significant results in the GWAS and subsequent analyses that suggest that the rs2653349 SNP (Val308Ile) could be a genetic factor related to severity of nicotine dependence and possibly pain, schizotypal personality traits, and goiter in the Japanese population.

SYMPOSIUM (S24-1)

The endocannabinoid system in schizophrenia

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Strong clinical, observational, experimental and associational evidence has linked cannabis to psychosis and specifically to schizophrenia. These data indicate potential mechanistic interactions between cannabinoids and systems relevant to the pathology of schizophrenia such as dopamine pathways. Central to the action of exogenous cannabinoids is the endogenous cannabinoid or endocannabinoid system. This poorly understood signalling system in the CNS consists of at least three endogenous ligands, anadamide, 2-AG and AEA and their synthetic and degradative enzymes and their cognate receptors, CB1 and CB2 as well as transient receptor potential channels and peroxisome proliferator activated receptors. The CB1 receptor is the most abundant G-protein coupled receptor in the CNS and is richly expressed in cortical and sub-cortical regions associated with schizophrenia. However, it's role in modulating neurotransmitter release and this relationship to psychosis remains imprecisely understood. A number of studies have investigated the endocannabinoid system in psychotic disorders and have mainly reported consistent changes in CB1 receptor expression and protein levels. In particular interactions with frontal and mid-brain dopamine systems links with mechanisms of psychosis. The potential to intervene through this system to ameliorate psychosis and related symptom domains through agents targeting the endocannabinoid system has attracted considerable recent interest.

SYMPOSIUM (S24-2)

Internet addiction in Indonesia: a challenging situation

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Internet addiction is a relatively new phenomenon in Asia especially among teenagers and young adults. Prevalence ranges from 2-40%, with the highest recorded in South Korea. Rapid improvement in technology makes the internet more easily accessible to teenagers and young adults nowadays and the latest study showed that 20% students in secondary and high schools in Jakarta suffer from internet addiction. Its symptoms are similar to those of substance addiction. Internet addiction can often co-occur with other mental disorders, for example ADHD, depression, bipolar disorder, social phobia and avoidant personality. It can generally be divided into online games addiction and social media addiction. Male teenagers tend to be addicted to online games. Online games addiction is associated with competitive nature, escape from reality (real world), and feeling connected to people without having to meet them in person. People who use the internet for more than 4 hours a day are more prone to experiencing internet addiction. During fMRI studies, the prefrontal cortex and amygdala are shown to be more active, similar to findings from the study on patients with substance addiction.

SYMPOSIUM (S24-3)

Association of Proopioimeranocortin gene polymorphism with vulnerability to alcohol dependence in Japanese

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Objective: Genetic contribution rate of alcoholic dependence is approximately 0.4-0.6, indicating that genetic variations can be markers for individual vulnerability to alcohol dependence. Racial and ethnic differences of genetic variations lead to different effect sizes in the analyses and would be expected to affect the results of association studies. The endogenous opioid system has been reportedly implicated in addiction including alcohol dependence. In the present study, we focused on the Proopiomeranocortin (*POMC*) gene which encodes β-Endorphin and non-opioid peptides including ACTH and examined the effects of genetic variations on alcohol dependence.
Method: This study included 437 male Japanese patients diagnosed with alcohol abuse/dependence by DSM-III-R and 353 healthy control subjects matched to alcohol dependent patients on gender and age. The statistical significance of associations between variances of single nucleotide polymorphisms (SNPs) in alcohol dependent patients and control subjects were evaluated with non-parametric methods.
Result: Genotype variation of the *POMC* C-1802T SNP was significantly different between alcohol dependent patients and control subjects. The frequency of C-allele carriers of the *POMC* C-1802T SNP in alcohol dependent patients was higher than that in control subjects. No linkage disequilibrium block including the SNP was identified in Japanese population.
Conclusion: A polymorphism in 5 flanking region of the *POMC* gene appears to be associated with alcohol dependence in Japanese. World Health Organization reported that the prevalence estimated for alcohol use disorders in Japan was similar to that in Indonesia among Asian countries. Therefore, genetic variations associated with alcohol dependence in Japanese would be useful information also for Indonesian. In the symposium, we also review epidemiology of alcohol dependence in Japan and discuss for genetic contribution to alcohol dependence.
Keywords: Alcohol dependence, Proopiomelanocortin, Genetic polymorphism

SYMPOSIUM (S24-4)

Impulsivity and Addiction

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Background
The magnitude of the world drug problem becomes more apparent when considering that more than 1 out of 10 drug users is a problem drug user, suffering from drug use disorders or drug dependence. Drug use disorders have many consequences relating with economic, morbidity, mortality, and risky behavior for transmitting blood borne diseases. Researches of impulsivity over the years become evident to function by determinant of drug use and vice versa.
Purpose of review
This review will discuss about tools to detect impulsivity and result from several researches in relation with addiction and impulsivity in Indonesia.
Finding
Impulsivity can be measured using questionnaires such as Barratt Impulsive Scale (BIS-11), *Sensitivity to Punishment & Sensitivity to Reward Questionnaire (SPSRQ), Behavioral Inhibition System/Behavioral Activation System Questionnaire (BIS/BAS)*; Brain Computer Interface (BCI); and electroencephalography (EEG). Research in 30 HIV-infected and 33 healthy men in Indonesia showed that HIV-infected individuals reported higher alcohol- and drug-related risk behavior, compared to healthy controls. HIV-infected men were more impulsive (mainly increased reward sensitivity) compared to controls, which predicted alcohol- and drug-related risk behavior.
Summary
Sensitive tools for impulsivity should be used to predict risk group for drug addiction and other mental disorders so early intervention can be applied.

POSTER (P1 -A1)

Association study of genetic polymorphisms in ABCB1, CYP2B6, CYP2D6 genes and efficacy dosage for methadone therapy in Han heroin dependence patients

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Objectives: Opioids dependence is one of the most serious problems affecting social norms and public health system. Methadone Maintenance Therapy (MMT) is now widely used to treat heroin dependence with high efficacy. Methadone is a synthetic opioid anesthetic, past studies showed that gene polymorphism and individual's differences may affect the pharmacodynamics of Methadone, which is majorly metabolized by Cytochrome P450 and P-glycoprotein. Studies also showed that genetic variations of CYP450 CYP2B6, G516T and A785G enzyme are related to Methadone blood concentration, and CYP2D6 * 10, with high variations in Asians, plays a major role in Methadone metabolism. Besides, ABCB1 C1236T, G2677T and C3435T gene variants of P-glycoprotein are confirmed to be related to effectiveness of MMT.
Methods: This study is to explore the relationship between CYP450 genetic polymorphism (ABCB1, CYP2B6, & CYP2D6 * 10) and effective dosage of Methadone. The study subjects were heroin dependence outpatient treated with MMT in LotungPoh-Ai and General Keelung Hospitals in northern Taiwan. The study protocol was approval by the Ethics Committees of Cathy Hospital. From January 2015 to September 2015, a total of 100 (82 men and 18 women, the average age is 42.53±6.65 years respectively,) heroin dependence patients were enrolled. Characteristics including daily Methadone dosage, BMI index, and other clinical data were collected; gene extraction from oral mucosa and was analyzed via Real-time PCR.
Results: Our study finds that the average Methadone dosage in different sex, BMI index, ABCB1 2677GG and CYP2B6 516GG variations is statistically significant. Male($p<0.009$), BMI>25($p<0.007$), and CYP2B6 516GG homozygote are related to higher average Methadone dosage($p<0.02$), while ABCB1 2677GG homozygote is related to lower dosage($p<0.05$). Multiple linear regression is done to examine the relationship between variants above and average Methadone dosage, and it can predict more than 30% of effective Methadone dosage in our study objects.
Conclusion: The future in-depth study to explore interactions between variants above and effective MMT dosage is warrant. This study outcome should be helpful to precisely dosing MMT for Taiwan Heroin dependence patients in the future.

POSTER (P1-A2)

Clinical Characteristics Associated with Concomitant Use of Benzodiazepine Hypnotics and Alcohol: Preliminary Findings

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Objectives: Concomitant use of benzodiazepines and alcohol seems prevalent in clinical settings; however, previous studies have not focused solely on psychiatric patients. The objectives of this study were three-fold: (1) to investigate the prevalence of concomitant use of benzodiazepine hypnotics and alcohol in outpatients with mixed psychiatric diagnoses, (2) to investigate the extent of awareness on the side of their psychiatrists about the concomitant use and (3) to examine the clinical characteristics related to the concomitant use.
Methods: A questionnaire survey was carried out for outpatients with schizophrenia, depression and primary insomnia (International Classification of Diseases, 10the edition) who were receiving benzodiazepine hypnotics at Kawasaki Municipal Hospital, Kanagawa, Japan. After providing informed consent, participants were asked to fill in a sleeping diary for seven days in which use of hypnotics and alcohol was also recorded. In addition, their treating psychiatrists were asked as to whether or not they thought their patients were using them concomitantly. CAGE test was used to assess their drinking problems.
Results: Fifty Patients (mean±SD age, 55.1±13.2 years; 23 females; schizophrenia [n=18], depression [n=15] and primary insomnia [n=17]) were included. The prevalence rates of concomitant use of hypnotics and alcohol were 50.0% (9/18) in schizophrenia, 33.3% (5/15) in depression and 41.2% (7/17) in primary insomnia. On the other hand, the concomitant use was suspected by their psychiatrists only in 55.6% (5/9), 20.0% (1/5) and 28.6% (2/7), respectively. In schizophrenia and depression, CAGE total scores were significantly higher in concomitants users than the others (mean±SD, 1.7±1.1 vs 0.3±0.7, $p=0.009$ in schizophrenia; 1.2±1.3 vs 0.0±0.0, $p=0.022$ in depression).
Conclusion: Nearly half of the patients concomitantly used benzodiazepine hypnotics and alcohol. which was frequently overlooked by their psychiatrists. CADE test may be useful to screen such concomitant users.

POSTER (P1-A3)

The Effect of *FKBP5* Gene Polymorphisms, Adverse Childhood Experience, and Their Interaction on Methamphetamine Abuse

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Objectives: Dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis is strongly linked to drug addiction, including methamphetamine seeking. Genetic association studies suggest the effect may be mediated by FK506 binding protein 5 (FKBP5) gene that regulates HPA axis function. We therefore hypothesized that the variant of FKBP5gene may increase the vulnerability of Methamphetamine (METH) abuse or genetic factors may contribute to different sensitivity to adverse childhood experiences (ACEs). The present study was a case-control study to examine the ACEs, single nucleotide polymorphisms (SNPs) of FKBP5 gene, and their interactions among methamphetamine (METH) abusers in Taiwan.
Methods: We genotyped SNPs of FKBP5 gene (rs1360780) in 401 METH users (336 males and 65 females) and 348 controls (288 males and 60 females).Self-administered Family Health History Questionnaires measured the ACEs.
Results: Compared to controls, the total numbers of ACEs in METH abuserswassignificantly higher ($p<0.0001$), the variantFKBP5 (rs1360780) genotypes in METH abusers had no significant difference ($p>0.5$).Theeffect from gene (FKBP5 genotypes) -environment interaction on METH use showed no significant interactions in current analyses.
Conclusions: Our study suggests ACEs are highly association with METH abuse, but SNPs of FKBP5 gene showed no significant association with METH abuse. We also fail to find significant interactions between ACEs and FKBP5 gene SNPs to influence METH abuse vulnerability

POSTER (P1-A4)

Atypical antipsychotic intervention for addiction drug cases in *Rumah Sakit Ketergantungan Obat Indonesia*, statistic of outpatient setting during August-October 2016. Is it prolonged abstinence?

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Addiction is a sense of high interest in a case within a desire to do so and accompanied by certain symptoms. Drug abuser increased faster nowadays. Indonesia as a growth country also impacted by, almost 3% people in this country become drug addictive. Symptoms of addiction closely related to mental disorder. The changes of behavior are one of feature, in the other hand also psychologic aspects include cognitive function and emotional. Drug addiction or substance dependency is similarly compulsion to seek and take drug, then loss of control for limiting intake and emergence of a negative emotional state when access to the drug is prevented. Drug addiction has been conceptualized as disorder that moves from impulsivity to compulsivity in a collapse cycle of addiction comprised of three stage preoccupation, intoxication and withdrawal affect. It is closely related to mental disorder. Abstinence is the destination of drug abuser in every stage.

Multidimentional disorder interm of cognitive and affective symptoms always needs psychofarmacology intervention. A number of potential therapeutic molecular target with varying degrees of serotonin, norephinephrine, dopamine and glutamat receptors. Atypical antipsychotic have an advantage over older conventional drug for covering positive and negative symptoms from psychotic as mental disorder related to drug abuser. *Rumah Sakit Ketergantungan Obat* (RSKO) is a drug dependency hospital in Indonesia which giving treatment in addiction cases. Outpatient setting treatment in RSKO receiving variety patient from variety cases, more than 40% has problem in drug abuser within recrational to situational user until dependency. Simple feature represents amongst 3 months observation in RSKO most in outpatient treatment settings. Statistic will present number of visiting patient, various of addiction drug cases, and psychofarmachology given. Atypical antipsychotic is used, first to decrease the psychotic symptoms induced by drug. Abstinence condition will be reached by its therapy as long as it can be, instead of another research needed to prove the efficacy of atypical antipsychotic for this abstinence.

POSTER (P1-A5)

The Effect of Chronic Alprazolam Use: Addiction, Tolerance and Psychotic Symptoms

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Introduction: Alprazolam is used as an anxiolytic drug for generalized anxiety disorder. Initial study of this drug indicated low rates of side effects. Several notions of adverse effects of alprazolam during both treatment and withdrawal periods have been reported. This study aimed to provide an additional description of psychopathologies in relation to chronic alprazolam use.
Method: Case report
Result and Discussion: A 38 years-old male was taken to the emergency room because he had behaved strangely since 6 hours before admission. He was suddenly frightened, mentioned about some people who would kill him, and said that he already died. He also appeared to be talking to himself and responded irrelevantly to questions. In addition, he tried to keep pushing the wall, saying that it should be straightened since it was tilted. He had been taking alprazolam for 2 years as suggested by his friend for his sleep problem, started with 0.5 mg, thenhe increased the dose himself up to 4 milligrams per day. However, he stopped taking alprazolam 2 weeks before admission, saying that the drug did no good because he still had sleeping problems. He had no other known previous psychiatric history. Thepsychotic symptoms he was experiencing were then attributed to the chronic alprazolam use followed by its sudden withdrawal.
Conclusion: The chronic administration of alprazolam followed by a sudden withdrawalmight induce psychotic symptoms. Alprazolam use should be under the supervision of a psychiatrist.
Keywords: alprazolam, addiction, tolerance, withdrawal, psychotic

POSTER (P1-A6)

Dealing with arising ketamine abuse in Taiwan

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Background: In recent years, ketamine became one of the most severe problem of drug abuse among young people especially in Asian Countires. In Taiwan, young people use ketamine due to peer influence, disturbed mood or recreational use. Ketamine misuse and abuse may lead to ulcerative cystitis and cognitive impairments. However, there is still no consensous on dealing with the ketamine abuse problems. This study aims to examine whether a life skill education has an influence on cessation contemplation of current Ketamine users.
Methods: Between January and March 2016, 285 ketamine users participated in a 6-hour program regarding skills of communication, decision making, refusal skills and HIV/AIDS prevention. Before and after the program, participants filled in a structured questionnaire, including age, gender, education, knowledge about ketamine and stage of ketamine abstinence.
Results: It showed that knowledge about Ketamine improved and a substantial number of participants motivated to prepare themselves abstain from using ketamine within the next 30 days.
Conclusion: It might be considered that life skill training could be integrated in the management of people with ketamine abuse problems to improve their motivation to keep abstinence

POSTER (P1-A7)

Involvement of CaMKII and ERK in nicotine dependence

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Nicotine is an active compound in tobacco and has a rewarding effect in the central nervous system (CNS), which may leads to dependence. Nicotine dependence is elucidated by brain mechanisms and molecular substrates associated with reward signaling. The reward signaling includes glutamate receptors and their downstream signaling pathways such as calcium/calmodulin-dependent kinase II (CaMKII) and extracellular signal regulated kinase (ERK). To investigate the roles of both CaMKII and ERK on nicotine dependence, we Measured CaMKII and ERK activities after nicotine dependence assessed by conditioned placed preference (CPP). Mice were firstly habituated to the CPP apparatus for five days, followed by a pre-conditioning test to determine the nicotine-paired compartment. Mouse entered conditioning training for one month in which 0.5 mg/kg nicotine was administered intraperitoneally followed by confinement in the designated compartment of CPP apparatus for 30 minutes. Four hours later, the same procedure was repeated, only this time saline was given instead of nicotine and the mouse was confined in the opposite of nicotine compartment. One day after conditioning, preference scores were measured to evaluate the nicotine dependence. The mice were sacrificed and mouse hippocampi were isolated for immunoblotting analyses of CaMKII and ERK. It was found that CaMKII and ERK phosphorylation significantly increase during nicotine dependence condition. The results offer a new pharmacological strategies to treat nicotine dependence based on the manipulation of CaMKII and ERK signal. In particular, disruption of reconsolidation of drug-related memories by disrupting CaMKII and ERK signaling may have a high therapeutic value in the treatment of nicotine dependence.

POSTER (P1-A8)

Induction system of Shati/Nat8L expression by methamphetamine via dopamine D1 signaling pathway

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Objectives: Shati/Nat8L is significantly increased in the nucleus accumbens (NAc) of mice after repeated methamphetamine (METH) treatment. We have reported that Shati/Nat8L overexpression in mice NAcattenuats METH-induced hyperlocomotion, locomotor sensitization, and conditioned place preference. However, it is unclear how mechanism lies in Shati/Nat8L induction by METH treatments in NAc of mice.
Methods: We performed a mouse Shati/Nat8L luciferase assay using PC12 cells. Next, we investigated the response of METH to Shati/Nat8L expression and CREB activity using mice brain slices of NAc, METH administration to mice, and Western blotting for CREB activity of specific dopamine receptor signals in vivo and ex vivo, respectivery.
Results: We found that METH activates CREB binding to the Shati/Nat8L promoter to induce the Shati/Nat8L mRNA expression. Furthermore, the dopamine D1 receptor antagonist SCH23390, but not the dopamine D2 receptor antagonist sulpiride, inhibited the upregulation of Shati/Nat8L and CREB activities in the mouse NAc slices. Thus, the administration of the dopamine D1 receptor agonist SKF38393 increased the Shati/Nat8L mRNA expression in mice NAc.
Conclusions: These results show that the Shati/Nat8L mRNA is increased by METH-induced CREB pathway via dopamine D1 receptor signaling in mice NAc. These findings might contribute to development of a clinical tool for METH dependence.

POSTER (P1-A9)

Psychotic symptoms induced by varenicline in a patient with alcohol and nicotine dependence: a case report

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Objective: Varenicline has been reported to case psychotic symptoms in patients with schizophrenia or mood disorders. The objective of this report was to present a case suffering from alcohol and nicotine dependence without any comorbid psychiatric condition who experienced psychotic symptoms only during the use of varenicline.
Method: A case report.
Results: A 44-year-old male inpatient with alcohol dependence and nicotine dependence according to the International Classification of Diseases, 10th edition, without any history of other psychiatric illnesses, was voluntarily hospitalized to receive alcoholism rehabilitation program (ARP). On the 2nd day of hospitalization, he started to take 0.5 mg/d of varenicline, and the dose was increased to 1.0 mg/d on Day 5. On Day 6, he experienced auditory hallucination and persecutory delusion, and showed loose association. These psychotic symptoms completely disappeared in three days by discontinuing varenicline and starting 6 mg/d of aripiprazole on Day 7. He wanted to resume varenicline due to exacerbation of craving for smoking, and started to receive it again at 1.0 mg/d on Day 17 and then the dose was maintained. On Day 31, he started to experience exactly the same psychotic symptoms. On Day 32, varenicline was discontinued and these symptoms were resolved on Day 35. Thereafter he did not show any psychotic symptoms also after quitting aripiprazole on Day 73. He was discharged on Day 86 upon completion of the ARP.
Conclusions: To our knowledge, this is the first case that presented varenicline-induced psychosis despite no history of schizophrenia and mood disorders. Causal relationship between use of varenicline and psychosis is very likely in light of the two-time appearance of psychotic symptoms only during the use of this medication. Physicians should be aware of potential occurrence of psychosis as a side effect of varenicline in the treatment of dependence in any patient.

POSTER (P1-A10)

The relationship between stress and alcohol consumption in female mice

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OBJECTIVE: A complex relationship exists between alcohol-drinking behavior and stress. There are well-known sex differences in the epidemiology of alcohol dependence; however, the relationship between stress and alcohol consumption is poorly understood. There obviously exist sex differences in sensitivity, perception, and responsiveness to stress, and then these differences will be reflected in drinking behavior.Genetic factors, such as differences in genes for **μ**-opioid receptor (MOP) systems, also have a substantial influence on alcohol consumption, but only a limited set of such genetic influences on stress-induced alcohol consumption have been examined. The current studies investigated the influence of MOP deletion on voluntary ethanol consumption in female wildtype (WT) and knockout (KO) mice with a chronic restrain stress or log-term social isolation stress.
METHODS: This study assessed the effects of isolation-rearing or restrain stress on later ethanol intake using a two-bottle home-cage consumption (ethanol 8% vs. water) paradigm in WT and MOP gene knockout female mice.
RESULTS: While restrain stress did not affect ethanol consumption in MOP-KO femalemice, it produced a reduction in ethanol consumption in WT mice. Socially-rearing MOP-KO mice alone consumed more ethanol than isolation-rearing female MOP-KO, socially-rearing WT mice, or isolation-rearing WT mice.
CONCLUSIONS: The present finding demonstrate that there is a tendency for stress types to correlate with drinking behavior in female mice.

POSTER (P1-A11)

Smartphone-Based Support System (SoberDiary) for Treatment-seeking Alcohol-dependent Patients

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Relapse prevention in patients with alcohol dependence (AD) has long been a clinical challenge. Providing a support system in place enabling continuous self-monitoring for maintaining abstinence may be beneficial. The aim of this study was to develop a smartphone application in conjunction with breathalyzers with data sensing via Bluetooth (SoberDiary) to enhance the clinical management for AD and then examine the benefits of the support system in patients with AD.

Methods

We established SoberDiary that contains a portable Bluetooth breathalyser, phone application, and back-end server, being developed based on empirically supported psychosocial interventions for AD that were deliverable on the platform of smartphones, including motivational enhancement therapy, cognitive-behavioral therapy, contingency management, and 12-step treatment. The participants regularly self-administered breath alcohol concentration (BrAC) tests using breathalyzers and input their momentary feedback on phones. To test the potential benefit of SoberDiary, we recruited 38 patients with AD who had detoxified and received maintenance treatment in the outpatient departmentfor 12 weeks. We divided the p**articipants** into highly adherent (HA) and less adherent (LA) groups according to the accumulated reward points that they obtained based on frequency of visits to and the amount of time spent using SoberDiaryand the completion rate of required BrAC tests.

Results

19 and 18 patients who had been followed for at least 2 weeks were classified as HA and LA group respectively. Although the retention rate was comparable between the two groups, the HA group exhibited a lower number of drinking days and drinks per week, lower craving and lower anxiety, increased cumulative abstinence days, and a higher abstinence rate and quality of life.

Conclusions

Increased SoberDiary compliance is associated with more favorable clinical outcomes. The preliminary findings suggest a smartphone-assisted support system might be feasible in supplementing conventional AD treatment in individuals' regular environments

POSTER (P1-A12)

Integrated genetics and proteomics research platform for internet game disorder

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Objectives: Biomarker is measurable indicator to predict the presence or severity of a disease state. Examples of biomarkers include levels of protein in the blood or patterns of activity in the brain. This study designs an IABio DB (Internet Addiction Bioinformatics Database), which is an integrated database for Biomarker research concerning an internet game group, a smartphone addiction group and their control group.
Methods: We develop the IABio DB to realize results of DNA and protein analysis from blood samples and information from the research subjects related to the internet game and smart phone addition using a web-based database.
Results: The study applied the OAuth2.0 to access the sensitive information of the subjects by authorized researchers. We attempted to make it possible for researchers to search, by individual or group, results including the internet and smart phone addiction index of subjects, the storage status of blood samples like SST, Plasma and DNA, data on usage, biomarker research results including DNA and protein.
Conclusions: The IABio DB enables the efficient management of information regarding subjects and blood samples. The IABio DB is significant to share research results between researchers in each field

POSTER (P1-A13)

Genome-wide association study identifies candidate loci associated with intraoperative remifentanil infusion rate in patients undergoing laparoscopic-assisted colectomy

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Background/Objective : The orexin system is well known to regulate feeding behavior andstates of sleep/wakefulness.Despitelack ofstudies that reportedly investigated genetic variations in the orexin systemaffectingfeeding behavior in humans, a growing number of human genetic studies have been accumulated targetingheadache and some psychiatric diseasesincluding those related to sleep, such as nalcorepsy. However, few such studies have focused on variations associated with reward-related traits, althoughtheorexin system has been suggested to be involved in the rewarding effects.In this symposium, we present a study that comprehensively explored genetic contributors to nicotinedependence by using whole-genome genotyping arrays in Japanese subjects.
Method : A two-stagegenome-wide association study(GWAS) was conductedfor 148 subjects using the Fagerström Test for Nicotine Dependence (FTND), Tobacco Dependence Screener(TDS), and number of cigarettes smoked per day (CPD) as indices of nicotine dependence. For the additionalassociation analyses, patients who underwent major abdominal surgery, patients with methamphetaminedependence/psychosis, and healthy subjects with schizotypal personality trait data were recruited. Autopsyspecimens with various diseases were also evaluated.
Result/Discussion : After the GWAS between more than 200,000marker single-nucleotide polymorphisms (SNPs) and the FTND, TDS, and CPD, the nonsynonymous rs2653349 SNP(located on the gene that encodes orexin [hypocretin] receptor 2) was selected as the most notable SNPassociatedwith FTND in the two-stage GWAS. This possibleassociation was replicated for independent 374 samples. This SNP was also associated withpostoperative pain, the initiation of methamphetamineuse, schizotypal personality traits, andsusceptibility to goiter.
Conclusion : We obtained significant results in the GWAS andsubsequent analyses that suggest that the rs2653349 SNP(Val308Ile) could be a genetic factor related to severity of nicotine dependence and possibly pain, schizotypalpersonality traits, and goiter in the Japanese population.

POSTER (P1-A14)

The correlation between the degree of insomnia with smooking behaviour and overtraining at FIK UNM collage students

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Smoking and overtraining is one of the cause of insomnia and it's often to be found in FIK collage students of UNM. So we need to do a research to know the correlation between the degree of insomnia, smooking behaviour and overtraining in FIK UNM collage students at Makassar. This study is an observational analytic with crosssectional perspective condected at FIK UNM with total sample 100 students. Variables used were insomnia, smooking behaviour intensity and overtraining sydromes. From this research, is found the caracteristic of 100 samples, insomnia according to age, 20-22 years old is 45 collage students and group of 23-25 is 17 collage student. According to departements, Ilara was 29 students, Kepelatihan 22 students, Penjaskesrek 11 students. To see the correlation between insomnia and smooking, we used Pearson correlation test with p 0,000 . It means that is possitive correlations between insomnia and smooking behaviour. We found p 0,161 for the for correlation between insomnia and overtraining,it means that is no correlation. While on the smooking group and was also get overtraining, only 7 person (22,5%) were not insomnia, and there were 24 person (77,4%) were insomnia. And at the not smooking group and not overtraining, 14 person (93,3%) were'nt insomnia and only 1 person (6,6%) were insomnia from 15 person. From the result, we can say that someone that is smooking insomnia will be worse if he was also overtraining. The conclusion from this research, that is correlation between insomnia and smooking behaviour, there's not correlation between insomnia and overtraining, but insomnia that is caused by smooking can be worse if the sample is also overtraining.

POSTER (P1-B1)

Association of cognitive impairment, psychotic symptoms and neurotrophic factors in elderly chronic schizophrenia patients

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Objectives: Some reports show the relationship with neurocognitive function in schizophrenia patients and neurotrophic factors (eg. brain derived neurotrophic factor, BDNF; glial cell line derived neurotrophic factor, GDNF). However no study has investigated those relationships in chronically medicated elderly patients with schizophrenia. The aim of this study was to examine the associations of serum BDNF and GDNF levels with the cognition or clinical characters in elderly chronic schizophrenia patients.
Methods: Schizophrenia were diagnosed using the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision criteria. The severity of schizophrenia was evaluated using the Manchester Scale for chronic psychoses (ManS). And cognitive function was measured by the Brief Assessment of Cognition in Schizophrenia Japanese version (BACS-J). Blood sampling and clinical evaluation were performed on the same day. The levels of serum BDNF and GDNF were assayed by ELISA using Milliplex MAP Kit (HNDG3MAG-36K and HNDG4MAG-36K) on a Milliplex Analyzer 4.2 MAGPIX machine (Millipore) according to the manufacturer's instructions.
Results: Fifty-six late-life chronic schizophrenia inpatients were enrolled in this study. There is no correlation between the scores of the BACS-J subcategories and neurotrophic factors (eg, BDNF, GDNF). There is no correlation between the scores of the ManS subcategories and BDNF but GDNF. GDNF shows significant negative correlation with psychomotor retardation. There is no correlation between the scores of the DIEPSS subcategories and BDNF but GDNF. GDNF shows significant correlation with sialorrhea and tremor.
Conclusions: The relationship among the psychotic symptoms, the neurocognitive impairment and neurotrophic factors is complicated. Our result suggests that GDNF is more sensitive state marker for extra pyramidal symptoms regarding sialorrhea or tremor than BDNF though neurotrophic factors do not reflex the cognitive dysfunction in chronically medicated elderly schizophrenics.

POSTER (P1-B2)

Computer- assisted Cognitive remediation in Schizophrenia and Bipolar disorder: a Prospective, Randomized, Double-blind, Sham-controlled study

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Objectives : Schizophrenia included not only positive and negative symptom, but also impaired cognitive function that was considered to be the core symptom of schizophrenia. In addition, several studies disclose that the cognitive function in bipolar patients would still be declining gradually. Computerized assisted cognitive remediation is documented for significant improvement in schizophrenia. However, those data in bipolar disorder was still in vague.
Methods : Twenty patients with each bipolar and schizophrenia were included in which 10 patients were assigned to active computer-assisted cognitive remediation group and 10 patients were assigned to control videos/games group. Twenty schizophrenia patients and eighteen bipolar patients (n=8 in controls) completed our cognitive remediation program (1.5 hours twice a week, over 12 weeks). We checked simplified PANSS or Young Mania Rating Score (YMRS), functional evaluation by social-adaptive functioning evaluation (SAFE) at baseline (T0), first month (T1), second month (T2), third month (T3) and sixth month (T6). Cognitive function was evaluated by using modified MATRICS at T0, T3 and T6.
Results : In schizophrenia patients, there was a significant improvement in auditory (Digit span test : p=0.04) and visual working memory(Spatial span test-forward: p=0.04). In bipolar patients, our study found a significant improvement in executive function (Wisconsin Card Sorting Test- Categories, p=o.o4; Preseverative Errors, p=0.038) and attention (Gordon Diagnostic System: p=0.045). There was no difference of functional evaluation between active and controls at baseline or T6 in both bipolar and schizophrenia group.
Conclusions : These preliminary findings suggest that computer-assisted cognitive remediation shows significant treatment effects on cognitive performance including elevated visual and auditory working memory in patients with schizophrenia as well as elevated executive function and attention in patients with bipolar disorder. Further study to individualize remediation program would be needed.

POSTER (P1-B3)

Association Between Serum Vitamin D Levels And Positive – Negative Symptoms Male Schizophrenic Patient In Sumatra Utara

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Background : Schizophrenia is one of the most disabling psychiatric disorders, with seriuos consequences on families and society. Although a genetic component in its a etiology is indisputable, environmental factors also play important role. Vitamin D plays crucial roles in neuroprotection and neurodevelopment, and low levels are commonly associated with schizophrenia. Lower vitamin D levels were correlated with more severe positive, negative, and overall symtoms in schizophrenia patient.
Methods: This study was an analytical study, conducted in RS Jiwa Propinsi Prof. Ildrem North Sumatra, RSUD Lubuk Pakam North Sumatra. The period May 2016 - September 2016, with a sample of the study 27 samples. Inclusion criteria: Were male schizophrenic patients, aged between 15-55 years old, the acute phase and no agitation, was willing to be the subject of research. Exclusion criteria: history of other psychiatric, medical conditions common history. The severity measured by the PANSS. Examination of serum vitamin D using ELFA. The statistical test used in relationship with of symptoms was measured with correlation.
Results: still on progress under study
Conclusion and Suggestion: still on progress under study

POSTER (P1-B4)

The Effect of Vitamin E as an Adjuvant Therapy to Improvement Tardive Dyskinesia in Schizophrenia Patients

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Background: Tardive dyskinesia (TD) is a syndrome of late-onset, abnormal choreoathetoid involuntary movements, that develops in some patients who receive chronic neuroleptic medications. The neurodegenerative hypothesis of TD derives support from different lines of evidence, including preclinical studies suggesting that neuroleptics may have a cytotoxic effect. In addition, some clinical studies have shown (1) some neuropathological changes in the basal ganglia, (2) biochemical changes possibly indicative of oxidative stress in patients with TD, and (3) the effectiveness of antioxidants in treating TD through medication trials.
Objective: To determine the effect of vitamin E as an adjuvant therapy to improvement of tardive dyskinesia in schizophrenic patients.
Methods: This research is a clinical trial. There are two groups of patients with tardive dyskinesia, One group of 10 people given vitamin E as an adjuvant therapy and the other group was not given Vitamin E. Tardif dyskinesia due to neuroleptic diagnosis is confirmed by DSM-IV-TR criteria and measured quantitatively by the Abnormal Involuntary Movement Scale (AIMS). Comparison AIMS collected and processed by a computer program.
Result: From the comparison between group 1 and group 2, the value P = 0.002 where P <0.05, so it concluded changes in AIMS scores were statistically significant.
Conclusion: 1. One of the etiology tardive dyskinesia is a biochemical change due to oxidative stress. 2. Vitamin E as an adjuvant therapy effect on improvement of tardive dyskinesia in schizophrenic patients with a decrease in the AIMS scale.

POSTER (P1-B5)

The role of doctor-patients relationship on medication adherence in young schizophrenia patients

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Objectives : Although quality of doctor patients relationship could influence in medication adherence, only small number of studies support it in case of schizophrenia. In this study, we investigated the relationship between medication adherence and several clinical factors including the quality of therapeutic relationship in non-chronic schizophrenia patients.
Methods:We performed a cross-sectional study that include 40 patients aged between 18 and 60 years with a diagnosis of schizophrenia according to the DSM-IV-TR. The sample included patients recruited from outpatient clinic in Korea. To exclude chronic-patients we included patients only who have been treated under 10yrs. Adherence rate and clinical factors were assessed with self-report measures, including the Medication Adherence Rating Scale(MARS), Scale To Assess the Therapeutic Relationship (STAR), Scale to Assessment Unawareness of mental disorder(SUMD), and LIVERPOOL UNIVERSITY NEUROLEPTIC SIDE EFFECT RATING SCALE(LUNSER). Pearson's correlation analyses between KMARS and STAR_K, KSUMD, KLUNSERS were performed. A multiple linear regression model was applied with KMARS scores as dependent variable and variables that were found significantly related to KMARS scores were used as independent variables.
Results: MARS total score was not associated with STAR total score and SUMD score but showed significant correlations with STAR-Non-supportive clinician input score($r=0.51$, $p<0.01$), and LUNSER score($r=-0.63$, $p<0.01$). With the results of regression, medication adherence was significantly predicted from non-supportive clinical input($\beta = 0.316$, $P<0.05$) and medication adverse effects($\beta = -0.486$, $P<001$). Theses variables explained 42% of the variance.
Conclusions: Clinician's supportive attitude to patients and effort to reduce the medication adverse effect could improve medication adherence in non-chronic schizophrenia patients.

POSTER (P1-B6)

Differences Total Score Simpson-Angus Scale (SAS) Based On Gender With Treatment risperidone in schizophrenic patients

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Background
Schizophrenia is a severe form of mental illness affecting about 7 per 1000 adults globally. Patients with schizophrenia appear to respond to lower doses of neuroleptics, and to be more sensitive to developing extrapyramidal side-effects by gender. The authors therefore compare the side effects based on gender with the total score of the Simpson-Angus Scale (SAS) in patients with low doses of risperidone extrapyramidal neuroleptic
Research Methodology
The study was performed on the month from Nopember until March 2016. This is the first study was conducted in Indonesia , especially in North Sumatra. This study is an analytical study comparative with the approach of eksperiment design. The number of samples is 31 subject female and 31 subject male in schizophrenic patients. Samples are affordable populations that meet the inclusion and exclusion criteria. Analysis of the data used is T test not paired to see the difference in the total score of the Simpson-Angus Scale (SAS) based on gender with risperidone treatment in schizophrenic patients

POSTER (P1-B7)

Representativeness of Clinical PET Study Participants with Schizophrenia: A Systematic Review

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OBJECTIVE: While brain imaging techniques such aspositron emission tomography (PET) have provided invaluable dataon antipsychotic effects, selection bias remains a serious concern, which was addressed in this systematic review.
METHOD:A systematic review of PET studies that measured dopamine D_2 receptor blockade with antipsychotics was conducted toexaminetheir inclusion/exclusion criteria, using PubMed, EMBASE, and Clinical Trials.gov (last search, July 2016). PET studies were included if they measured D_2receptor occupancy in patients with schizophrenia and included introduction of antipsychotic treatment or antipsychotic regimen change in a systematic manner.
RESULTS: Twenty-six studies were identified; of these second-generation antipsychotics were examined in 21 studies. Age limit was included in 13 studies; one study solely included geriatric patients while others targeted younger adults. Eleven, 6, and 3studies specifically targeted clinically stable patients, patients with severe psychopathology, and antipsychotic-free patients, respectively. Nineteen and 18 studies excluded patients with physical comorbidity and substance abuse, respectively.As a result, the mean age of subjects ranged from 23 to 42 years when one study that targeted geriatric patientswas excluded.Mean Positive and Negative Syndrome Scale total scores ranged from 54 to 95. The average Clinical Global Impression - Severity of Illness score was below 4 in 7 studies, 4 or more but less than 5in 5 studies, and 5 or more in 1 study. No comparison active-drug or placebo arm was employed in 24 studies. Blind assessment of symptomatology was performed only in 5 studies.
CONCLUSION: In general, subjects participating in clinical PET studies were relatively young, presented with mild symptomatology, and were free from either substance abuse or physical comorbidities. These characteristics need to be taken into account when interpreting the results of PET studies and translating the findings into actual clinic.

POSTER (P1-B8)

Intranasal oxytocin does not modulate jumping to conclusions in schizophrenia: Potential interaction with baseline social functioning

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Background: Oxytocin is a neuropeptide implicated in maintaining trust and affiliative behaviours in humans. Currently, there is great interest in exploring the therapeutic potential of oxytocin as an adjunct to conventional antipsychotic treatment for improving clinical and social cognitive symptoms in patients with schizophrenia. It has been well established that patients with schizophrenia show deficits in probabilistic reasoning tasks, such that they quickly jump to conclusions without sufficient evidence. Since performance on this task is related to activation of prefrontal areas also implicated in social cognition, we explored whether intranasal oxytocin could improve probabilistic reasoning performance in stable medicated patients with schizophrenia.
Methods: Forty-three male, medicated patients with schizophrenia (Mean Age ± SD: 40.81 ± 11.44) and sixteen matched healthy controls (Mean Age ± SD: 30.38 ± 9.85) participated in a double-blind, placebo controlled, cross-over study. Participants were required to complete the “Jumping to Conclusions” probabilistic reasoning task on two separate study visits (minimum 20 days apart). For each study visit, participants were randomized to receive either intranasal oxytocin (50IU in solution) or intranasal placebo (saline).
Results: Consistent with previous findings, patients with schizophrenia showed deficits in probabilistic reasoning, jumping to conclusions more often than healthy controls ($t(57)=2.78$, $p=.007$). Oxytocin did not significantly change probabilistic reasoning performance in patients ($t(42)=-1.11$, $p=.27$), nor in healthy controls ($t(15)=-.62$, $p=.55$). However, there was great variability in change in performance given oxytocin in patients. Exploratory analyses found that patients with lower bassline social functioning, as assessed by the Social Functioning Scale, showed more change on the probabilistic reasoning task given oxytocin, characterized by a reduced tendency to 'jump to conclusions.'
Conclusion: Acute oxytocin does not appear to modify probabilistic reasoning in healthy controls and patients with schizophrenia. However, future studies should explore the potential confound of baseline social functioning.

POSTER (P1-B9)

Electroconvulsive shock affected the schizophrenia-like behavior and the glial activation in the hippocampus of Gunn Rat

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Objective:Electroconvulsive therapy (ECT) is regarded as one of the efficient treatments for intractable psychiatric disorders, but the mechanism of therapeutic action remains unclear. Recently, many studies indicate that ECT affects the immune system, including the immune-related cells, such as microglia and astrocytes. Moreover, microglial and astrocytic activation has been implicated in postmortem brains of schizophrenia patients. We previously demonstrated that Gunn rats showed schizophrenia-like behavior and microglial activation in their brains. In this study we examined the effects of electroconvulsive shock (ECS), an animal counterpart of ECT, on schizophrenia-like behavior, microgliosis and astrogliosis in the hippocampus of Gunn rats. We also examined the behavior and the gliosis late after the chronic ECS.

Methods :The rats were divided into 4 groups, i.e., Wistar sham, Wistar ECS, Gunn shamand Gunn ECS. ECS groups received ECS once daily for 6 consecutive days.Subsequently, prepulse inhibitiontest (PPI) was performed on all animals. After PPI, immunohistochemistry analysis was carried out to determine microglial activation and astrocytic activation, using anti-CD11b and anti-GFAP antibody, respectively.

Results :We found PPI deficit in Gunn rats compared to Wistar rats, and it was significantly improved by ECS. In immunohistochemistry analysis revealed that there is significant higher expression of CD11b and GFAP in Gunn rats compared to Wistar rats. ECS attenuated the expression of both CD11b and GFAP in Gunn rats. Long-lasting effect of ECS on PPI deficit and glial activation in the hippocampus will be shown in the poster presentation.

Conclusion :Our findings indicate that ECS ameliorates schizophrenia-like behavior in Gunn rats and attenuates both microglial activation and astrocytic activation in the hippocampus of Gunn rats. Accordingly, therapeutic effects of ECT may be exerted, at least in part, by inhibition of glial activation.

POSTER (P1-B10)

Insight and risk factors for suicide in schizophrenia : a casestudy at Mental Hospital, Bali

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Background

Insight in schizophrenia is defined as awareness into illness, symptoms, and need for treatment and has long been associated with cognition, other psychopathological symptoms. Poor insight has been recognized as a potent barrier to treatment adherence and a risk factor for a range of poorer outcomes. However insight improvement also has been proposed to increase risk of depression and suicide. Does insight improvement is risk factors for suicide in schizophrenia?

Method

Male, 25 years, a Balinese, diagnosed with schizophrenia paranoid, had done completed suicide by hanging while hospitalizedat Bali Mental Hospital. Patient was admitted to the hospital due to rampage and killed his family member. Patient was suffered from schizophrenia paranoid since teenager and had been restrained for several years. During treatment at the hospital, patient was given anti psychotic and gained his insight on what had happened. Insightscore was evaluated using G12 PANSS.

Results

A direct link between insight and suicide in schizophrenia disorder remains uncertain but may be mediated by other variables. Some insight dimensions may lead the patientwith schizophrenia to a more depressive state that would lead the patient to think more pessimistically about their life. In this case patient realized that he had harmed his family and would be exiled from his family therefore committed suicide.

Conclusion

There is little evidence to support the suggestion that insight may represent a risk factor for suicide in patients with schizophrenia. Further studies with larger samples and longer follow-up periods in naturalistic conditions is needed to evaluate the role of insight in risk of suicide; given that the important implications to develop a model for suicide prevention in schizophrenia.

Keywords : insight, suicide, schizophrenia

POSTER (P1-B11)

Differences in social functioning among patients with major psychiatric disorders: Interpersonal communication is impaired in patients with schizophrenia and correlates with an increase in schizotypal traits

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Impaired social functioning is a hallmark of major psychiatric disorders. The purpose of this study was to detect a disorder-specific factor of social dysfunction among patients with major psychiatric disorders (PSY), including schizophrenia (SCZ), bipolar disorder (BIP) and major depressive disorder (MDD). Social functioning was assessed in patients with SCZ (n=80), BIP (n=27) or MDD (n=29) and healthy controls (HC, n=68) using the Social Functioning Scale (SFS). Compared to HC, the SCZ, BIP and MDD patient groups showedlowertotal SFS scores. No differences in the total scores forsocial functioning were observed between patient groups. We next investigated seven subscales of the SFS among PSY and observed significant diagnostic effects on all subscales of the SFS.Notably, patients with SCZ have poorer interpersonal communication than patients with MDD. Furthermore, the poorerinterpersonal communication score was significantly correlated with an increase in schizotypal personality traits,as assessed by the Schizotypal Personality Questionnaire (SPQ) in HC.Although there were no differences in overall social functioning among PSY, disorder-specific factors, such as interpersonal communication, were impaired among PSY.The correlation between poor interpersonal communication and the increase in schizotypal traitssuggests that poor interpersonal communication may be an intermediate phenotype of SCZ.

POSTER (P1-B12)

Effect Of Low Impact Aerobic Exercise To Calgary Depression Scale For Schizophrenia (CDSS) Total Score In Schizophrenic Patient In Mental Health Hospital In North Sumatera

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BACKGROUND
Mental disorder constitute a huge socioeconomic burden for health care systems worldwide, raising the question about effective and lasting treatment. Schizophrenia is one of the most important public health problems in the world. A survey by World Health Organization ranks schizophrenia among the top ten illnesses that contribute to the global burden of disease. Recently, there has been an increased prevalence of anxiety, depression, and substance abuse disorders in patients with schizophrenia, leading distortion of its clinical representation.
In the general population, several epidemiological studies have found significant cross sectional correlation between mental health and physical activity levels. In an adults population, regular physical activity is associated with a significantly decreased prevalence of current major depression, panic disorder, agoraphobia, social phobia, and specific phobia.
To date, physical exercise has attracted attention for improving cognitive functioning and avoiding medication side effects in psychiatric patients. Systematic reviews demonstrated that aerobic exercise can reduce primary symptoms in patient with schizophrenia, and attenuate secondary symptoms such as depression, self deprication and social withdrawal.
AIM OF THIS STUDY
Aim of this study is to know the effect of low impact aerobic exercise to Calgary Depression Scale for Schizophrenia (CDSS) total score in women schizophrenic patient.
METHODOLOGY
This study is cross sectional study with experimental pretest posttest non randomized design, which is to compare total score of CDSS before and after low impact aerobic exercise between women schizophrenic patient whose take medication and low impact aerobic exercise and women schizophrenic patient with medication only. The respondents is women schizophrenic patients in mental health hospital North Sumatera by using non probability sampling techniques purposive sampling types.
RESULT
Follow
CONCLUSION
Follow

POSTER (P1-B13)

The Correlation Between Cognitive Function And Personal Social Performance In Male Schizophrenic Patients

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Schizophrenia is perhaps the most dramatic and tragic manifestasion of mental illness known to mankind. The consequences of the illness is for the individual, affected his or her family and society. Schizophrenia is one of twenty of the illness that cause Years Lost due to Disability. Treating the symptom is not enough. The aim of treatment must be include the quality of life of schizophrenic person totally. This study aim to examine the relationship between cognitive impairement and performance of the person with schizophrenia. Cognitive test is scaled with Indonesian version of Montreal Cognitive of Assesment called MoCA-Ina, while personal and social performance scaled with Personal and Social Performance scale. There are many study that search the relationship of cognitive impairement and social functioning of schizophrenic patients, but this is the first study that using PSP and MoCA-Ina. Both PSP and MoCA-Ina is known to be simple easy use rating scale but still have good sensitivity and specificity, and perhaps can build people's interest to use it in clinical practice.

25 male schizophrenic patients were assesed in Prof. M. Ildrem Mental Hospital of North Sumatera Province of Indonesia. Positive correlations between MoCA-Ina and PSP score were identified. Since that,clinicians should pay attention to cognitive, and might give some early intervention to it.

POSTER (P1-B14)

Oxidation And Nitration In Dopaminergic Areas Of The Prefrontal Cortex From Patients With Bipolar Disorder And Schizophrenia

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Objectives: Increased oxidative stress is strongly implicated in bipolar disorder (BD), where protein oxidation, lipid peroxidation and oxidative damage to DNA have been consistently reported. High levels of dopamine (DA) in mania are also well-recognized in patients with BD, and DA produces reactive oxygen species and electron-deficient quinones that can oxidize proteins when it is metabolized.
Methods: A literature search was conducted in BMC Psychiatry and PubMed.
Results: We found increased oxidation of DAT-immunoreactive regions in patients with BD and decreased nitration of TH- immunoreactive regions in both patients with Bipolar Disorder and schizophrenia. On the other hand, we found increased global levels of oxidation in patients with BD and schizophrenia, although nitration levels did not differ between the groups.
Conclusion: These findings suggest alterations in levels of protein oxidation and nitration in DA-rich regions of the prefrontal cortex in patients with BD and schizophrenia, but more markedly in those with BD.
Key word: oxidation, nitration, bipolar disorder, schizophrenia , TH- immunoreactive, DAT-immunoreactive

POSTER (P1-B15)

Treatment Resistant Schizophrenia: a Case Study

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Introduction: Studies have shown that 20% to 30% of all schizophrenia patients are resistant to drug treatment. Treatment resistant schizophrenia (TRS) is defined by an inadequate response to a succession of treatments. The International Psychopharmacology Algorithm Project criteria of TRS: no period of good functioning in previous 5 years, prior non-response to at least 2 antipsychotic drugs of 2 different chemical classes for at least 4-6 weeks each at dosages equivalent to ≥ 400 mg/d of chlorpromazine (CPZ) or 5 mg/d of risperidone, and moderate to severe psychopathology, especially positive symptoms: conceptual disorganization, suspiciousness, delusions, or hallucinatory behaviors.
Case Illustration: Ms. FY, a 47 years old woman with continuous paranoid schizophrenia since 1992. She was hospitalized multiple times and since 2011 there are major function impairments in several areas. She was treated with combinations of 2 antipsychotic drugs of different chemical classes for at least 4 weeks each. She still have persistent positive and negative symptoms such as persecutory delusions and delusions of being controlled, conceptual disorganizations, hallucinatory behavior, suspiciousness, blunted affect, emotional and social withdrawal. During her latest hospitalization in Rumah Sakit Cipto Mangunkusumo, symptoms were evaluates weekly with Positive and Negative Syndrome Scale (PANSS) of Schizophrenia.
Results: According her medical reports, since 2011 she received oral combinations of antipsychotics, such as, haloperidol-olanzapine, to haloperidol-clozapine, to haloperidol-aripiprazole, with equivalent dosages between 550 mg to 1550 mg of CPZ and good adherence. Her latest PANSS score show less than 20% improvement and Global Assessment of Functioning scale is 31-40.
Discussion: We should more aware about TRS when patients exhibit slow improvement after 4-6 weeks of oral combination of 2 antipsychotics. Reconsider to adjunct other treatment modalities such as long-acting injectable antipsychotic or electroconvulsive therapy. Also, non-pharmacological interventions, including behavioral therapy should be used to their maximal potential.

POSTER (P1-B16)

The Relationship between cognitive impairment and brain volume in Schizophrenia

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Background: Previous studies have suggested that brain structure in Schizophrenia (SZ) related to their intellectual and cognitive impairments. We investigated the relations of current and estimated premorbid Intelligence Quatient (EIQ) with brain structure in Japanese.
Method:176 patients with SZ and 662 healthy controls (HC) underwent neuropsychological assessment. EIQ evaluated with Japanese adult reading test and current IQ evaluated with Wechsler Adult Intelligent Scale. Patients were divided into 3 intellectual groups which were Preserved, Deteriorated, and Compromised group. Deteriorated group displayed meaningful decline in IQ (⩾ 10 points) as evidenced by the difference between current IQ and EIQ. Compromised group displayed EIQ below 90, and Preserved group displayed EIQs above 90 and who demonstrated less than a 10-point difference. Existence of a 10-point IQ decline took precedence to either of cutoff strategies described. As Compromised group was too small, we excluded it from the analysis. We compared structural imaging data (3D T1 volumes) of the brain acquired at two different scanners (1.5- or 3-Tesla) and processed by FreeSurfer software.For each segmented structure, Preserved, Deteriorated, and **HC group** compared using an ANCOVA analysis, including age, gender, type of MRI scanner as covariates. This study was approved by the ethics committee at Osaka University.
Result: Deteriorated group had significantly smaller whole brain, total cortical gray matter and cortical thickness compared with HC. Moreover, Deteriorated group had significantly symmetrically smaller hippocampus, amygdala, nucleus accumbens and asymmetrically smaller right thalamus and larger left globus pallidus compared with HC,. Especially, only left globus pallidus was larger in Preserved or in Deteriorated group compared with those in HC.
Conclusion: These findings provide additional evidence that impairments in cognition associated with reduced EIQ in SZ related to aberrant brain structure.

POSTER (P1-B17)

Correlation of Serum Levels of BDNF and Montreal Cognitive Assessment Score Version Indonesia (MoCA - Ina) In Schizophrenic Patients

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Background : Schizophrenia is a complex neurodevelopmental disorders with impaired cognitive function as the main part. BDNF can be a marker of abnormal neurological development and neurotransmission in schizophrenia. BDNF regulate aspects of developmental plasticity in the brain and is involved in cognitive function.
Research Methodology: The study was performed on the month from October 2016 until March 2017. This is the first study was conducted in Indonesia , especially in North Sumatra. This study is an analytical study of numerical correlative with the approach of cross sectional design. The number of samples is 48 subject. Levels of serum BDNF was analyzed by using the quantitative sandwich enzyme immunoassay.Cognitive function was assessed by scores of MoCA-Ina. Analysis of the data used are numerical correlation test to examine the correlations between serum levels of BDNF and Montreal Cognitive Assessment Score Version Indonesia (MoCA-Ina) in schizophrenic patients.
Result : We identified that the mean total serum BDNF in patients with schizophrenic is 27729.6 standard deviation = 5626.5. The mean total score of Moca-Ina in schizophrenic patients was 20.6 with a standard deviation of 5.
Conclusion: There is correlation of serum levels of BDNF and Montreal Cognitive Assessment Score Version Indonesia (MoCA-Ina) in schizophrenic patients. Pearson correlation value levels of serum BDNF and Moca-Ina Score of 0.780 showed a positive correlation with the strength of a strong correlation (r = 0.6 - <0.8).

POSTER (P1-B18)

White matter connectivity related to amisulpride treatment response in patients with schizophrenia

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OBJECTIVES
Although previous studies reported the effectiveness of amisulpride in treatment of schizophrenia, no study investigated white matter (WM) connectivity of patients with schizophrenia in relation to the treatment response after amisulpride. The objective of this study is to explore any association between the WM connectivity at early stage of amisulpride treatment and the treatment response in patients with schizophrenia.
METHODS
Twenty patients with schizophrenia and 17 age- and sex-matched healthy control (HC) subjects were included in this study. Brain magnetic resonance scans at 3 Tesla were conducted and the tract-based spatial statistics were used for image analysis. All patients began treatment with 200mg of amisulpride per day and the dosage increased to 1200mg/day. At baseline and 8 weeks after treatment, patients were assessed using the Positive and Negative Syndrome Scale, the Scale for the Assessment of Positive Symptoms (SAPS), and the Scale for the Assessment of Negative Symptoms.
RESULTS
The group comparison of fractional anisotropy (FA) showed that patients group has lower FA values in the extensive WM regions than the HC group. Among the patients with schizophrenia, the FA values of genu of corpus callosum, superior longitudinal fasciculus, external capsule, posterior limb and retrolenticular part of internal capsule and posterior thalamic radiation showed significant negative correlations with scores of the SAPS treatment response (all $P<0.05$).
CONCLUSIONS
The current study suggests that the treatment response after amisulpride may be associated with the fronto-temporo-limbic WM connectivity at early stage of treatment in patients with schizophrenia.

POSTER (P1-B19)

Vitamin D Deficiency of Schizophrenic Patient by Characteristic Demographic in North Sumatera

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Objectives : Vitamin D levels are sub-optimal in people with schizophreniaand other psychotic disorders, being lowerthan matched controls even from the first episode of psychosis. Lifestyle and physical health factors associatedwith low vitamin D, such as smoking, increased body mass index, inactivity, and social withdrawal(likely resulting in deceased sunlight exposure), are allmore frequent in people with psychosis.
Aims : To determine Vitamin D Deficiency of Schizophrenic Patient by Characteristic Demographic in North Sumatera
Methods : This study was an analytical study to measure serum vitD relationship between the ethnicity batak and malay on schizophrenic patients who are out-patients in RS Jiwa Propinsi Sumatera Utara and RSUD Deli Serdang the period in May 2016 and ended in June 2016. Inclusion criteria were schizophrenic patients male and female, aged between 18 to 60 years old, the acute phase no agitation or abstinence antipsychotic drugs for two weeks, ethnicity batak and malay, and willing to be the subject of research. Exclusion criteria were the history of other psychiatric, comorbidities with other common medical condition, and history of substance abuse. The total sample is 40 subjects (20 batak and malay). Blood sample for serum vitD using ELFA method. Statistical analysis using numeric comparative T- independent test.
Results: still on progress under study
Conclusion and Suggestion: still on progress under study

POSTER (P1-B20)

Working Memory Deficit in Sibling of Schizophrenia Patients

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Introduction: It has been well established that cognitive function is altered in schizophrenia patients. Several studies found that deficits in cognitive function has already been shown in the early phase of psychotic disorder. Among those cognitive aspects declining in psychosis patients, working memory deficit is the core feature of this disorder. Several meta-analyses on cognitive deficits in families of patients with schizophrenia have been published in the past few years. Whether assessment of working memory deficits in unaffected sibling of schizophrenia patient may appear as risk indicator or interpretable factor for developing schizophrenia is currently under debate and under extensive studies.
Method: literature review from medical database to search the relationships between working memory impairment in sibling of schizophrenia patients
Result: A candidate endophenotype for an illness is associated with unaffected family members. The abnormal activity of the prefrontal cortex in the fMRI and gene catechol-o-omethyltransferase (COMT), affected the activity of regulation of dopamine when working memory is activated. It is also found genetically inherited, and affected the working memory sibling of schizophrenia patients.
Conclusion: Cognitive deficits, perhaps those involving executive control, working memory, and inhibition, in particular, may continue to provevaluable in the search for specific genes conferring risk for schizophrenia.Assessment of working memory function in siblings of people with schizophrenia become important for early prevention strategies.

POSTER (P1-B21)

The number of hospitalization and cognitive function in schizophrenia

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Objectives: We hypothesized repeated hospitalization leads to reduce neurocognitive function in schizophrenia patients. We investigated the retrospective chart review about the relationship between the number of hospitalization and neurocognitive function in the patients.
Methods: Cognitive performance in patients was assessed using Brief Assessment of Cognition in schizophrenia Japanese language version (BACS-J) . We assessed 282 patients with BACS-J. 119 patients were excluded for the following reasons: (1) no diagnosis of schizophrenia; (2) without hospitalization; (3) insufficient data..
The recruited patients were divided into three groups according to the number of hospitalization; (i) on 57 patients who had experienced only 1 hospitalization, (ii) on 47 patients with 2 hospitalizations, (iii) on 59 patients with 3 or more hospitalizations.
Comparison of between-patient groups was conducted using an analysis of covariance (ANCOVA) that allowed variance from clinical factors to be partialled out in the comparison.
Results: The number of hospitalization was positively associated with poorer performance on the score of BACS-J. Any associations were not observed regarding sex, education, disease onset, antipsychotic dosage and benzodiazepine dosage. Significant differences in motor function, attention and processing speed were found between three groups.
Conclusions: The number of hospitalization is associated with poorer cognitive performance. It is speculated the recurrence of psychotic episode influences worsening neuropsychological impact in the schizophrenia patients. Prospective cohort study with larger sample should be done to reconfirm the preliminary findings.

POSTER (P1-B22)

The differences in knowledge level score based on the level Expressed emotion female relatives of schizophrenic patients Batak tribe in Prof. Dr. M. Ildrem Psychiatric Hospital North Sumatera

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Background :Expressed emotion (EE) status has been proven to be a good predictor of relapse in schizophrenia. However, there is no data knowledge level score based on the level Expressed emotionfemale relatives of schizophrenic patients Batak tribe yet.
Aims : To assess the differences in knowledge level score based on the level Expressed emotion female relatives of schizophrenic patients Batak tribe
Method : This research is a comparative analytic research with cross sectional approach that uses questionnaires Family Questionnaire and Knowledge About Schizophrenia Test to determine the differences in knowledge level score based on the level Expressed emotion female relatives of schizophrenic patients Batak tribe
Results : in process
Conclutions: in process

POSTER (P1-B23)

The combination of presynaptic cytomatrix protein Piccolo knockdown in the prefrontal cortex and mild social defeat stress induces schizophrenia-like behaviors in mice

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Objectives: The multiple risk factors such as a genetic predisposition and an environmental insult are involved in the onset of schizophrenia. The alteration of PCLO mRNA expression is reported in the postmortem brain of the patients with psychiatric disorders including schizophrenia. The PCLO gene encodes presynaptic cytomatrix protein Piccolo served to vesicle trafficking on exocytosis and endocytosis. Alternatively, traumatic event is known to lead harmful psychological consequences in humans and animals. In the present study, therefore, we investigated the combinational effects of Piccolo knockdown and mild social defeat stress on emotional behaviors in mice.
Methods: Male C57BL/6J mice were injected AAV-miPCLO or AAV-Mock vectors into the bilateral prefrontal cortex. These mice were exposed mild social defeat stress (three times of 5-min physical contact with aggressive male ICR mouse at 15-min intervals) 3 weeks after the AAV vector injection, and then assessed by various behavioral tests.
Results: The non-stress-exposed Piccolo knockdown mice exhibited increased locomotor activity in a novel environment and decreased prepulse inhibition of the acoustic startle responses. These abnormal behaviors were ameliorated by administration of an antipsychotic drug, risperidone. Furthermore, the Piccolo knockdown mice showed cognitive dysfunctions including object recognition, spatial learning and working memory. Alternatively, in the mild social defeat stress-exposed Piccolo knockdown mice but not Mock mice, the behavioral impairments on social interaction to a stranger mouse and motivation to escape from water were additionally observed.
Conclusions: These results suggest that the vulnerability of PCLO gene in the prefrontal cortex induces the phenotypes like the positive symptom and cognitive dysfunction in schizophrenia, and the combination of social stressful event and its gene manipulation adds the similarity to the negative symptom in schizophrenia. Thus, our observations indicate that the mild stress-exposed cortical Piccolo knockdown mice are useful animal model containing the face, construct and predictive validities for schizophrenia.

POSTER (P1-B24)

The Influence Of Ocimmum sanctum as an adjuvant therapy on clinical features and cognitive function improvement in schizophrenia patients treated risperidon

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Background : Ocimum sanctum has already known worl wide as traditional herbal medicine. Long time ago people have using Ocimum sanctum to cure diseases. Ocimum sanctum is one of Indonesian tradional medicine. Previous syudy in animal laboratory (rats) showed significant association between Ocimum sanctum (Basil Leaf) and stress. Ocimum sanctum known to have property as an antioxidant, anti inflammation, anti psychotic, neurprotector, etc. Few studies evaluated effect of Ocimum sanctum in Schizophrenia patients.
Methods : In this experimental study we analyzed 2 groups of patients. Each group contains 10 (ten) Schizophrenia patients. One group take Risperidon only and the other group take Risperidon combine with Ocimum sanctum. Each group was given Risperidon 2 mg per day each 12 hour via oral. One group combine with Ocimum sanctum, every patients take 2 pils of Ocimum sanctum leaf per day each 8 hour via oral. All of the procedura was done after meal time. After 2 hours taking Risperidon, we give the patients Ocimum sanctum. Patients were evaluated using PANSS and MOCA-INA score admission and after 14 (fourteen) days of treatment.
Results : PANSS score significantly decreasedafter 14 days taking Ocimum sanctum compared to control group that take Risperidon only (p = 0,000). MOCA-INA score significantly increased after 14 days taking Ocimum sanctum compared to control group that Risperidon only (p = 0,000).
ANSS score significantly decreasedafter 14 days taking Ocimum sanctum compared to control group that take Risperidon only (p = 0,000). MOCA-INA score significantly increased after 14 days taking Ocimum sanctum compared to control group that Risperidon only (p = 0,000).
Conclusion : By giving Ocimum sanctum as an adjuvant therapy in Schizophrenia patients can help in improvement of clinical features and cognitive function in Schizophrenia patients.

POSTER (P1-B25)

Comparison Serum Vitamin D by the Residence Between Highland and Lowland inSchizophrenic Male Patient in Sumatera Utara

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Background: The most common of psychotic disorders is schizophrenia. Vitamin D is made endogenously in the skin from UVB radiation from sunlight. Vitamin D deficiency is common in patients with severe mental illness such as schizophrenia. Schizophrenia is a debating chronic mental illness characterised by positive symptoms, such as hallucinations and delusions, and negative symptoms including flat affect and lack of motivation. Several environmental risk factors for schizophrenia, such as season of birth, latitude, and migration, have been linked to vitamin D deficiency. There also seems to be relationship between the risk of schizophrenia and latitude, with an increased incidence rate of schizophrenia seen at a higher latitude.
Methods: This study was an analytical study, conducted in BLUD RS Jiwa Propinsi Sumatera Utara and RSUD Deli Serdang, the period in May 2016 and ended in June 2016 with a sample of the study 60 sample (20 patients live in the Highland and Lowland, 20 healthy controls). Inclusion criteria were schizophrenic patientsboth men and women, aged between 18 to 60 years old, acute phase no agitation or abstinence antipsychotic drugs for two weeks, live in the Higland and Lowland, and willing to participate this study. Exclusion criteria were history of other psychotic disorders, comorbidities with other common medical condition, a history of substance abuse. Sample inspection for serum vitamin D using ELFA method. Statistical analysis using numeric comparative T independent test.
Results: still on progress under study
Conclusion and Suggestion:still on progress under study

POSTER (P1-B26)

Exploring functional polymorphisms in a schizophrenia risk locus of DRD2 using prolactin concentration in healthy subjects

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Objectives: Previously, we reported that rs7131056 and rs4648317 in intron 1 of the dopamine receptor D2 gene (DRD2) were related to plasma prolactin levels of health Japanese subjects (Fukui N et al. 2011). This result suggested these SNPs were functional polymorphisms of DRD2. A recent genome-wide association study showed that rs2514218 in the 5′ region of DRD2 was strongly associated with schizophrenia (Schizophrenia Working Group of the Psychiatric Genomics Consortium 2014). Interestingly, rs7131056, rs4648317, and rs2514218 are located in the same LD block in the HapMap database. Furthermore, it was reported that the rs2514218 genotype could predict antipsychotic response (Zhang JP et al. 2015). However, according to the HapMap data, there are large differences in the rs2514218 allele frequency between Caucasian and Asian populations. In this study using Japanese subjects, we aimed to identify candidate functional polymorphisms in the 5′ region of DRD2 for future pharmacogenetic studies of antipsychotic drugs in East Asian populations. **Methods:** 231 healthy Japanese subjects participated in this study after providing written informed consent. The studies were approved by the ethics committee of Niigata University School of Medicine. Fasting blood samples were collected at 9.00 am Prolactin concentrations were measured by enzyme immunoassay (SRL, Tokyo, Japan). Tagging SNPs for the 5′ region of DRD2 (chr11: 112818310–112918309) were selected from the HapMap database. Tagging SNPs, rs7131056, rs4648317, and rs2514218 were genotyped by TaqMan 5'-exonuclease assay. We performed multiple regression analysis with prolactin concentration as the dependent variable and genotype, age, and sex as independent variables. Statistical significance was set at P <0.0036. **Results:** Two SNPs [rs7131056 (β = 0.23, P = 0.0034) and rs10891564 (β = 0.24, P = 0.0017)] were significantly correlated with prolactin concentration. **Conclusions:** In East Asian populations, pharmacogenetic studies dealing with antipsychotics probably should examine the rs7131056 and rs10891564 polymorphisms rather than rs2514218.

POSTER (P1-B27)

Patient's knowledge of prescribed psychotropics and medication adherence in schizophrenia: A cross-sectional survey

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Objectives : While medication adherence is critically important in the pharmacological treatment of schizophrenia, it remains unclear how patient's knowledge of prescribed psychotropics affect medication adherence. The objectives of this cross-sectional study were to assess patient's knowledge on their prescribed psychotropics and to explore associations between the knowledge and the adherence. **Method :**Outpatients with schizophrenia or schizoaffective disorder according to the International Classification of Diseases, 10th Edition were included. Their knowledge on therapeutic effects, types, and mechanisms of action of each of psychotropics that they were receiving were assessed, using a multiple-choice questionnaire developed for this study. A Pearson correlation coefficient was calculated between percentage of correct answers in each category and the number of psychotropics prescribed or medication possession ratio (MPR) as an index of adherence. **Results :**83 outpatients participated in this study. Fifty subjects (63.3%) were male. The mean±SD age of the subjects was 46.1±11.4 years old, the number of psychotropics prescribed was 3.2±2.0, the number of antipsychotics prescribed was 1.7±0.9, the PANSS total score was 54.7±14.5, and the MPR was 0.96±0.15.The mean rates of correct answers on effects, types, and mechanisms of action of prescribed psychotropic drugs were as low as 40.4%, 35.2%, and 6.9%, respectively. Those rates for antipsychotics were generally lower with 33.3%, 29.7%, and 7.8%, respectively. No significant correlation was found between MPR and rates of correct answers on any of effects, types, or mechanisms of action of prescribed psychotropic drugs. Lack of significant correlation was also observed between MPR and the number of prescribed psychotropics. **Conclusion:** Although any effect of patient's knowledge about psychotropics on medication adherence was not observed in the present study, insufficient knowledge on prescribed medications may need to be paid attention to in outpatients with schizophrenia so as to improve their insight into the illness and the treatment.

POSTER (P1-B28)

Antipsychotic use is a risk factor for hyponatremia in patients with schizophrenia: a 15-year follow-up study

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Objectives : Hyponatremia affects 10% of patients with chronic schizophrenia and can lead to severe consequences. However, the role of antipsychotics and other risk factors in hyponatremia occurrence has remained inconsistent. This study examined the association between antipsychotic use and hyponatremia occurrence in patients with schizophrenia.
Methods : We utilized the National Health Insurance Research Database to follow 2051 patients with schizophrenia from 1998 to 2013. Among them, 137 (6.7%) developed hyponatremia. Sociodemographic characteristics, physical comorbidities, and psychiatric treatment experiences were compared between those who had hyponatremia and those who did not. A Cox proportional hazards model was used to examine the hazard ratios (HRs) of these characteristics.
Results : In patients with hyponatremia, the mean age at first hyponatremia occurrence was 54.7 ± 13.9 years, an average of 9.5 ± 4.0 years after schizophrenia diagnosis, and 32.9% of them were off antipsychotics before hyponatremia occurrences. Age at schizophrenia diagnosis (HR = 1.1), low-income household (HR = 2.4), comorbidities (HR = 1.2), and psychiatric admissions (HR = 1.04) were associated with the risks of hyponatremia. Compared with no antipsychotic use, atypical (HR = 2.1) and typical antipsychotics (HR = 3.1) were associated with an elevated risk of hyponatremia, after adjustment for age, sex, and physical comorbidities. Carbamazepine use (HR = 2.9) was also a significant risk factor for hyponatremia ($p < 0.05$).
Conclusions : Antipsychotic use in patients with schizophrenia with polypharmacy should be monitored for hyponatremia occurrences. Clinicians should pay attention to the impact of poor living conditions on hyponatremia occurrence.

POSTER (P1-B29)

Safety of Lurasidone in Schizophrenia: A Systematic Review and Meta-Analysis of RCTs with Active Comparators

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Background: The objective of this study was to evaluate the effects of lurasidone (LUR) on body weight and other metabolic parameters as this information is relevant to guide clinical decision making.
Methods: Systematic review and meta-analysis of short-term (≤6 weeks) randomized controlled trials (RCTs) comparing LUR and other antipsychotics (APs) head-to-head in schizophrenia. Co-primary outcomes were body weight change and ≥7% weight gain in the safety population. Secondary outcomes included metabolic adverse events.
Results: Across 5 RCTs (n=1,604), LUR had significantly lower body weight change (WMD=-1.135, 95%CI: -2.240 to -0.030, p=0.044).
Regarding ≥7% body weight gain, LUR had significantly lower frequency than active comparators (N=4, n=1,302, RR=0.275, 95%CI: 0.155 to 0.486, p<0.001). LUR was also associated with significantly lower weight increased patients, waist circumference, total cholesterol and LDL cholesterol gain than active comparators
(N=4, n=1,328, RR=0.222, 95%CI: 0.070 to 0.701, p=0.010,
N=2, n=695, SMD=-0.272, 95%CI: -0.462 to -0.081, p=0.005,
N=4, n=1,303, SMD=-0.361, 95%CI: -0.608 to -0.114, p=0.004,
N=2, n=691, SMD=-0.362, 95%CI: -0.522 to -0.203, p<0.001, respectively).
Conclusions: These meta-analysis indicate that LUR was found to be less problematic in body weight gain and metabolic disturbances than other antipsychotics.

POSTER (P1-C1)

The Effect of Acceleration Study During High School to Depression Level of Medical Students

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Introduction: In many studies, medical students score high ratio of depression than any other college student because of the workload and stressor they deal each day during their study. Student in acceleration program that cause them to be systematic also felt these workload and stressor. High intelligence is needed in this case, along with creativity and responsibility to make the task and the study easier which can help them if they are being medical student. This study will compare severity of depression in student with acceleration study during high school with student without acceleration study.
Material and Method: Case control study was use with inclusion criteria of 18 years old or over, batch 2013 in faculty of medicine UniversitasAirlangga with acceleration background at junior or senior high school, and willing to participate in this research. Research will compare the student with another group of 18 years old or over, batch 2013 in faculty of medicine UniversitasAirlangga without acceleration background. The result from each group will be compared using Mann-Whitney U test.
Result : From 17 accelerate student, only two of them have categorize in Beck Depression Scale as mild depression with a scoe of 14 each. From the non accelerate group, 3 out of 24 categorize as mild depression. When compute statistically using spearment correlation for beck depression scale and social rating scale there's no correlation being an accelerate student induce depression with $p>0.05$ ($p = 0.536$). But from the ranks from the Mann-Whitney U test conclude that the non acceleration group more prone to depression with mean rank of 21.96 to 19.65 for the acceleration group respectively.
Conclussion: There is no correlation between being an accelerate student during high school with depression.

POSTER (P1-C2)

Assessment of Depression, Anxiety and Stress among Postnatal mothers

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Background & Objectives:
Depression often exists co-morbidly with otherconditions like anxiety, irritability and stress. Objectives are to assess the levels of depression, anxiety and stress among postnatal mothers and to find the correlation between depression, anxiety and stress.
Methods:A descriptive survey approach was selected for the study and non-probability convenient sampling technique was used to select 100 postnatal mothers at M.S.Ramaiah Medical Teaching Hospital, Bangalore, India.
Results: From the total subject, 16% of the subjects as mild Depression, 13% as moderate depression, 5% as extremely severe Depression and only 1% as in severe Depression. Likewise, 29% as moderate anxiety, 11% of mothers as severe anxiety, 10% as extremely severe anxiety and only 3% as mild anxiety. Considering into the levels of stress, 11% as mild stress, 6% as moderate stress 4% as severe stress and about 2% as extremely stress. The mean percentage of anxiety and stress was higher than depression. The correlation between depression and anxiety showed highly significant with "r"= 0.643 at $p<0.01$. Likewise the correlation between anxiety and stress showed a satisfactory significant with "r"= 0.719 at $p<0.01$. Also the correlation between depression and stress was highly significant with "r"= 0.824 at $p<0.01$.
Conclusion: Recently delivered mothers are vulnerable to the whole spectrum of general psychiatric disorders, as well as those resulting from the physical and psychological changes of childbirth. Midwives, and public health nurses need to screen for depression, anxiety and stress at every opportunity early in the postpartum period.

POSTER (P1-C3)

The Differences of Depression Prevalencein Elderly Patients with Type II DM treated with Oral antidiabetic drug and Insulin Injectionin Ngemplak Yogyakarta

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Objectives: To determine there is correlation between consumption oral diabetes drugs with depression scores in elderly patients with type II DM in Ngemplak, Yogyakarta.
Methods: This study was a descriptive analytic study with cross sectional design. The sampling method used was purposive sampling. Data were taken secondary from medical record from Family Doctor. All DM patients with oral anti-diabetic visiting from July until December 2016 were included. Depression score was measured using Geriatric Depression Scale (GDS). The exclusion criteria were the presence of other organic mental disorders and brain infections. Data will be analyzed statistically using chi-squared test.
Results: DM is a chronic disease requires long-term therapy that can influence psychological. This study of elderly patients with DM studied and analyzed from some variables such as age, sex, occupation, work, marital status, fasting blood glucose, two hours postpandrial blood glucose. This study is still in progress and result will be reported later.
Conclusions: Elderly patients with diabetes have an increased risk for depression. This condition requires attention and a comprehensive management. Early detection of depression in elderly patients with DM would improve prognosis.

POSTER (P1-C4)

Korean Medication Algorithm for Depressive Disorder 2017: Non-Pharmacological Biological Treatments

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Objectives: The basis of treating depression pharmacological treatment method is widely used. Korean Medication Algorithm Project for Depressive Disorder (KMAP-DD) was developed in 2002 and revised in 2006 and 2012. Since the last revision five years ago the third revision reflected the new research result and the latest trends in the areas of pharmacological treatment. **Methods:** 144 psychiatrists who have vast clinical experiences in depressive disorder are primary selected then survey was sent to them via mail, 67 surveys were retried. This survey is constructed with 44 questionnaires in which contained from overall treatment strategies to treatment strategies under the specific circumstances. Each treatment strategy or treatment option is evaluated with the overall score of nine and the following 95% confidence interval result treatment option were divided into three phases of recommendation; primary, secondary, thirdary. **Results:** Electroconvulsive therapy(ECT) was recommended as an initial strategy for major depressive disorder, severe without psychotic features with urgent suicidal risk, and as a second strategy for non-responders on antidepressant monotherapy or combination therapy and combined with physical illness. In the patient of major depressive disorder, severe with psychotic features, ECT was preferred as an initial strategy for urgent suicidal risk patients, but as a second strategy for non-responders on antipsychotics and antidepressants combination therapy and combid with physical illness. TMS was not recommended as an initial treatment strategy for major depressive disorder, but could be a second strategy for non-responder on antidepressants combination therapy in severe episodes without psychotic features, and non-responders on pharmacotherapy in moderate episodes. **Conclusions:** ECT was an initial strategy in severe episode with/without psychotic features who has an urgent suicidal risks, and secondarily preferred in case of non-responders, comorbid with physical illness and pregnants.

POSTER (P1-C5)

Effectiveness of local wisdom-based games and neurofeedback treatment in decreasing depression of post schizophrenic depression patients admitted to Prof. Dr. SoerojoMagelang mental hospital

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Objective: Schizophrenia is severe mental disorder often coexisting with depressive symptoms. Local wisdom games and neurofeedback are non-pharmacological treatments for decreasing depression level on post-schizophrenic depression patients. We aimto analyze effectiveness of local wisdom-based games and neurofeedback for decreasing depression level in post schizophrenic depression.
Method: Our study isexperimental with a relation type of pre-test and post-test control design.Research tools: local cultural wisdom game equipments; neurofeedback device; Beck Depression Inventory (BDI); and socio-demographic questionnaire. 100 post-schizophrenic depression patients in Prof. dr. Soerojo Magelang Mental Hospital were divided into: group that was given local wisdom-based game, group that was given neurofeedback, group that was given both treatments, and control group that was given pharmacotherapy only. We analyzed depression level before and after treatment using F-test with $\alpha = 5\%$.
Result: Depression level significantly decreased in group given local cultural wisdom games (-61,6%; Fh=336.135; $p<0.01$), neurofeedback (-64,8%; Fh= 265.283; $p<0.01$), both treatments (-74,5%; Fh=397.093; $p<0.01$), and control group (-47.4%; Fh=106.333; $p<0.01$).
Conclusion: Local wisdom-based games and neurofeedback are effective to decrease depression level in post-schizophrenic depression patients.

POSTER (P1-C6)

The Association between Fasting and 2 Hours Post Prandial Blood Glucose Levels and Depression Score in Elderly Patients with type II Diabetes Mellitus Treated with Insulin and Oral Antidiabetic drug in Ngemplak Yogyakarta

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Objectives: The aim of this study was to determine the association betweenfasting and 2 hours post prandial blood glucose levels and depressionscore in elderlypatients with type II Diabetes Mellitus in Ngemplak Yogyakarta
Method: This study was a descriptive analytic study with cross sectional design. The sampling method used was purposive sampling. Data were taken secondary from medical record from Family Doctor. All DM patients visits from July until December 2016 were included. Depression score was measured using Geriatric Depression Scale (GDS). Fasting and 2 hours post prandial blood glucose levels were measured at the time of data collection. The exclusion criteria were the presence of other organic mental disorders and brain infections. Data will be analyzed statistically using chi-squared test.
Results: Depression is associated with poor glucose control in patients with DM. In this study,the association between glucose level and depression was studied and analyzed, particularly in regard to anti-diabetic treatments used.This study is still in progress and result will be reported later.
Conclusions: Depression is common in elderly, particularly in those with chronic disease such as DM. Depression will interfere with the disease management and affect the outcome. Therefore early detection and proper management is important for these patients.

POSTER (P1-C7)

Investigation of cognitive dysfunction of both post-traumatic stress disorder and major depressive disorder using current source analysis of P300 event-related potential

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Introduction: Researches upon the classification criteria to differentiate similar symptoms of post-traumatic stress disorder (PTSD) and major depressive disorder (MDD) have been attempted. This study investigates differences using P300 in sensor and source level and to discover relationships between current source density and symptom scores to develop quantitative biomarkers.
Methods: Fifty-three PTSD patients, 77 MDD patients, and 39 healthy controls (HCs) were recruited. Current source analysis of P300 ERP components elicited by the auditory oddball paradigm was conducted using sLORETA (standardized low-resolution electromagnetic tomography) software. The difference of current source activities between patients with PTSD, MDD and HCs and relationships between P300 current source density values and severity symptom scores including Hamilton Anxiety Rating Scale, Beck Anxiety Inventory (BAI), Hamilton Depression Rating Scale, Beck Depression Inventory (BDI), Pain Anxiety Symptoms Scale (PASS), and Impact of Event Scale-Revises (IES-R) was investigated.
Results: PTSD showed significantly reduced P300 amplitudes at Fz, Cz, Pz and T8 electrode compared to HCs, and also significantly reduced P300 amplitude of PTSD at Fz, Cz, and Pz electrode and prolonged latency at T8 electrode were found compared to MDD. Also, PTSD showed significantly reduced current source densities in medial frontal gyrus, anterior cingulate cortex, cingulate gyrus, posterior cingulate cortex, parahippocampalgyrus, insular, Inferior temporal gyrus, cuneus, lingual gyrus, and precuneus compared to HCs; while diminished source activation of PTSD compared to MDD was found only in cingulate gyrus. Finally, lingual gyrus negatively correlated with BAI and BDI, ACC had negative correlation with PASS, and parahippocampalgyrus and Inferior temporal gyrus showed negative correlation with BAI and IES-R.
Discussion: Results suggest that reduced amplitude and prolonged latency would reflect declined automatic cognitive processing of PTSD compared to MDD, and the reduced current source density and relationships with symptom scores would be related to impaired cognitive system of PTSD.

POSTER (P1-C8)

Rumination as a mediator of the influence of childhood trauma on depression and anxiety in non-clinical samples

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Objectives: Although there is strong evidence that childhood trauma is associated with the development of depression and anxiety, relatively few studies have explored potential mediating factors of this relationship. We aimed to evaluate the mediating role of rumination in the relationship between childhood trauma and mood status such as depression and anxiety using structural equation modeling.
Methods: Two hundred seven healthy participants completed the Childhood Trauma Questionnaire; the Ruminative Response Scale; the Beck Depression Inventory; the State Anxiety Inventory; and the Affective Lability Scale. Structural equation modeling was used to evalute this relationship.
Results : Results supported rumination as a mediator of relations between childhood trauma and depression and anxiety in non-clinical samples. The mediation model indicated that childhood trauma and its subtypes are linked to depression and anxiety through three subtypes of rumination, thereby supporting a significant indirect relationship (Standardized coefficient = 0.56, $p<0.001$ for the path from trauma to rumination; 0.67, $p<0.001$, from rumination to mood). The direct relationship between childhood trauma and mood symptoms was also significant in a model including rumination (Standardized coefficient = 0.68, $p<0.001$).
Discussion: The present study found that rumination mediates the influence of childhood trauma on developing mood symptoms in non-clinical participants. Childhood trauma appears to be a critical determinant for developing symptoms of depression and anxiety.

POSTER (P1-C9)

Role of Terstosteron in treatment of depression

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ABSTRACT
Depression is a leading cause of disability throughout the world and affects approximately 2%to 5% of the population. While depression is generally twice as common in females as in males, studies have found no gender difference between older men and women in theprevalence of clinically significant depression.
While the prevalence of depression in men increases with age, so does the prevalence ofhypogonadism. It has been reported that roughly 39% of men over the age of 45 years suffer fromandrogen deficiency and roughly 8% of men over the age of 50 years suffer from symptomatic androgendeficiency. Depression and anxiety are the most common psychopathological symptoms associatedwith male hypogonadism. The question is whether the age-related gradual decline in testosterone levels contributes to the rising rate of depression in older men.
Testosteron replacement therapy has been shown to improve depressive symptoms in most men. This could be due to the fact that testosterone is a modulator of gabaa receptors and inhibits 5-ht3 receptors centrally. However there appears to be a subpopulation of depressed male patients that tend to respond best to testosteron replacement therapy.
Men with depressive symptoms and testosterone deficiency syndrome should be given a trial of testosterone replacement therapy for at least 3 months as total replacement therapy alone may improve clinical symptoms of depression. Furthermore, men already on SSRIs may also experience further improvement in depressive symptoms after initiating total replacement therapy.

POSTER (P1-C10)

The Efficacy of Folic Acid as Adjuvant Therapy in Improving Depressive Symptom

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BACKGROUND: Depression is recognized as an important cause of disability and mortality worldwide. Evidence suggests that folate deficiency is causatively linked to depressive symptoms because folate plays an important role in the one-carbon metabolic pathway involved in methylation processes and the synthesis of neurotransmitters in the central nervous system. Some studies also indicate that folic acid maybe a very helpful add-on to other prescription antidepressants.
The aim : To compare the improvement of clinical symptom in depressive patients that given fluoxetine only and fluoxetine with folic acid.
METHODS: This clinical trial conducted on 20 participants, devided into two groups. 10 participants was treated with fluoxetine 20 mg daily and 10 participants was treated with fluoxetine 20 mg + 800 mcg folic acid daily. Hamilton Depression rating Scale is used for evaluate depressive symptom, before treatment and during treatment at 2^{nd}, 4^{th}, and 6^{th} weeks. Measurements are then analyzed the comparison result.
RESULTS : Both of groups showed a significant decrease in score HDRS, on the 2^{nd}, 4^{th}, and 6^{th} week after treatment ($p < 0.05$). From the comparative analysis between both of groups, HDRS score in fluoxetine + folic acid group have more significant decrease than fluoxetine group and especially at the 4^{th} week ($p=0,024$)
CONCLUSION: Folic acid as adjuvant therapy is more effective in improving depressive symptoms than fluoxetine only. Another research is needed to bo done with more respondend and more varied doses

POSTER (P1-C11)

Prevalence of depression and its associations with demographic and clinical characteristics and quality of life among university students in China

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Objectives: This study aimed to determine and compare the prevalence of depressionamong university studentsinHong Kong, Macao and Mainland China and its relationship between the depression and quality of life (QOL).
Methods: A random cluster sample of 2312 subjects (928 from the Macao, 446 from HongKong and 938 from mainland China) was recruited and interviewed using standardized instruments. Depression was measured with the Beck Depression inventory(BDI).
Results: Altogethersubjects of the sample (28.9%) were classified as moderate depression or above.The proportion of depression of university students in Hong Kong,Macao and Mainland Chinawas 41.0%,35.2% and 16.8% respectively. On multivariate analyses, much academic stress (p<0.001, OR=2.75, 95% CI: 2.20-3.44), insomnia (p<0.001, OR=3.10, 95% CI: 2.28-4.23), Internet addiction (p<0.001, OR=2.45, 95% CI: 1.99-3.02) and be scolded by others (p<0.001, OR=1.47, 95% CI: 1.18-1.83) were positively associated with depression.Medical student (p<0.001, OR=0.66, 95% CI:0.53-0.83) ,interested in major (p=0.001, OR=0.74, 95% CI: 0.59-0.92), better physical situation (p<0.001, OR=0.38, 95% CI: 0.29-0.50) and highlyGrade Point Average(GPA) (p<0.001, OR=0.55, 95% CI: 0.44-0.67) were negatively associated with depression. After controlling for the confounders,depression was significantly associated with lower physical, psychological, environment and social QOL.
Conclusions: Depression is common amonguniversity students in China. Given its negative effect on QOL, more attention should be paid to university students who had much academic stress□insomnia□internet addiction or be scolded by others.Appropriate strategies should be carried out reducing their occurrence.

POSTER (P1-C12)

Depression in Myasthenia Gravis Patient

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Objectives
Myasthenia gravis is an autoimmune disease and potentially disrupted brain function causing depression as a results of the disease or treatment side effect. Biologically, depression in Myasthenia gravis patient correlated with cortisol failure to give the physiologis effects and anti inflammation effects in peripheral level due to lack of glucocorticoid receptor sensitivity. Other study showed that depression correlated with decrease of lymphosit proliferation stimulated by natural killer cell activity and referred to cytokine level study. Psychological aspect in Myasthenia gravis because the frustrated, physically unsatisfied, activity limitation, and lack of disease information. This study
Methods
Case study with anamnesis and mental status check in 1st year Myasthenia gravis patient.
Results
Patient, NK, female, 26 years old, a nurse with 1 year old baby, actively socialized, history of Myasthenia gravis since 1 year ago, with main complain diplopia, fatique and asphyxiate. Now, patient quit from her job, could not take care of her baby, and retracted from social life. Patient had depression symptoms which were depressive affect, lack of energy, insomnia, loss of appetite, guilty and feeling useless, more than 2 weeks and it was her first episode. Patient was diagnosed with moderate depression episode with somatic symptoms (F31.11 PPDGJ III).
Conclusion
Depression in Myasthenia gravis patient strongly correlated with chronic stressor and anhedoniaas a results of decreasing gene expression for cell proliferation and differentiation. Social and environment factors also important for patient with chronic stressor. Chronic Myasthenia gravis condition causing psychopatologicall problem as a result of neurotransmitter dysregulation

POSTER (P1-C13)

The Role Oxidative Stress and Antioxidant in Depression

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Objectives: It is suggested that many factors contribute in the mechanism of depression including increased oxidative stress and decreased level of anti-oxidants
Methods:A literature search was conducted in PubMed and BMC Psychiatry. Studies assessing the association of stress oxidative model and anti-oxidant in depression were included in this review.
Results: Compared to healthy subjects, people with depression have higher serum peroxide in free radical levels and oxidative damage products. Oxidative damage products included red blood cells (RBC), malondialdehyde (MDA), serum MDA, 8-Hydroxy-2′-deoxyguanosine (8-OHdG) and F2-isoprostanes levels. Lower anti-oxidant levels were also shown by decreased serum paraoxonase, uric acid, albumin, high-density lipoprotein cholesterol, zinc, vitamin A, C, and E levels. Antidepressant therapy has anti-oxidant activity in increasing serum uric acid, albumin and vitamin C levels; and decreasing RBC and serum MDA levels. The addition of dietary supplementation of vitamins A,C, and E for 6 weeks, had significant reduction in depression scores and improvement of blood levelantioxidants was observed in patients.
Conclusion: There is evidence of higher stress oxidative and lower anti-oxidant activity in people with depression disorder. Antidepressants and adjunctive anti-oxidant supplementsshow significant reduction of stress oxidation level in those patients.

Key word: stress oxidative, anti-oxidant, depression, malondialdehyde, 8-Hydroxy-2′-deoxyguanosine, F2-isoprostanes

POSTER (P1-C14)

Dose-related effects of ketamine infusion on suicidal ideation in patients with treatment-resistant depression: a randomized double-blind controlled study in Taiwan

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Objectives: Suicidal ideation and treatment-resistant depression (TRD) are serious problems of public health worldwide. Our aims are 1) to evaluate dose-related antidepressant effect of ketamine on mood and suicidal ideation in patients with TRD; 2) to investigate the association between decreasing of depression score and degree of suicidal ideation. **Methods:** Seventy-one patients with diagnosis of TRD (female 75.2%), which was defined by at least two failed antidepressant responses, received three doses of ketamine (0.5mg/kg, N=24, 0.2mg/kg, N=23, and placebo, N=24) in a double-blind, randomized controlled clinical trial. MADRS and HAMD_17 mood ratings were assessed at baseline and 11 time-points post ketamine infusion until day 14. **Results:** There was a significant dose-related ketamine effect on scores on HAMD_17. The responder analysis (>50% reduction from baseline HAMD on at least two days between days 2 and 5) also revealed a significant dose-related effect (saline:12.5%, 0.2 mg/kg: 39.1%; 0.5 mg/kg: 45.8%).Primary outcomerevealed a robust and fast antidepressant and antisuicidal effect with significant reduction of ratings by high dose vs. placebo from 40-minute to day 7. Symptom attenuation in HAMD_17 rating within one week post-infusion was not only seen in depression (43%) but even greater (59%) in suicidal ideation. Significant greater percentage reduction of suicidal ideation than of HAMD_17 score (remove item 3 (suicidal ideation) and anxiety somatization factor) and MADRS Item 10, under high dose 0.5mg/kg were found (all ps from D1 to D7) < 0.05, correlations for these two changes were from 0.531 to 0.591). Regression analysis elicited decrease percentage at 240 min accounted for 34% of reduction of suicidal ideation. **Conclusions**: Improvements of suicidal ideation after ketamine infusion are related to, but not completely driven by, improvement in depression. There might have other neural substrate influenced by ketamine to account for decreasing suicidal ideation
Key words: ketamine, dose-related, depression, suicidal ideation

POSTER (P1-C15)

Gene expression-based diagnostic marker for bipolar disorder

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Objectives: The purpose of the present study is to develop a multi-assay diagnostic test for bipolar disorder (BD) based on leukocyte gene expression profiles.
Methods: 41 BD subjects and 42 age-and-sex matched non-psychiatric subjects were recruited from the Tokushima University Hospital in Japan. All subjects who participated in this study were of unrelated Japanese origin and signed written informed consent forms approved by the institutional ethics committee of the Tokushima University Graduate School. RNA gene blood tube (Qiagen) and RNA PAX gene Blood RNA kits (Qiagen) were used to extract total RNA from peripheral leukocytes. Real-time quantitative RT-PCR analysis was performed using a customized PCR array plate which was consisted of 40 BD candidate genes. A Discrimination score (D-score) was calculated for each subject by multiplying the coefficients of the linear discriminants, obtained using the lda() function of the MASS package in R, to the standardized values of expression after Z-score transformation of the selected genes.
Results: Among 40 candidate genes examined, five had expression values that differed significantly between BD patients and control subjects. We were able to segregate the patients with BD from control subjects by calculated D-scores with a sensitivity and specificity of 71.4%and 68.8%, respectively.
Conclusions: Further researches will be needed to improve the performance of the present biological test for BD.

POSTER (P1-C16)

Treatment after hospitalization and three-year mortality in people with bipolar disorder: a cost-effectiveness analysis

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***Objective*:**There is a lack of clarity in the literature regarding the cost-effectiveness comparisons between the different outpatient treatment patterns following the psychiatric hospitalizations for bipolar disorder (BD).
***Method*:**Adult patients diagnosed with and hospitalized for BD treatment in 2008 were identified from the National Health Insurance Research Database in Taiwan and were followed up for the consecutive three years (2008-2011). The recruited patients were grouped according to the number of psychiatric outpatient clinic visits (OPD) within the first year after the index hospitalization. With death as the effectiveness measure, a cost-effectiveness analysis was conducted comparing the groups with different outpatient treatment patterns after hospitalizations for BD, over a three-year follow-up period.
***Results*:**Those with 13-17 OPD visits within the 1st year of index hospitalization had the lowest psychiatric and total healthcare costs over a three-year follow-up period (compared to OPD 1-7, 8-12, and >=18). The three-year mortality rates were 4.1% (OPD 1-7), 3% (OPD 8-12), 2.4% (OPD 13-17), and 3.9% (OPD >=18), respectively. In terms of death outcomes, having 13-17 OPD visits within the 1st year was the more cost-effective option compared to OPD 1-7 and OPD>=18 as revealed in the incremental cost-effectiveness ratios (ICERs). From the perspective of psychiatric treatments, the ICER for OPD 8-12 over OPD 13-17 was NTD 110,400 per one percentage point decrease in the death rates.
***Conclusion*:** Those patients hospitalized for BD treatments were associated with higher mortality rates. A post-discharge outpatient treatment at a frequency of 13-17 OPD visits within the 1st year of index hospitalization was associated with lower psychiatric and total healthcare costs in the following three years. Besides, having an adequate frequency of OPD visits after discharge may be considered a cost-effective strategy to reduce future death outcomes in this group of BD patients.

POSTER (P1-C17)

Psychotic bipolar disorder and suicide risk: A case-control study

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Bipolar disorder (BP) is a severe neuropsychiatric disorder with a course of recurrent episodes of mania and depression and a high lifetime suicide rate around 15%. Compared with other types of depression, we ever found that bipolar depression was related to a significantly increased risk for all-cause mortality, suicide, and accidental death during a 10-year period. However, our previous search for genetic basis of BP did not led to a clear insight into its pathogenesis. Clinical phenotype refinement to identify promising sub-phenotypic seems needed for the future study. Psychotic features frequently occur in BP and may be indicative of a more homogeneous and also with possible etiologic ties to schizophrenia. We therefore aim to investigate the different characteristics of psychotic bipolar disorder from the non-psychotic cases, using a national health insurance dataset.
At beginning, a case-control design was used to extract cases of suicides (n=56,473) from National Mortality Registry in Taiwan from 2000 to 2012. Each case was matched by age, gender, and place of residency with 4 randomly selected controls (n=225,892). Conditional logistic regression was used to analyze the case-control data.
We found that bipolar disorder without and with psychotic feature exerts 2-fold odds for suicide than the cases without bipolar disorders (adjusted Odds Ratio 3.43 and 6.09, respectively), after controlling for sociodemographic factors and other comorbidities. Age at suicide is younger for psychotic bipolar disorder than the non-psychotic patient. Compared with the non-psychotic patient, bipolar disorder with psychosis was more likely to receive psychosocial intervention in the past one year and to come from low-income family.
Our findings from the large dataset imply that psychotic bipolar disorder might be treated as a sub-phenotype in the future biological study in psychiatry.

POSTER (P1-C18)

Distinguishing Major depression and anxiety disorder in self-report: Result from psychometric analysis of Clinically Useful Anxiety Outcome Scale

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Background: This study aimed to examine the differential severity of anxiety and depressive symptomsbetween major depressive disorder (MDD) andanxiety disorders.
Methodology: In total, 838 psychiatric outpatientswere analyzed at their intake appointment. Diagnostic characteristics wereexamined using the structured clinical interview from the DSM-IV. We examined anxiety and depression severities indicated by Clinically Useful Outcome Scale (CUXOS) and Beck Depression Inventory (BDI) scores in patients with MDD only, anxiety disorder only, both MDD and anxiety disorder, and no MDD or anxiety disorder.
Results:The prevalence of patients with a new episode of MDD, current anxiety disorders, and both conditions in psychiatric outpatient samples were 41.4%, 33.4% and 18.5%, respectively. The self-reporting tests, CUXOS and BDI, were both able to accurately distinguish pure MDD, pure anxiety disorder, and both disorders.With regard to the CUXOS score, the patients with pure anxiety disorder had significantly higher scores than the patients with pure MDD. With regard to the BDI score, the patients with pure MDD had significantly higher scores than the patients with pure anxiety disorder.
Conclusions: Previous studies have argued that it is difficult to distinguish MDD from anxiety disorder based on depression and anxiety scores obtained with a self-reporting scale. However, these results mean that MDD can be significantly distinguished from anxiety disorder using a self-reporting test if an accurate diagnosis of either MDD or anxiety disorder is made and diagnostic comorbidity is considered.

POSTER (P1-C19)

Korean Medication Algorithm for Bipolar Disorder: changes in preferred medications for mania over 12 years

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Introduction: Many treatment guidelines for bipolar disorders have been introduced to assist clinical decision. Majority of these guidelines are based on evidences from clinical trials. The Korean Medication Algorithm Project for Bipolar Disorder (KMAP-BP) was developed to adopt and maintain an expert-consensus paradigm which was more practical and specific to the atmosphere in Korea.

Objective: In this research, preferred medication strategies for acute mania over four consecutively published KMAP-BP guidelines (2002, 2006, 2010, and 2014) were investigated.

Methods: The KMAP-BP questionnaire using a nine-point scale had covered some specific clinical situations divided into subsections with many treatment options. A written survey asked about the appropriateness of various treatment strategies and treatment agents commonly used by clinicians as the first-line.

Results: The most preferred initial treatment strategy for all subtypes of mania was a combination of mood stabilizer (MS) and atypical antipsychotic (AAP) in every edition. In contrast to MS monotherapy, the preference of combination therapy has been increased over time. Among MSs, lithium and valproic acid are almost equally preferred except in the mixed subtype where valproic acid is the most recommended MS. Carbamazepine was the first-line MS only in the first edition. Olanzapine, quetiapine, and aripiprazole were the preferred AAP for acute manic episode in later editions. This change might depend on the recent research results and safety profile. In cases of unsatisfactory response to the first-line medications, we recommended switching or adding another first-line agent. In KMAP-BP 2014, adding different type of drugs (MS to AAP or AAP to MS) was preferred for partial responders.
Discussion: The Korean experts have been increasingly convinced of the effectiveness of a combination therapy. There have been evident preference changes: increased for AAP and decreased for carbamazepine.

POSTER (P1-C20)

Korean Medication Algorithm Project for Depressive Disorder 2017 (KMAP-DD 2017) to make sure of the ; 3rd revision.

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Aim: This study isconstitutes a third revision of the guidelines for the treatment of major depressive disorder (MDD) issued by the Korean Medication Algorithm Project for Depressive Disorder 2017 (KMAP-DD 2017) to make sure of the). It incorporates changes of experts'in the expert consensus that occurred between 2012 and 2016 in company with the development of new drugsas well as information regarding newly developed and publication of recentrecently published clinical trials.
Methods: Using a 44-item questionnaire, an expert consensus was obtained on pharmacological treatment strategies for 1) nonpsychotic MDD, 2) psychotic MDD, 3) persistent depressive disorder (dysthymia) and depression subtypes, 4) continuous and maintenance treatment, and 5) special populations; consensus was also obtained regarding 6) the choice of an antidepressant(AD) according to in the context of safety and adverse effects, and 7) non-pharmacological biological therapies.
Results: AD monotherapy was recommended as treatment of choice (TOC) for nonpsychotic depression in adults, children and adolescents, elderly adults, and patients with postpartum depression or premenstrual dysphoric disorder. The combination of AD and atypical antipsychotics (AAP) was recommended for psychotic depression. The duration of the initial AD treatment for psychotic depression depends on the number of depressive episodes. Most experts recommended stopping the initial AD and AAP therapy after a certain period in patients with one or two depressive episodes. However, for those with three or more episodes, maintenance of the initial treatment was recommended for as long as possible. Monotherapy with various selective serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs) was recommended for dysthymic disorder and melancholic type MDD.

POSTER (P1-C21)

Alterations of the cortisol and dehydroepiandrosterone in perinatal depression

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Objectives: The purpose of this study is to investigate the alterations of the hypothalamic-pituitary-adrenal axis hormones, especially salivary cortisol and dehydroepiandrosterone (DHEA) in perinatal depression.
Methods: 44 patients with depression and 217 normal subjects in perinatal period were included in this study. Edinburgh Postnatal Depression Scale(EPDS) and Beck Depression Inventory II(BDI-II) were performed. The subjects below 10 points of EPDS score or below 13 points of BDI-II score were classified to normal subjects. Among the subjects more than 11 points of EPDS score or more than 14 points of BDI-II score were diagnosed depression by DSM-IV TR by psychiatrists. All subjects were to collect their saliva in each 4 collecting tubes, immediately upon awakening(IA), 30 minutes after awakening(30A), 60 minutes after awakening(60A) and before bedtime(BB).
Results: The number of subjects in antenatal period were 103, and antenatal depression(AD) patients were 21, antenatal normal(AN) subjects were 82. The number of subjects in postnatal period were 114, and postnatal depression(PD) patients were 23, postnatal normal(PN) subjects were 91. Salivary cortisol levels in subjects with AD collected IA, 30A and 60A were lower than with AN subjects significantly except BB. Salivary cortisol levels in subjects with PD collected 60A only were lower than with PN subjects significantly. Salivary DHEA levels in subjects with both AD and PD were lower than with normal subjects significantly. Also cortisol/DHEA ratio(F/D ratio) in subjects with both AD and PD were much higher than with normal subjects significantly.
Conclusions: These results suggest that the blunted response was shown in AD, and the characteristics between AD and PD are different. Also the differences of salivary DHEA levels and F/D ratio between subjects with PD and normal subjects are suggested the one of the key points of difference among both groups.

POSTER (P1-C22)

Differences Anxiety Symptoms And Depression Symtoms In Mother Of Children Undergoing Maintenance Therapy For Childhood Acute Lymphoblastic Leukemia

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Methods
Participants
This study is an analytical study with cross-sectional approach to see the comparation in HADS score between 20 mothers of children with ALL with control group in Rumah sakit haji adam malik medan, using instruments Hospital and Depression Scale (HADS). Total sample was 40.
Mothers were matched by their children's sex and age. Inclusion :criteria were as follows: (a) mothers were primary caregivers of the children between the age of 3 and 12 years.(b)mothers spoke and wrote bahasa indonesia, (c)children were in the maintenance phase of therapy and had no other concurrent, major illness or disability, (d) children were standard risk, and (e) mothers in the control group had children without chronic disease or disability. Exclusion criteria were as follows: (a) serious, unstable physical or mental illness in mother or child or (b) mothers taking steroid medication.
Instruments
Hospital Anxiety and Depression Scale (HADS)—The HADS is a self-report questionnaire consisting of 14 items divided into 2 subscales, anxiety and depression (Zigmond & Snaith, 1983). The maximum score for each subscale is 21.A score of 7 or greater on each subscale suggests the presence of clinical levels of anxiety or depression. Scores between 8 and 10 suggest the presence of anxiety or depression, while scores greater than or equal to 11 indicate probable mood disorder (Snaith, 2003). Moorey et al. (1991) reported internal consistency of .93 for anxiety and .90 for depression. Concurrent validity (assessed by comparison with psychiatric rating scales) is r= .54 for anxiety and r= .79 for depression (Zigmond&Snaith, 1983). Validity also has been shown when used with a community sample. Sensitivity was 88% for the anxiety subscales and 90% for depression, while specificity was 91% for both subscales (Abiodun, 1994). When used in primary care, internal consistency was α= .89. Convergent validity between the Patient Health Questionnaire-9 and the HADS anxiety scale (r= .81) and HADS depression scale (r= .77) was adequate (Cameron, Crawford, Lawton, & Reid, 2008)
Results: still in the progress of under study
Conclusions and Recommendations: still in the progress of under study

POSTER (P1-D1)

Distinguishing Quantitative Electroencephalogram Findings between Generalized Anxiety Disorder and Panic Disorder

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Objectives: Generalized anxiety disorder(GAD) and panic disorder(PD) are common diagnoses in anxiety disorders. However, it is difficult to distinguish GAD from PD. Neurobehavioral markers that differentiate GAD and PD would be helpful in ongoing efforts to refine classification schemes based on neurobiological measures. The aim of this study was to determine the distinguishing neurophysiological characteristics between GAD and PD using quantitative analysis of an electroencephalogram(QEEG).
Methods: The study included 36 patients with GAD and 25 patients with PD. Resting (eye closed) vigilance controlled EEG recordings were assessed at 64 electrode sites according to the international 10/20 system. QEEG were compared between GAD and PD groups by frequency bands (delta 1-3 Hz, theta 4-7 Hz, alpha 8-12 Hz, beta 12-25 Hz, high beta 25-30 Hz, gamma 30-40 Hz and total 1-40 Hz) made by spectral analysis.
Results: The absolute powers of theta and alpha bands at the frontal area differed between GAD and PD group. The absolute power of the theta activity was decreased in FP1 and FP2 ($p<0.05$) and the absolute power of the alpha activity was decreased in F3 ($p<0.05$) in cases with GAD compared to PD.
Conclusions: The differences in QEEG power in our investigation suggest that underlying pathophysiologic mechanisms may be different between GAD and PD. The findings that the decreased absolute powers of the theta and alpha activity at the frontal area in GAD may be the main neurophysiological characteristics of the GAD.

POSTER (P1-D2)

ECT in a severe OCD patient

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Objectives: ECT (electroconvulsive therapy) is not currently the fist-line treatment for OCD (obsessive-compulsive disorder) patients, but small studies have found it effective in treatment-refractory group.We report a severe OCD patient in her third year of once-a-year-ECT after poor response of medications. Her data during most recent admission of BAI (Beck anxiety inventory), BDI (Beck depression inventory), and YBOS (Yale-Brown obsessive compulsive scale) are described in the text.
Methods:
Ms. A is a 52-yaer-old woman suffering from OCDfor 15 years. Her symptoms, including obsession, compulsion, anxiety, easily fatigued, depressive feeling, insomnia and somatic complaint, did not improve with medication, so she has been admitted in July, 2014 for ECT. After discharge, she was regularly followed up in our out-patient clinic with tolerable symptoms. However, her symptoms became worse 9 months later, so she was admitted for ECT on July, 2015. Symptoms improved except depressive feeling and insomnia this time. Then obsession and compulsion became worse 7 months later, so she was admitted on July, 2016. During most recent admission, her scores according to BAI, BDI and YBOS were 37, 45 and 21 respectively before ECT.

Results:

Ms. A underwent bitemporal ECT three times per week for four weeks during this admission. Her scoreswere 33, 36, 21 respectively after 6 times of ECT, and 19, 30, 29 after 9 times. Obsession and compulsion disturbed Ms. A more even though her anxiety and depression ameliorated. Then her scores were 42, 44, 34three weeks after last ETC.
Conclusion: ECT seems to be effective initially to the symptoms of Ms. A, but obsession and compulsion progressed gradually; besides, anxiety and depression also fluctuated. The effectiveness of ECT in treatment-refractory OCD patients needs further study.

POSTER (P1-D3)

Serotonin modulated the correlations between obsessive-compulsive (OC) trait and heart rate variability in normal healthy subjects

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Objectives: The impact of serotonergic system on OCD is well studied. However, the correlation between OC presentations and autonomic nervous system (ANS) is still unclear. Furthermore, whether the correlation might be modulated by serotonin is also uncertain.
Methods: We recruited eight-nine healthy subjects. Serotonin transporter availability (SERT) by [^{123}I]ADAM and HRV tests were measured. Symptoms checklist-90 (SCL-90) was measured for the OC presentations. The interaction between HRV and SERT availability were calculated and the correlation between ANS and OC symptoms were analyzed after stratified SERT level into two groups (Low and high groups of BDNF were split at medium (2.15)).
Results: The interactions between OC symptoms and SERT were significantly correlated with low frequency (LF), high frequency (HF), total power (TP) and root mean square of successive differences (RMSSD). Furthermore, the significant inverse correlations between OC symptoms and the above HRV indexes existed only in subjects with higher SERT availability (LF: r=-0.36, p=0.01 ; HF: r=-0.45, p=0.002 ; TP: r=-0.35, p=0.01 and RMSSD: r=-0.43 p=0.003). The results remained significant after controlled age and sex.
Conclusions: OC symptoms might be correlated with ANS regulations in subjects with low extracellular serotonin levels.
Keywords: obsessive compulsive symptoms, autonomic nervous system, HRV, SERT availability

POSTER (P1-D4)

Resting-state functional connectivity of the thalamus as a possible predictor of treatment response in obsessive-compulsive disorder

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Objectives: To investigate thecorrelation between baseline resting-state functional connectivity of the thalamus and treatment resposne in obsessive-compulsive disorder (OCD)

Methods:To investigate the functional connections of each thalamic subregions, we used thalamic atlas which divides thalamus into 7 subregions. Resting-state functional magnetic resonance imaging was obtained from 44 drug-naïve or unmedicated OCD patients and demographically matched 44 healthy controls. We investigated resting-state functional connectivity of the individuals through the seed-to-voxel analyses using aforementioned thalamic subregions. The clinical symptoms were measured by Yale-Brown obsessive-compulsive scale (Y-BOCS) at baseline and 1 year follow-up aftertreatment. Spearman correlation between baseline thalamic functional connectivity and improvement of Y-BOCS score at 1 year follow-up was analyzed.

Results:Majority of patients were treated with serotonin reuptake inhibitor, mainly escitalopram and fluoxetine, except 7 patients who received nonpharmacologic treatment such as psychotherapy, psychoeducation and cognitive-behavioral therapy.In seed-to-voxel analyses of thalamic subregions, the OCD group showed significantly higher baseline connectvity in middle temporal gyrus, middle frontal gyrus, putamen, insular cortex, and postcentral gyrus. In Spearman correlation analyses, baseline thalamicfunctional connectivity and improvement of Y-BOCS score at 1 year follow-up showed signicant negative correlation in middle temporal gyrus, middle frontal gyrus. In simple regression analyses, these negative correlations were also identified.

Conclusions:Consistent with recent neuroimaging studies, these data suggest that the pathophysiology of OCD may involve extensive large-scale brain systems, including the temporal, parietal areas, rather than conventional orbitofronto-striatal model. Furthermore, these findingssuggest that thalamocortical functional connectivity could be used as a predictor of treatment response in OCD patients.

POSTER (P1-D5)

Fornix Integrity Associated with Early Trauma in Panic Disorder

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Background : People who have experienced childhood abuse are more likely to experience frequent or generalized anxiety or panic disorder (PD). Although previous studies have used magnetic resonance imaging (MRI) to demonstrate structural abnormalities of brain in subjects with PD, no study about the brain white matter (WM) connectivity differences between PD with and without early trauma. The objective of this study is to find out the brain WM correlates with early trauma. **Methods** : 53 right-handed patients with PD who met the diagnostic criteria in Structured Clinical Interview for DSM-IV were examined by means of MRI at 3 Tesla. We used correlational analysis between major limbic white matter such as fornix, stria terminalis and cingulum Fractional Anisotropy (FA) and Early Trauma Inventory (ETI) in PD. Panic Disorder Severity Scale (PDSS), Beck Depression Inventory (BDI) and Anxiety Sensitivity Index-Revised (ASI-R), Albany Panic and Phobia Questionnaire(APPQ) were administered in PD patients. **Results** : Regression analysis showed that fornix FA scores of the major limbic white matter were significantly correlated with ETI socres. (p=0.024, Benjamin Hochberg FDR correction). The scores of APPQ, ASI were significantly correlated with Fornix FA scores. **Conclusion** : This study suggests that early trauma could influence the connectivity in fornix of major limbic structures in PD. Further investigation will be needed.

Key words: Panic Disorder, Early Trauma, White Matter

POSTER (P1-D6)

Reduced Cortical Thickness of Temporal Pole, Insula and Pars Triangularis in Patients with Panic Disorder

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Objectives
Recent neuroimaging findings have revealed that several paralimbic and prefrontal regions are involved in panic disorder (PD). However, no imaging studies have compared differences in the cortical thickness between patients with PD and healthy control (HC) subjects.
Methods
Forty-seven right-handed patients with PD who met the diagnostic criteria in the Diagnostic and Statistical Manual of Mental Disorders-IV-Text Revision and thirty HC subjects were enrolled. We used the FreeSurfer software package for estimating the cortical thickness of regions of interest, including the temporal pole, insula, and pars triangularis (mid-ventrolateral prefrontal cortex).
Results
The cortical thickness of the temporal pole (P=0.033, right), insula (P=0.017, left), and pars triangularis (P=0.008, left; P=0.025, right) in patients with PD was significantly lower compared with HC subjects (Benjamini-Hochberg false discovery rate correction). Exploratory Pearson's correlation analysis revealed a significant negative correlation between the cortical thickness of the right temporal pole and Beck Depression Inventory scores (r=-0.333, P=0.027) in patients with PD, and a positive correlation between the cortical thickness of the left pars triangularis and Panic Disorder Severity Scale (r=0.429, P=0.004), Anxiety Sensitivity Index-Revised (r=0.380, P=0.011), and Beck Anxiety Inventory (r=0.421, P=0.004) scores.
Conclusions
Ours is the first study to demonstrate cortical thickness reduction in the temporal pole, insula, and pars triangularis in patients with PD compared with the HC subjects. These findings suggest that the reduced cortical thickness can play an important role in the pathophysiology of PD.

POSTER (P1-D7)

Anxiety Factors Associated with Obsessive-Compulsive Disorder: A Population Based Case-Control Study in Taiwan.

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Objectives: Obsessive-compulsive disorder (OCD) is a chronic debilitating anxiety disorder significant in intrusive thoughts and compensation repetitive behaviors. Few studies have reported on this condition Asia. The relationship among OCD and anxiety disorders remained unknown.Thefirst part of specific aim in this study was to estimate the prevalence, incidence and psychiatric comorbidities of OCD in Taiwan.The second part purpose of this study was to investigate whether specific anxiety disorders correlate with the risks of obsessive-compulsive disorder (OCD).

Methods.

We designed a population-based case-control study from the Taiwan National Health Insurance Database, which consisted of 2662 patients with newly diagnosis of OCD as cases and 13310 subjects without OCD controls during 2000 to 2011. Age, sex, demographic variables and covariate psychiatric disorders were compared between OCD cases and control using the chi-square test and t test. Anxiety disorders were classified into four groups: Generalized anxiety disorder (GAD), Post-traumatic stress disorder (PTSD), Social phobia, and Panic disorder.

Results.

Multivariable logistic analysis showed no association was detected between PTSD and OCD (OR 1.91, 95% CI, 0.49 to 7.48). GAD (OR 3.77, 95% CI, 2.95 to 4.8), panic disorder (OR 5.16, 95% CI, 3.61 to 5.76), social phobia (OR 17.8, 95% CI, 3.69 to 85.97) were significant comorbidities associated with increased risk of OCD. The further analysis was performed using only the GAD and panic disorder. After adjusting for variables, GAD and panic disorder durations were not significantly related to the risk of OCD.

Conclusions.

The study confirms the association between OCD and three specific anxiety disorders, including GAD, social phobia and panic disorder. PTSD does not correlate with the risk of OCD. Future studies should focus on finding the additional psychosocial and genetic factor between OCD and anxiety disorders.

POSTER (P1-D8)

Factors Associated with the Response to Combination Therapy of Psychological and Pharmacological Treatment in Panic Disorder

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Introduction The factors associated with the response to psychological treatment and pharmacotherapy in panic disorder are still little known. This study was intended to examine if the serotonin transporter linked polymorphic region (5-HTTLPR) or other genetic variants can affect the response to combination of Mindfulness-based cognitive therapy (MBCT) and pharmacotherapy on relapse in patients with panic disorder (PD).

Methods 107 patients with PD treated with pharmacotherapy alone (pharmacotherapy group) and 101 patients with PD underwent 8-week MBCT as an adjunct to pharmacotherapy (combination therapy group) were enrolled and provided blood samples to extract genomic DNA for classifying individuals according to two genotype subgroups (SS, non-SS) of the 5-HTTLPR and other additional 5-HTR1A, BDNF, COMT polymorphisms. Patients were followed up to additional 5 years and differences in time to relapse were compared. Factors influencing time to relapse were assessed using Cox proportional survival regression, and Kaplan-Meier survival analysis.

Results There were no significant differences in sociodemographic findings between combination therapy and pharmacotherapy alone group. The result demonstrated by Cox proportional survival regression model showed that combination therapy group has longer time to relapse than pharmacotherapy group (P=0.043) and SS genotype group also has longer duration to relapse respectively (P=0.042). Furthermore, among the patients in combination therapy group, SS genotype revealed outstanding longer time to relapse compared to non-SS genotype (P=0.041)

Conclusions Our findings suggest that MBCT and SS genotype of 5-HTTLPR each has potentially benefit effects on reducing the probability of relapse risk of panic disorder. Further investigations are needed for discovering the relationship between genotype and treatments

POSTER (P1-E1)

Placebo effects in Alzheimer Disease: analysis of the CATIE-AD data

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OBJECTIVES: The aim of this study was to compare symptom trajectories between placebo and active drug responders and to examine whether early placebo improvement at week 2 would be associated with placebo response at week 8, so as to provide evidence to guide systematic screening of potential placebo responders with BPSD.
METHODS: The data of 371 patients with Alzheimer disease (DSM-IV) in Phase 1 of the Clinical Antipsychotic Trials of Intervention Effectiveness for Alzheimer disease (The CATIE-AD) [1] were analyzed. The patients were randomly assigned to treatment with olanzapine, quetiapine, risperidone, or placebo in a double-blind condition. Trajectories of Brief Psychiatric Rating Scale (BPRS) total scores were compared between placebo and active drug responders (i.e. those who achieved a ≥25% BPRS total score reduction). Prediction performance of binary classification in improvement at week 2 for placebo response at week 8 was examined; sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the consecutive cut-off points in increments of 5% between 5% and 25% in the BPRS total score reduction at week 2 were calculated.
RESULTS: There were no significantly differences in symptom trajectories between placebo and drug groups. The cut-off of 10% at week 2 presented with the highest precision of 0.66 with sensitivity, NPV, specificity, and PPV of 0.53, 0.65, 0.77, and 0.68, respectively.
CONCLUSION: Symptom trajectories of BPSD in responders follow a similar pattern irrespective of treatment modalities. The 10% cut-off at week 2 seems robust for the prediction of subsequent placebo response at week 8, which may need to be considered in future clinical trials to reduce failure trials for BPSD.

POSTER (P1-E2)

Clozapine Induced Shock, QTc Interval Prolongation, And Worsening of Extrapyramidal Syndrome In 58 Years Old Woman With Early Onset Dementia, A Case Report

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Introduction: The prevalence of dementia increases with age, which could occur under 65 years old (early onset dementia). Early onset dementia could have comorbidity with psychiatric disorders. This paper present about a case 58-year-old female with early onset dementia developing clozapine induced shock, QT prolongation, worsening of extrapyramidal syndrome. After the discontinuation of clozapine, the side effect progressively declined over 3 days.
Objective: To determine the most safe antipsychotic in early onset dementia
Method: The search is conducted in Pubmed, Cochrane, Proquest, Trip, with keyword "clozapine", " QT prolongation", "extrapyramidal syndrome", "dementia, early onset" and "antipsychotic" through MeSH engineering with limitations issue 10 years. Limitation of research on humans, type of article from Case Report, Randomized Controlled Trial, Cohort, and published in English.
Result: The risk in developing QTc prolongation is similar between clozapine, olanzapine, risperidon and aripiprazole. Other antipsychotics rated as high and medium risk. At present, no alternative treatments appear to be quite safe and effective for dementia.
Conclusion: Even clozapine has been claimed more safe, the following are factors to be seriously considered: the presence of cardiovascular diseases, QTc interval, electrolytic imbalances, familiar history with torsades des pointes, use of another drugs, hypotension, extrapyramidal syndrome, and observation on another side effect. Careful use of antipsychotic drugs at proper dosage and for the closely necessary time requested for trying to timely control behavioral symptoms is the most reasonable way of facing this condition
Keyword: early onset dementia, qt interval prolongation, extrapyramidal syndrome, clozapine

POSTER (P1-E3)

Anosognosia for a Visible Facial Tumor in Frontotemporal Dementia: a case report

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Background : Anosognosia is a condition without awareness of impairment of function or illness and denial is a strategy used to reject something. Both are barriers for patients to receive medical investigation. Here we present a case of frontotemporal dementia who lack of awareness to his visible tumor on cheek.
Case : Mr.C is a 65 year-old male retired patient. He suffered from right nasal inverted papolloma and received completed resection in 2004. Then he could do job well without discomfort until retirement in 2014. Since that, he started to present agitation, personality change and bizarre behavior as hoarding trash. Dementia was suspected but he didn't get define diagnosis. In 2015, the computerized tomography(CT) showed suspicious recurrent right nasal tumor but he refused to receive further evaluation. Although his children repetitively pointed out the increasingly protruding mass, making him barely to open his right eye, he still insisted disease-free himself and could not cooperate with therapeutic procedure. Therefore, he was referred for his denial. Psychiatric interview revealed he has poor attention, memory impairment, disinhibition, lack of awareness for the nasal tumor with emotional indifference. Brain CT on June 2016 showed severe bilateral temporal atrophy and left thalamus lacunar infarction. Frontotemporal dementia is impressed.
Discussion
To distinguish from anosognosia to denial may be a challenge and important part for treatment strategy, which former is organic etiology and latter is psychological defense mechanism. In literature, anosognosia was documented to be associated with deficit in parieto-temporal cortex, and insula in stroke patents, and functional disconnection between cortical midline structures and medial temporal lobe in Alzheimer's dementia.
Conclusion: Our case reminds physicians to pay more attention to the differentiation of anosognosia and denial. Planning ahead, performing smooth transition to whatever tasks need to occur next, and working with.

POSTER (P1-F1)

Beneficial Effect of Aerobic Exercise on Emotion, Cognition, and Physical Function in Children with Attention Deficit / Hyperactivity Disorder

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Objectives: Considering the clinical importance of an improvement in cognitive functions and behavior on the functional adaptation of children with ADHD, the objectives of this study is to assess the effects of a moderate- to high-intensity physical activity program lasting 12 weeks on ADHD-related behaviors, cognitive functions and fitness in children with ADHD compared with healthy controls. **Methods:** Participants were children with ADHD according to DSM-IV and Healthy children with no psychiatric problems. Exercise programs were composed of an hour of exercise with bike riding, once every week, for 3 months. Program were delivered uniformly according to a strict protocol and supervised by a psychomotor therapist and monitored by nurses, social workers specialized in psychiatry. To prevent dropout of patients due to injury and exhaustion, exercise intensity will be increased gradually. Psychiatric assessments included Child Behavior Check List (CBCL), Korean version of the ADHD Rating Scale (K-ARS), and Parent Stress Index (PSI). Cognitive function were assessed by Trail making test (TMT), Comprehensive Attention Test (CAT). Test of Gross Motor Development (TGMD) and Shuttle run (SR) were used to check the physical functions. **Results:** Thirty two patients with ADHD and 29 healthy controls participated in exercise programs. After exercise programs, ADHD group showed significant improvement in K-ARS score ($t=5.73$, $p<0.001$), CBCL subscore and TMT, CAT,TGMD and SR. Control group showed improvement in CDI ($t=2.26$, $p=0.032$). In ADHD group, Parent Stress Index of ADHD participants was significantly reduced after exercise programs. Between group comparisons, ADHD group showed more significant improvement in ARS, CBCL, TMT and TGMD than control group. **Conclusions:** Present study support that physical activity engendered through aerobic exercise has notable beneficial effects in the improvement of ADHD-related behavioral symptoms, cognitive functions and motor coordinating abilities for the children with ADHD.

POSTER (P1-F2)

The Influence of Psychosocial Factors to Eating Behaviour in Children and Adolescents: An Evidence Based Case Report

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Background: The effects of eating behavior in child and adolescent phases and will define the health status related nutrition intake later in adulthood. Psychosocial stress factors and dyadic emotion regulatory processes have been linked with food consumption, but the relation's direction remains unclear. Understanding the correlation of dietary intake is necessary in order to effectively promote healthy dietary behavior and increase mental health wellbeing among children and adolescents. **Case Report:** A mother brought her 8 years old child to the health care provider, with a chief complain of her child was very skinny and took a little portion of meals almost everyday starting at age 5 and known as fussy eating. Another mother came with her 7 years old child who had a problem of too much eating which known as binge eating. **Aim:** The aim of this review is to explore and explain the psychosocial factors that influence the eating behavior in children and adolescents be based on evidence based medicine. **Method:** We included literatures of research articles such as cross-sectional studies, prospective studies, randomized control trials, and systematic reviews using Medline/PubMed, Embase, and PsychINFO. The articles published between January 2009 and April 2017. All studies include subjects ranged at age 5-19 years old. The selection and review process were based on the relevancy of population, intervention, and outcome. **Results:** From 16 articles that have been abstracted, there were similar psychosocial factors that influence the eating behavior in child and adolescent. Appropriate eating behavior associated with normal BMI with adequate nutritional intake is influenced by some psychosocial factors, which are: feeding practice process at infancy, perceived modeling and variety of diets from parents or caregivers, guidance of social cognition about food and its intention, emotional regulation, personality trait, perceived stress and self-regulatory capacity, transactional process to close relationships, social support, self-esteem, and body image related to social and media influence. **Conclusion:** Knowing contributing factor in building eating behavior in children and adolescent is important to make strategies in the prevention and treatment of maladaptive eating behavior. Parents should know their child temperament in association to achieve the goodness of fit. However, more investigation on the assessment and intervention is needed to address this.

POSTER (P1-F3)

The effect of Nigella sativa increase levels of superoxide dismutase in passive smokers (Study in Sprague Dawley rats)

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Objective: Many schizophrenia patients are exposed to smoke around 83-85%. Schizophrenia smokes around 10-25 cigarette per day. Exposure to cigarette or cigarette smoke may disrupt inbalance of pro and antioxidant in human body. Black cumin seeds (Nigela sativa) has the effect of antiinflamatory and exogenous antioxidants. Nigella sativa (NS) with the molecule active thimoquinone. Endogenous antioxidant levels can be measured of catalase, superoxide dismutase enzyme.
Aim: to analyze the effect of Nigella sativaon plasma levels of superoxide dismutase in Sprague Dawley rats that were exposed to smoke.
Methods: A true experimental design with post test only control group design study using Sprague Dawley as animal model. After adapted for 7 days, 18 samples were randomly divided into three groups (n=6 per group). K1 (negative control), K2 (positive control) was given exposure to cigarette smoke 4 cigarettes / day, P was given exposure to cigarette smoke and black cumin extract 2 g/KgBW/day. Examination SOD was measured using ELISA kit on the day 29th, using blood sample from retroorbita vein. Statistical test using Kruskal Wallis.
Results: The mean ± SD SOD each group were K1 = 6.34 ±3.64, K2 = 3.43±0,34, P = 5.08 ±2.92, there were no significant differences between groups. (P = 0,208)
Conclusion: Nigella sativaextract increases plasma SOD levels in Sprague Dawley rats by exposure to cigarette smoke and black cumin seed extract.

POSTER (P1-F4)

Correlation between Marker Oxidative Stress and Histopathology Hepar (Manjaroenigk Score) (Study in Wistar Rat Induced by Fluhpenazine decanoate)

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Objective: Fluphenazine decanoate is an long acting injection drug anti psychotic grouppprescribed for typical schizophrenic.The use of long-term antipsychotic can increased oxidativestress that can lead to cell death. Imbalance prooxidant and antioxidant severe can be causing cell death. Catalase and superokside dismutase are an enzyme that can be used as a marker for oxidative stress. Cell damage caused by oxidative stress can be evidenced from the histopathology of liver cells by HE staining in value with ManjaRoenigk score.
The aim to know correlation between oxidative stress marker (enzym catalase levels) anddamage ofhistopathologyhepar.
Methods: This experimental research used post test only control group design. 15 of male wistar rats divided randomly into 3 group, namely the control group (K) which is given with the standard diet and the injection of sesame oil,and the group treatment I (P1) is given with fluphenazine decanoate 1 mg/kgBB, whereas the group treatment II (P2) is given with fluphenazine decanoate 2 mg/kgBB. In the day of 28, rats were terminated and the heparwere taken to be made extracts for the measurement of levels of catalase with 10% H_2O_2 and to be made histopathological slides with HE staining.
Results: Percentage of catalase levels from high to low : K group 62,5%> P1 group 25%> P2 group 12,5%. Damage ofhistopathologyheparwith catalase levels from high to low: K group (r=0,667)> P1 group FD 1 mg (r=0,564)> P2 group FD 2 mg (r=0,410).
Conclusion There is weak correlation betweencatalase levels and damage of histopathology hepar caused by fluphenazine decanoate exposure.

POSTER (P2-G1)

Musical hallucination associated with the superior temporal gyrus in non-dominant hemisphere

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Objective : Musical hallucination is a rare subtype of auditory hallucination characterized by the perception of musical sounds, instrumental music, or songs. Some studies reported that musical hallucination was improved with the administration of antiepileptics. Here we report six cases with musical hallucinations associated with hearing difficulty, and hyperperfusion in the temporal gyrus in non-dominant hemisphere correlated with musical hallucination and hallucination were improved by carbamazepine (CBZ) therapy.
Methods : A total of six patients with musical hallucinations (male n=2, female n=4, mean age 81 years) underwent cerebral perfusion single photon emission computed tomography (SPECT) studies with N-isopropyl-p-[(123)I] iodoamphetamine to measure regional cerebral blood flow (rCBF) before and after CBZ treatment. In addition, z-score maps were acquired using 3-dimensional stereotactic surface projections (3D-SSP) of SPECT data. The ratios of rCBF in the superior temporal gyrus, the middle temporal gyrus, the supramarginal gyrus and the angular gyrus were compared between before and after treatment. In order to determine the dominant hand, the Edinburgh handedness test was conducted. The left-handed case (case 4) underwent fMRI to identify the dominant hemisphere. The strength of musical hallucination was evaluated with Auditory Hallucination Rating Scale before and after treatment.
Results : Cerebral perfusion SPECT detected hyperperfusion in temporal gyrus in the non-dominant hemisphere during musical hallucinations in all cases. CBZwas effective on musical hallucination and improved the above hyperperfusion. In addition, hyperperfusion in the temporal gyrus in non-dominant hemisphere correlated with strength of hallucinations.
Conclusion : Hyperperfusion in the superior temporal gyrus in non-dominant hemisphere and hallucination were improved by CBZ therapy. These results suggest that the superior temporal gyrus in non-dominant hemisphere is pathologically associated with musical hallucination.

POSTER (P2-G2)

Ventral hippocampus outputs modulate stress-provoked aggression

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Objectives : Accumulating evidence shows that the ventral hippocampus (VH) modulates stress responses. However, whether the VH modulates stress-evoked aggression remains elusive.
Methods : Here, we used the optogenetic and chemogenetic approaches to examine whether the VH activation involves stress-evoked attack behavior inpost-weaning social isolated mice, an animal model of aggression. The lentivirus carrying CaMKII-NpHR3.0-eYFP or CaMKII-ChR2-eYFP were transducted into the VH of separate groups of post-weaning social isolated mice. After 4 weeks of resting, these mice performed behavioral tests.
Results : After 30 min of footshocks as acute stress, NpHR-expressing mice recieved amber light of 589 nm laser to inhibit the VH activation in OFF-ON-OFF states of the resident-intruder (RI) test, a well-known agression test.The result indicated the inhibition of VH activation blocked stress-induced attack behavior. Moreover, the optogenetic stimulation of the VH by blue light of 473 nm laser induced attack behavior of ChR2-expressing mice but not NpHR-expressing mice. In addition, we transducted adenoassociated virus (AAV5) carrying hSyn-HA-hM3D$_{(Gq)}$-IRES-mCitrine, hSyn-HA-hM4D$_{(Gi)}$-IRES-mCitrine, or hSyn-EGFP (as control) into the VH of separate groups of post-weaning social isolated mice. CNO injection (1mg/kg) to activate hM3D$_{(Gq)}$ induced attack behavior of hM3D$_{(Gq)}$-expressing mice but not of control mice. On the other hand, CNO injection blocked stress-induced attack behavior of hM4D$_{(Gi)}$-expression mice but not one of control mice.
Conclusions : These reults of optogenetic and chemogenetic approaches suggest that the VH activation modulates attack behavior in mice. Our findings provide the evidence which the VH activation regulates the neural circuits of aggression in mice

POSTER (P2-G3)

Pharmacological profiling of several μ-opioid receptor agonists based on the changes in theligand-biased intracellular signaling

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“Ligand-biased efficacy” provides new opinions for differences among ligands that act at the same receptor. However, the relationship between the ligand-biased signaling and a wide variety of pharmacological differences amongindividual μ-opioid receptor (MOR) agonists has not yet been to be fully elucidated. In the present study, we investigated thepharmacological profiles of several MOR agonists based on the changes in the ligand-biased intracellular signaling. The treatment with MOR agonists, such as morphine, tramadol and M1, to the HEK293 cell over-expressing Halo-fused MORs failed to produce the internalization of MORs, whereas other MOR agonists including oxycodone, fentanyl and methadone dramatically induced MOR internalization. In addition, the treatment of fentanyl and methadone to CHO cells over-expressing MORs showed the dramatic increase in β-arrestin recruitment of MORs. These results suggest that each ligand acting at MORs can differently activate its signaling through MORs. We will also discuss the more detailed difference of intracellular signaling induced by several μ-opioid receptor agonists.

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POSTER (P2-G4)

Dentate gyrus cells count and memory retention in Sprague Dawley rats post vascular cognitive impairment induction and after treatment with haloperidol and olanzapine

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Abstract
Aims This study was aimed to examine the effect of haloperidol and olanzapine administrations on dentate gyrus cells and memory retention in *Sprague Dawley* rats after VCI induction.
Methods This study was a quasi experimental study with a post test only control group design. Subjects were male *Sprague Dawley* rats weighing 200-250 grams. VCI was induced with bilateral carotid ligation method. Memory retention was measured with *novel object recognition test* (NORT). Each group received intramuscular injection of haloperidol (1mg/kgBW), olanzapine (2mg/kgBW) and aqubidest injection (sham and control) for three days. The brains were then evacuated and analyzed histopathologically for cell counts.
Results Cellular analyses showed that cell count was lowest for sham groups and highest for the haloperidol group. But the difference was not statistically significant. There were no significant difference in the time spent exploring old and new objects for all groups ($p > 0.05$). Comparisons between groups showed similar results. Control group spent more time exploring new objects as shown by DI value, but it was not statistically significant.
Conclusion The administration of either olanzapine or haloperidol did not significantly affect dentate gyrus cells and rat cognition post VCI induction.

POSTER (P2-G5)

The relationship between thalamic functional connectivity and general intellectual functioning in individuals at ultra-high risk for psychosis

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Abstract
Objectives: General intellectual functioning has previously been reported to buffer against deficits of social cognition in individuals at ultra-high risk for psychosis (UHR). However, little is known of the neurobiological link between neurocognition and social cognition in UHR. Recent studies have demonstrated that thalamic networks play critical role in cognitive functions and thalamo-cortical connectivity is altered in UHR subjects. The current study aimed to evaluate the relationship between thalamo-cortical connectivity and general intelligence in individuals at UHR.
Methods: Fifty-five individuals at UHR participated in the present study and underwent a resting-state functional connectivity magnetic resonance imaging at 3T. Participants were recruited from a longitudinal cohort study from April 2010 until December 2014. We measured the baseline IQ and whole-brain thalamic functional connectivity maps using the anatomically defined left and right thalamic seeds. Correlation analyses were performed to investigate the association between subject's connectivity intensities and IQ.
Results: The 55 UHR participants were predominantly male (74.5%), with a mean age of 20.73 ± 3.27 years. The average IQ score was 109.60 ± 12.02 (ranging from 84 to 136). The IQ scores demonstrated negative relationship with strength of resting state functional connectivity between thalamus and right supramarginal gyrus (SMG) of inferior parietal lobule.
Conclusions: This result demonstrate that higher general intelligence in UHR is associated with reduced connectivity between thalamus and right SMG. Considering that SMG is known to be related with social cognition, our finding could be give insights into the relationship between neurocognition and social cognition in UHR subjects.

POSTER (P2-G6)

Acute Psychosis in “Asymptomatic” Malaria

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Abstract
Objectives Acute Psychosis, with symptoms of excitement or sudden behavioral changes, is a common psychiatric emergency that may encourage patient seeking for professional help. Good clinical skills are needed to rule out psychosis as a symptom related to underlying diseases. Clinicians may be unfamiliar with diseases that is rare in practice, e.g. malaria in non-endemic area. “Asymptomatic” malaria, without presence of common obvious symptoms: fever and chills, has recognized as a result from partial immunity, which restrain but does not completely eliminate the infection. Studies found 5.4-12% psychosis case of Falciparum Malaria, and delays in recognition can lead to a worse prognosis.
Method Case reports 22-years old male, presents with excitement and sudden behavioral changes within a week. Patient experienced auditory and visual hallucination, and delusion of reference. There was no fever, chills, or other physical symptoms. Further investigation obtained history of visiting endemic area of malaria a year before, without any complain ever since. Laboratory examination has requested, and found *Plasmodium falciparum* as a marker of malaria infection. Patient had received intramuscular 5 mg of Haloperidol and 10 mg of Diazepam to control excitement in first 48-hours, followed with peroral 10 mg/day of Haloperidol in 2 divided dose, and malaria was treated with Dihydroartemisinin-Piperaquine and Primaquine.
Result Psychotic features diminished after 5-days treatment. After recovery, patient back to his daily activities as a college student and there was no relapse on psychotic symptom.
Conclusion A thorough history, physical and mental state examination are essential for the initial approach to acute psychosis. Acute psychosis could be presentation of malaria and should be thought as a differential diagnosis in sudden psychotic symptoms with history of visiting endemic area. Comprehensive analysis on acute psychosis may lead to appropriate diagnosis and treatment, in order to prevent further complication.

POSTER (P2-G7)

Activation of astrocytes in the anterior cingulate cortex corresponds to sleep disorder under neuropathic pain

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It has been reported that sleep problems and daytime sleepiness are commonly found in primary care patients with chronic pain and cancer pain, and seem to be related mainly to depression and the severity of pain. In the present study, we evaluated whether neuropathic pain could activate astrocytes in the mouse anterior cingulate cortex (ACC), leading to sleep disorder. We used functional magnetic resonance imaging to visualize the increased blood oxygenation level-dependent signal intensity in the ACC of mice with sciatic nerve ligation under mild noxious stimuli. Such stimuli significantly increased the release of glutamate in the ACC of nerve-ligated mice compared to sham-operated mice. In addition, sciatic nerve ligation and mild noxious stimuli changed the morphology of astrocytes in the ACC. Using primary cultured glial cells from the mouse cortex, treatment of glutamate caused astrocytic activation, as detected by a stellate morphology, and promoted the translocation of GAT-3 to astrocyte cell membranes. In the ACC of nerve-ligated mice, the GABA level at the synaptic cleft was significantly decreased by exposure to mild noxious stimuli. Finally, we investigated with the optogenetic tool whether astrocytic activation in the ACC could directly mediate sleep disorder. The selective photostimulation of these astrocytes triggered sleep disturbance. Taken together, these results suggest that neuropathic pain-like stimuli activated astrocytes in the ACC and decreased the extracellular concentration of GABA via an increase in the release of glutamate. Furthermore, these findings provide evidence that astrocytic activation in the ACC may correspond to sleep disturbance in mice with nerve injury.

POSTER (P2-G8)

Spontaneous Parkinsonism in First-Episode Psychosis: Case Report

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Objectives: There is now growing evidence that parkinsonism and other extrapyramidal signs are highly prevalent in patients with first-episode psychosis prior to antipsychotic drugs treatment. Association between spontaneous parkinsonism with cognitive impairment are also observed in recent studies.
Method: A 56 years old woman presents with first-episode psychosis and has no history of taking antipsychotic drugs. Neurologic examination demonstrates tremor in both hands and bradykinesia. Executive function, verbal and visual memory impairment also found in neurocognitive examination. There is no evidence of related structural damage in non-contrast brain CT SCAN. Patient is diagnosed as paranoid schizophrenia after a series of examination rule out metabolic, endocrine or neurologic disease as an underlying disease. She is treated with 15 mg olanzapine daily and 3 mg trihexyphenidyl twice daily.
Results: Acute psychosis symptoms have improved in the third week of hospitalization. Parkinsonism symptoms have diminished by the time the patient is discharged. She is planned for cognitive remediation in outpatient setting.
Conclusions: Studies have consistently identify first-episode psychosis with no exposure to antipsychotics had abnormalities in function and brain structure, primarily the medial temporal, prefrontal, thalamic, and basal ganglia areas, also had extrapyramidal signs. Spontaneous parkinsonism in first-episode psychosis indicates an intrinsic feature of the disease process and implicates dysfunction in cortical-basal ganglia-cortical circuitry, not just medication related. Cognitive impairment associated with dyskinesia and parkinsonism may become predictive value for further cognitive impairment.

POSTER (P2-G9)

Influence of carbonyl stress on neural cells derived from induced pluripotent stem cell

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Schizophrenia (SZ) is a devastating mental illness in which initial and major risks of the disease during neurodevelopment may disturb postnatal brain maturation, which results in the onset after puberty. However, mechanistic understanding of schizophrenia is not well developed. One major limitation that has blocked the progress is the difficulty of accessing relevant tissues/cells for the investigation. First, although mental disorders affect the brain, it is almost impossible to obtain biopsied brains or neurons of central nervous system origin that are relevant to the diseases. Second, because the onset of these disorders is relatively young (adolescence or young adulthood), there is no guarantee that autopsied brains from aged patients with long-term medication reflect disease pathologies. For these reasons, there is expectation that induced pluripotent stem cells (iPS cells) will be a major advance for understanding of mental disorders.Astrocytes facilitate neuronal maturation by regulating exogenous stress. Antioxidant defense is one example of this type of astrocyte function.Previous study from our laboratory reported that the carbonyl stress in a subpopulation of SZ patients, leading to a failure of metabolic systems with plasma pentosidine accumulation and serum pyridoxal depletion. However, the molecular mechanisms of the relationship between carbonyl stress and SZ are still unknown. We hypothesize that astrocytes may have a deficit in energy metabolism resulting in neuronal damage in SZ, which might be involved in SZ pathology in carbonyl stress context.As a first step of the study, we examined how pentosidine accumulation affects to neuron and astrocyte using human iPS cells. We generated TUJ1 positive neurons and GFAP positive astrocyte from human iPS cells of normal control subjects. And then we measured the energy metabolism such asglycolysis and mitochondrial respirationin the cells. Our strategy will provide important clues for understanding of SZ.

POSTER (P2-G10)

The Difference of Serum Tumor Necrosis Factor-Alpha (TNF-α) Levels Between Patients Schizophrenic Male with Smoking and Control

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Objectives : The exact cause of schizophrenia is not known, although several aetiological theories have been proposed for the disease, including immune dysfunction or autoimmune mechanisms. Cytokines including TNF-α has an important role in the pathophysiology of schizophrenia and the effects of pharmacological treatment with antipsychotics. Nicotine is widely affect the brain, the immune system and cytokine levels. There is a hypothesis that the smoker in schizophrenic patients can play a role in the changes in cytokine profiles including TNF-α in schizophrenia.
Aims : To determine differences of serum TNF-α levels between schizophrenic patients with smoking in male and control.
Methods : This study was a comparative analytic study with approach cross-sectional study, divided into two group: 1) group of male schizophrenic patients with smoking (n_1=30) with inclussion criteria were patients who have been diagnosed schizophrenic based PPDGJ-III, 20-60 years old, male, smoking, chronic schizophrenic patients in the stable phase and Willing to participate this study. Exclusion criteria were have other mental disorders and comorbidity with other medical illnesses. 2) control group (n_2=30) with inclussion criteria were 20-60 years old, male, smoking, Willing to participate this study.Exclusion criteria were have mental disorder, a family history of psychiatric disorders, the other medical illnesses, a history of alcohol and other substances abuse (except caffeine and nicotine). Conducted in BLUD RSJ.Prof.Dr.M.Ildrem Medan. Levels of serum TNF-α were analyzed using the Luminex Assay Performance High Sensitivity TNF-α. Statistical analysis using numeric comparative T-Independent Test.
Results : still on progress under study
Conclusions : still on progress under study

POSTER (P2-G11)

Single Nucleotide Polymorphisms in the 5'Flanking Region of Interleukin-17A Gene Significantly Associate with Pain Sensitivity

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Abstract
Objectives : Pain correlates immune system through reward system (1, 2). Furthermore, interleukin (IL)-17A upregulation after lipopolysaccharide injection correlates with pain sensitivity (3, 4). Based on these, we examined associations between pain sensitivity and IL-17A/F gene polymorphisms.
Methods : We examined 80 single nucleotide polymorphisms (SNPs) around the coding region of both the human IL-17A gene and adjacent IL-17Fgene. Phenotypes examined were clinicallymeasured endpoints that were related to pain sensitivity (PPLpre)with the preoperativecold pressor test. The groups analyzed were 280 Japanese patients who were scheduled to undergo cosmetic orthognathic surgery for mandibular prognathism at Tokyo Dental College Suidoubashi Hospital.Genotype data for the IL-17A/F generegion were extracted from whole-genome genotyping data obtained in a previous study (5) and were statistically analyzed by nonparametric tests with SPSS software.
Results : We examined associations between PPL pre and the SNPs around the coding region of the human IL-17A/Fgene. Two SNPs in the 5' flanking region of IL-17A gene showed a significant association between the genotypes and a clinical endpointwith the preoperative cold pressor test (rs1937146: $P=9.2 \times 10^{-6}$ in total, $P=3.4 \times 10^{-5}$ for male, P=0.017 for female and rs9357726: $P=7.9 \times 10^{-5}$ in total, $P=1.2 \times 10^{-4}$ for male and P=0.047 for female). The genotypes in the rs1937146 and rs9357726 SNPs were A/C and A/G, respectively, and A alleles were associated with elevated pain threshold in PPLpre (longer time until pain sensation inthe preoperative cold pressor test) for both SNPs.
Conclusions : IL-17A SNPs associate with pain sensitivity, suggesting that IL-17A would affect pain sensitivity.

POSTER (P2-G12)

GIPR gene polymorphism in schizophrenia and metabolic syndrome : a cross-sectional study

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Abstract
Objectives : Metabolic syndrome (MetS) is characterized by abdominal obesity, insulin resistance, hypertension, and blood lipid disorders. Higher prevalence of MetS in schizophrenia compared with general population has been reported. Also, antipsychotic drugs are known as cause glucose abnormalities and weight gain. On the other hand, we have reported on the association between Gastric inhibitory polypeptide receptor (GIPR) gene polymorphism and insulin concentration and weight gain. In this study, we examined the relationship of MetS and GIPR gene polymorphism in patients with schizophrenia.
Methods : Two hundred eighty six schizophrenia patients participated in this study after providing written informed consent. The studies were approved by the Ethics committee of Niigata University School of Medicine. Patients aged 18–65 years were included in this study if they fulfilled the diagnostic criteria for schizophrenia according to the DSM-IV. MetS criteria was used Japanese Diagnostic Criteria for Metabolic Syndrome organized by Japan's eight societies for internal medicine specialties and International Diabetes Federation Worldwide Definition of the Metabolic Syndrome. Fasting blood samples were drawn after an overnight fast to examine fasting plasma glucose, triglyceride, and HDL-cholesterol. Demographic assessment of age, sex and BMI was also conducted. The serum analyses were performed by standard methods (SRL Inc., Tokyo, Japan). The GIPR gene polymorphism rs10423928 (T/A) was genotyped using a TaqMan 5'-exonuclease assay. One- way ANOVA or the chi-square test was used for comparisons among three groups according to genotype.
Results : The mean age of the subjects was 40.0± 13.1 years. The genotype frequencies of the GIPR gene polymorphism rs10423928 are T/T 186 samples, A/T 87 samples and A/A 13 samples. The genetic variation was in the Hardy–Weinberg equilibrium. There was no significant difference in prevalence of MetS among 3 groups.
Conclusions : No association detected between GIPR gene polymorphism in schizophrenia and prevalence of metabolic syndrome.

POSTER (P2-G13)

Seven cases of autoimmune limbic encephalitis with psychiatric symptoms

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Abstract

Objective : Recently, autoimmune limbic encephalitis such as anti-N-methyl-D-aspartate receptor (NMDA-R) encephalitis and anti-voltage-gated potassium channel complex (VGKC-complex) encephalitis, which often present as acute psychosis during the initial phase of illness, have been a focus of attention. Here we report definite 5 cases and suspicious 2 cases with autoimmune limbic encephalitis with acute psychiatric symptoms.

Case reports, Methods and Results : Case 1, 2 and 3 were 18, 30 and 42-years-old females, respectively. They suffered from hallucination, delusion, convulsive seizure, consciousness disturbance, and subsequent respiratory failure within 2 weeks. Case 4 was 63 year-old-male presenting with parkinsonism including finger tremor and rigidity and visual hallucination at the onset. Subacutely, these symptoms progressed to an akinetic mutism. Case 5 was 65-year-old female presenting with rigidity, hallucination, delusion, convulsive seizure and consciousness disturbance after complete remission of acute myelocytic leukemia (AML). Case 6 was 68 year-old-female with a previous history of o variectomy of teratoma. She suffered from depression, hallucination, delusion and consciousness disturbance. Case 7 was 35 year-old-female presenting with mannerism and consciousness disturbance. All cases were examined for anti-NMDA-R and anti-VGKC-complex antibodies and treated with immunotherapies. After immunotherapy, their neuropsychiatric symptoms were partially improved or had nearly remission. Anti-NMDA-R antibodies were detected in case 1, 2, 3 and 7. Anti-VGKC-complex antibodies were detected in case 1 and 4. Although anti-NMDA-R and anti-VGKC-complex antibodies were not detected in case 5 and 6, they were suspected to be associated with unknown autoimmune mechanisms because of their clinical symptoms, complications of neoplastic disease and response to the immunotherapy.

Conclusion : All cases presented psychiatric symptoms which resemble the ones of schizophrenia. Since autoimmune limbic encephalitis has possibilities developing life-threatening respiratory failure, psychiatrists should have correct knowledge about clinical course and treatment options for early diagnosis and intervention.

POSTER (P2-G14)

Vasculardiametersin CA1 area of hippocampus and memory retention in SpragueDawley rats post vascular cognitive impairment induction and after treatment with olanzapine

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Objectives This study was aimed to examine the effect olanzapine administrations on CA1 blood vessels and memory retention in *Sprague Dawley*rats after VCI induction.

Methods This study was a quasi experimental study with a post test only control group design. Subjects were male *Sprague Dawley* rats weighing 200-250 grams. VCI was induced with bilateralcommoncarotidarteryoclusionmethod. Memory retention was measured with *novel object recognition test* (NORT). Each group received intramuscular injection of olanzapine (2mg/kgBW) and aqubidest injection (sham and control) for three days. The brains were then evacuated and analyzed histopathologically for vessels diameter.

ResultsVascular analyses showed that vessel diameters was greater in olanzapine groups and smallest in the sham group. But the difference was not statistically significant. There were no significant difference in the time spent exploring old and new objects for all groups ($p > 0.05$). Comparisons between groups showed similar results. Control group spent more time exploring new objects as shown by DI value, but it was not statistically significant.

Conclusion The administration olanzapine did not significantly affect the blood vessel diameter in CA1 and rat cognition post VCI induction.

POSTER (P2-G15)

Associations between polymorphisms close to the cAMP responsive element binding protein 1 (CREB1) gene and the activating transcription factor 2 (ATF2) gene and fentanyl sensitivity

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Abstract

Background: Our previous study reported that genetic polymorphisms within a linkage disequilibrium block that spans 2q33.3-2q34 were strongly associated with the requirements for postoperative opioid analgesics after orthognathic surgery. Moreover, rs2952768 the most associated single-nucleotide polymorphism (SNP) close to cAMP responsive element binding protein 1 (CREB1) gene in this region was significantly associated with the expression level of CREB1 mRNA. Among CREB family genes the Activating transcription factor 2 (ATF2) gene is relatively located near the CREB1 gene around 2q31-33. ATF2 was previously called CREB2, ATF2 gene encodes a kind of activating transcription factor which is CRE binding transcription factor similar to CREB1. Thus, the present study examined associations between the analgesic effect of fentanyl in the preoperative cold pressor-induced pain test and polymorphisms in the ATF2 gene in 355 Japanese patients who underwent orthognathic surgery.

Results: In the present study, 33 SNPs were selected, and a total of two linkage disequilibrium blocks with six Tag SNPs (rs1153702, rs7583431, rs2302663, rs3845744, rs268214, and rs1982235) were observed in the region within and around the ATF2 gene. Thus, we further analyzed associations between these Tag SNPs and clinical data. Even after multiple testing such as Bonferroni adjustments, for the rs7583431 SNP, the analgesic effect of fentanyl in the preoperative cold pressor-induced pain test was found to be significantly greater with increase in the copy number of carried A allele (Linear-regression test, P = 0.001), although, preoperative and postoperative pain was not significantly associated with this SNP.

Conclusions: The present findings may contribute to adequate postoperative pain relief in individual patients. Although more research on the genetic factors that influence opioid sensitivity is necessary, fentanyl sensitivity may be predicted by analyzing the CREB1 and the ATF2 SNPs.

POSTER (P2-G16)

Recent Findings in the Neurobiology of Anxiety Disorders : Implications for Novel Treatments Approaches

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Anxiety disorders are complex mental disorders that place an enormous burden on individuals and society. Recent advances in basic and clinical research have shown the role of the amygdala and the cortico-striatal-thalamic-cortical circuits. Anxiety disorders are characterized by alterations in a diverse range of neurochemical systems suggesting novel approaches for drug treatments. Novel treatment that are widely studied in anxiety include serotonin and GABA system, glutamate modulators (ketamine, riluzole and D –cycloserine), α2δ ligands for voltage-gated calcium channels, corticotropin releasing factor,neuropeptide Y, and adrenergic agents. Corticotropin releasing factors concentrations which are elevated in a subset of anxiety disorders, suggests the potential utility of CRF receptor antagonists.

Novel treatment approaches to anxiety disorders seek to facilitate fear extinction rather than just suppress the fear response triggered by fear conditioning, which is how current anxiolytic drugs work. Glutamatergic receptor agonists (e.g., D-cycloserine) have an emerging role in the treatment of anxiety as facilitators of fear extinction during concurrent behavioral interventions.

POSTER (P2-G17)

Dysfunction of GPR40/FFAR1 signaling exacerbates pain behavior in mice

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Objectives: G-protein-coupled receptor 40/free fatty acid receptor 1 (GPR40/FFAR1) is activated by middle to long-chain fatty acids such as DHA, and is expressed abundantly in the central nervous system.Previously, we have shown that the activation of GPR40/FFAR1 signaling relates to the modulation of the descending inhibition of pain. Here, we investigated the involvement of fatty acid-GPR40/FFAR1 signaling in the transition from acute to chronic pain.
Methods: We used GPR40/FFAR1 knockout (GPR40KO) mice or wild type (WT) mice. A plantar incision was performed, and mechanical allodynia and thermal hyperalgesia was evaluated using von Frey filaments and plantar test, respectively. The localization of GPR40/FFAR1 was estimated by immunohistochemistry, and the levels of free fatty acids in the hypothalamus were analysed by LC-MS/MS.
Results: The repeated administration of GW1100, a GPR40/FFAR1 antagonist, had exacerbated incision-induced mechanical allodynia compared to vehicle treated mice. These mice had also significantly increased amount of phosphorylated ERK in the spinal cord after low threshold touch stimulation. The level of the long chain free fatty acids such as docosahexaenoic acid, oleic acid and palmitate, which are GPR40/FFAR1 agonists, significantly increased in the hypothalamus at two days after surgery, compared to the sham group. Furthermore, incision-induced mechanical allodynia, but not response in the plantar test, was exacerbated in GPR40KO mice compared to WT mice.
Conclusions: Our findings suggest that the dysfunction of this signaling pathway might induce functional alteration of endogenous pain control system and may be associated with the development of chronic pain.

POSTER (P2-G18)

Pharmacological and genetic inhibiton of protein kinase C δ attenuates against serotonin syndrome-induced by dextromethorphan via inactivation of 5-HT_{1A} receptor and activation of Nrf2-dependent glutathione induction; comparison with 5-HT_{1A} receptor agonist 8-OH-DPAT

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Abstract
Objective: Our pilot study showed that 5-HT_{1A} receptor mainly contributed to DM-induced serotonin syndrome in mice. Earlier reports suggested that 5-HT_{1A} receptor activates protein kinase C (PKC) in vitro. In the present study, we investigated whether the DM-induced up-regulation of 5-HT_{1A} receptor requires specific induction of PKC isoform.
Methods: Mice received a high dose of DM (80 mg/kg, i.p.). Serotonin syndrome scores were immediately evaluated over 30-min period of DM treatment. In addition, rectal temperature was measured 30 min after DM. Then, we examined changes in PKC expression of isoforms, serotonin receptors mRNA expressions, Nrf-2-dependent GSH-synthetic process, serotonin level and serotonin turnover rate after DM or 8-OH-DPAT.
Results: Treatment with DM resulted in a selective increase in PKCδ expression out of PKC isoforms, and in a significant phosphorylation in PKCδ. In addition, treatment with DM resulted in a significant production of oxidative stress. DM treatment impaired Nrf-2-dependent glutathione synthetic system (i.e., decreases in Nrf-2 nuclear translocation, Nrf-2 DNA binding activity, GSH level, glutathione-immunoreactivity, while increase in GSSG). This impairment paralleled intensity of serotonin syndrome. These signaling processes were attenuated by pharmacological (i.e., rottlerin) or genetic inhibition of PKCδ (i.e., PKCδ knockout mice).
Conclusion: PKCδ is a therapeutic target for attenuating serotonin syndrome induced by DM via modulating Nrf2 transcription factor and 5-HT_{1A} receptor

POSTER (P2-G19)

MK-801, but not naloxone, attenuates high-dose dextromethorphan-induced convulsive behaviors; possible involvement of NR2B receptor

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Objectives : Dextromethorphan (DM, 3-methoxy-17-methylmorphinan) is a dextrorotatory optical isomer of levomethorphan, a typical morphine-like opioid. Fatal poisonings due to large amounts of DM have been reported in Korea. Recently, we demonstrated that high-dose DM produced neuropatholgical features including myelinoid bodies in the hippocampus of rats. To extend our knowledge, we investigated DM-induced neuroexcitotoxic mechanism.
Methods : We have assessed whether N-methyl-D-aspartate (NMDA) receptor antagonist MK-801 or opioid receptor antagonist naloxone affects DM-induced seizure behaviors. We examined DM-induced changes in c-Fos level, proapoptotic parameters, and ultrastructural changes in the hippocampus of rats.
Results : Treatment with DM resulted in initial seizures. Seizure intensity and seizure latency induced by DM were significantly attenuated by MK-801, but not by naloxone. DM-induced increase in NR2B expression was more pronounced than that in NR1 or NR2A expression. Importantly, MK-801 significantly inhibited DM-induced NR2B receptor expression. In addition, MK-801 or NR2B receptor antagonist traxoprodil protected c-Fos expression, c-Fos immunoreactivity, proapoptotic parameters, and ultrastructural degeneration induced by DM in the hippocampus of rats.
Concusions : Convulsive behaviors associated with proapoptosis and ultrastrucrural degeneration induced by high-dose DM require NR2B/NMDA receptor activation, although we cannot rule out unknown neurotoxic effects induced by DM.

POSTER (P2-G20)

Hyperforin triggers apoptosis through a caspase-dependent pathway in hepatocellular carcinoma SK-Hep1 cells

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Objectives: Hyperforin, a polyprenylated acylphloroglucinol isolated from St. John's wort,has been shown to possess antidepressant activity and anti-cancer effect. However, whether hyperforin can induce apoptosis in hepatocellular carcinoma (HCC) cells is not ambiguous. Therefore, we investigated the anticancer effects and mechanism of hyperforin in HCC SK-Hep1 cells *in vitro*.
Methods : SK-Hep1 were treated with different concentration (0-10 □M) of hyperforin for different time. Effects of hyperforin on cell viability, apoptotic and anti-apoptotic mechanism were evaluated with 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay, flow cytometry, and western blotting assay.
Results: The results indicated that hyperforin significantly inhibits cell proliferation and enhances accumulation of Sub-G_1 phase and activation of Caspase-3.
Hyperforin also reduces expression of anti-apoptotic and proliferative proteins X-linked inhibitor of apoptosis protein (XIAP) and Cyclin-D1 in SK-Hep1 cells. Student's t-test was used for statistical analysis.
Conclusion: We suggested that hyperforin triggers apoptosis through a caspase-dependent pathway in HCC SK-Hep1 cells.

POSTER (P2-G21)

CROSS CULTURAL ASPECTS OF PSYCHOPHARMACOLOGY: Relevancies for Indonesia from a Pharmacogenetics Perspective

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Objective: The objective of this review was to provide evidence for cross cultural psychopharmacology of antipsychotics and discuss its relevancies for Indonesia.
Methods: We searched for literature discussing cross cultural aspects of antipsychotic treatment within the last 10 years with keywords cross cultural, psychopharmacology, and pharmacogenetics in Pubmed and SCOPUS database. We omitted keyword Indonesia since its produce no results. We selected only relevant articles.
Results: Based on published literatures, we found that culture will affect the presentation of psychiatric disorders and diagnoses made by psychiatrist. This will affect the drugs used for the treatment. The genetic variations contribute to drugs metabolism and efficacy of drugs used to treat psychiatric disorders. Genetic content of certain culture will interact with various environmental factors. Epigenetic regulations also played similar role. Both genetic and epigenetic factors contribute to the etiology of psychiatric disorders, drug metabolism, and vulnerability to undesired effects of psychotropic. They contribute to both the disorder presentations and drug metabolisms used to treat them. Indonesia is a country of various culture and diverse environmental factors. The same drugs might produce different outcome in different region in Indonesia which in turn affect the prescription pattern. Indonesian psychiatrists should take these into account when treating their patients. Indonesian policy maker should also consider these in providing drugs supply in various regions in Indonesia.
Conclusion: Culture can influence disorder presentation, drug metabolism, and prescription pattern. Genetic and epigenetic factors contribute to the variability of psychotropic responses and vulnerability to side effects. These should be taken into account in psychiatric disorders management.

POSTER (P2-G22)

Association between genetic polymorphisms in $Ca_v2.3$ (R-type) Ca^{2+} channels and fentanyl sensitivity in patients undergoing painful cosmetic surgery

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Objectives: Individual differences in the sensitivity to fentanyl, a widely used opioid analgesic, lead to different proper doses of fentanyl, which can hamper effective pain treatment. Voltage-activated Ca^{2+} channels (VACCs) play a crucial role in the nervous system by controlling membrane excitability and calcium signaling. $Ca_v2.3$ (R-type) VACCs have been especially thought to play critical roles in pain pathways and the analgesic effects of opioids. However, unknown is whether single-nucleotide polymorphisms (SNPs) of the human *CACNA1E* (calcium channel, voltage-dependent, R type, □1E subunit) gene that encodes $Ca_v2.3$ VACCs influence the analgesic effects of opioids.
Methods: We examined associations between fentanyl sensitivity and SNPs in the human *CACNA1E* gene in 355 Japanese patients who underwent painful orofacial cosmetic surgery, including bone dissection.
Results: We first conducted linkage disequilibrium (LD) analyses of 223 SNPs in a region that contains the *CACNA1E* gene using genomic samples from 100 patients, and a total of 13 LD blocks with 42 Tag SNPs were observed within and around the *CACNA1E* gene region. In the preliminary study using the same 100 genomic samples, only the rs3845446 A/G SNP was significantly associated with perioperative fentanyl use among these 42 Tag SNPs. In a confirmatory study using the other 255 genomic samples, this SNP was also significantly associated with perioperative fentanyl use. Thus, we further analyzed associations between genotypes of this SNP and all of the clinical data using a total of 355 samples. The rs3845446 A/G SNP was associated with intraoperative fentanyl use, 24 h postoperative fentanyl requirements, and perioperative fentanyl use. Subjects who carried the minor G allele required significantly less fentanyl for pain control compared with subjects who did not carry this allele.
Conclusions: Although further validation is needed, the present findings show the possibility of the involvement of *CACNA1E* gene polymorphisms in fentanyl sensitivity

POSTER (P2-G23)

Survey of the Relationship Between Internet Use and Social isolation (Hikikomori) in Japan. - blood flow change by the RI study-

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The Internet was originally designed to facilitate research activities. However, there has been a dramatic increase in the use of the Internet for education, entertainment, including video games. problematic internet use and related behaviors have been attracting the attention of mental health researchers and clinicians, although this field is still in its infancy.
Social isolation (Hikikomori) has increasingly become a problem in Japan and has been hypothesized to be related to problematic internet use.

Particularly amongst students, problematic internet use may be a major factor of social withdrawal. We conducted a survey of internet addiction and social withdrawal among students for different purposes to examine this hypothesis. And evaluate their blood floor level by the nuclear medicine scan. Methods: Subjects were 864 high school students for 5 different cities from Japan. And divided into three group for different purposes (1: Online game, 2: Social networking service(SNS), 3: The others). To examine the relationship between internet addiction and social withdrawal, we administered the Internet Addiction Test (IAT) and the UCLA Loneliness Scale (ULS), a measure of social isolation, to all subjects. And Focus on the severe case, we conduct a RI survey using a 3D-SSP assay. Results: Online game group tended to score higher than SNS group on the IAT (Online game μ= 50.7, SNS μ = 44.9). And online game group tended to score higher on the ULS than SNS group (Online game μ=49.2, SNS μ =36.2). For online game users considered addictive internet users, we found a significant correlation between the ULS and the IAT ($r=0.682$, $p<0.05$), suggesting that social isolation and internet addiction are associated with each other. Focus on the high IAT and ULS group, we found a significant reduction of the blood flow at medial frontal lobe. We will show the detail contents in this presentation.

POSTER (P2-G24)

Complement Factor H as a Plasma Inflammatory Marker of Geriatric Depression

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Objectives : Geriatric depression may be associated with inflammation. The aim of the study was to investigate this association by determining the levels of complement component 3 (C3) and complement factor H that represent markers of inflammation in elderly individuals with depression.
Methods : A total of 152 elderly subjects (MDD group, n =76 ; controls, n = 76) were selected from the Ansan Geriatric study. Blood C3 and complement factor H level were measured. MDD was diagnosed on the basis of the DSM-IV. Severity of depression were evaluated with geriatric depression scale.
Results : Serum complement factor H level was significantly higher in MDD patients than in normal control subjects (289.51±21.16 vs 339.67±66.23, $p<0.001$). In a regression model adjusted for possible confounders, complement factor H associate with geriatric depression ($p<0.001$).
Conclusion : This study reveals that there is an association between high serum levels of complement factor H and geriatric depression. It may be suggestive of alternative pathway of complement system contributing to develop geriatric depression

POSTER (P2-G25)

Functional change of serotonin 2C receptors in N-Methyl-D-aspartate (NMDA) receptor hypofunctional condition

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Background : N-Methyl-D-aspartate (NMDA)receptor hypofunctionmay contribute to the pathophysiology of schizophrenia. Clozapine, a highly effective treatment for schizophrenia, targets serotonin 2C receptors (5-HT2CR) with high affinity. 5-HT2CR modulatedopamine release. The interaction between 5-HT2CR and dopamine in an NMDA receptor hypofunctional condition, however, is not fully understood. We evaluated 5-HT2CR function for dopamine levels in an NMDA receptor antagonist-induced rat model of schizophrenia.
Method : Schizophrenia model rats were treated chronically with the NMDA receptor antagonist MK-801. We prepared four groups: 1) Naïve rats with single administrationof MK-212; 5-HT2CR agonist, 2) Naïve rats withsingle administrationof MK-801, 3) ChronicallyMK-801-treated rats withsingle administrationof MK-212, and 4) ChronicallyMK-801-treated rats withsingle administrationof MK-801. Extracellular dopamine levels in the prefrontal cortex (PFC) were measured using *in vivomicrodialysis*.An open field test was used for behavioral assessment
Results : The PFC dopamine levelwas significantly increased by single administration of MK-801 in naïve rats, but not inchronically MK-801-treated rats.The PFCdopamine level was not affected by single MK-212 administration in naïve rats, but was significantly increased inchronically MK-801-treated rats. Total distance traveled in the open field test tended to be increased by single MK-801 administration in naïve rats, and was significantly increased in chronicallyMK-801-treated rats. It was not affected by single MK-212 administration in naïve or chronicallyMK-801-treated rats.
Conclusion : These findings indicate that function of 5-HT2CR is altered to regulate excitatory the PFC dopamine in NMDA receptor hypofunctional condition.

POSTER (P2-G26)

BDNF Gene Polymorphisms as A Susceptibility Factor for Schizophrenia: literature

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Background: Increasing evidence suggest that Brain-derived neurotrophic factor (BDNF)is involvedinpathophysiology of schizophrenia. The most recent meta-analysis study reported significant association between BDNF Val66Met single nucleotide polymorphism and schizophrenia. Several other SNPs were tested for the association with schizophrenia, such as 3 other tag-SNPs located in gene (rs12273539), (rs2030324 and rs10835210) with conflicting results, and therefore needs to be clarified further.
Aim : To investigate the potential association of BDNF gene polymorphisms with susceptibility to schizophrenia and its clinical symptom severity.
Methods: Literature review.
Results: A literature review with updated references demonstrated the BDNF gene polymorphism significant (P=0,005) association for valine (Allele G) with schizophrenia compared to control group in Scottish population. Met-1 haplotypehighly significant associated decreased P,1x10^{-8}, OR=0,03, upper 95% CI= 0,47, lower CI=-0,77). BDNF gene polymorphism has been linked to attention impairment was specific to schizophrenic patients, also found AA (P= 0,004; effect size 0,29)) and AC (P=0,045; effect size=0,06) genotype showed significantly associated with positive symptom. BDNF gene polymorphism may no tbea major risk-conferringagent for the development of schizophreniaperse, but this polymorphism might modulate arange of clinical features of the illness and seems to contribute to the susceptibility to schizophrenia. However, further controlled studies are needed.
Conclusion: The present literature review provides evidence for the contribution of the BDNF gene polymorphism to schizophrenia susceptibility, associated with a higher prevalence of neuropsychiatric symptoms specifically with the presence positive symptom, decreased BDNF serum levels and cognitive impairment.

POSTER (P2-G27)

GPR40/FFAR1 deficient mice increase noradrenaline levels in the brain and exhibit abnormal behavior

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Abstract
Objectives: Polyunsaturated fatty acids (PUFA) are associated with emotional function in healthy or pathological conditions. In fact, the nutritional deficiency of these fatty acids causes vulnerability to stress. Moreover, the reduction of PUFA levels in the brain are observed in subjects with neuropsychiatric disorders. However, the molecular mechanisms remain unknown. Recent studies have indicated that free fatty acid receptor 1 (GPR40/FFAR1), which is activated by middle and long chain fatty acids, contributes to physiological function in the central nervous system. We have previously demonstrated that activation of brain GPR40/FFAR1 exerts an antinociceptive effect and antidepressant-like effect. However, it is unclear whether brain GPR40/FFAR1 contributes to emotional function. In this study, we investigated the involvement of GPR40/FFAR1 in emotional behavior using GPR40/FFAR1 deficient (knockout, KO) mice.
Methods: The emotional behavior in wild and KO male mice was evaluated at 9-10 weeks of age by the elevated plus-maze test, open field test, social interaction test, and sucrose preference test. Brain monoamines levels were measured using LC–MS/MS.
Results: The EPM and open field tests revealed that the KO mice reduced anxiety-like behavior. There were no differences in locomotor activity or social behavior between the wild and KO mice. In the sucrose preference test, the KO mice showed reduction in sucrose preference and intake. The level of noradrenaline was higher in the hippocampus, medulla oblongata, hypothalamus and midbrain of KO mice.
Conclusions: Therefore, these results suggest that brain GPR40/FFAR1 is associated with anxiety- and depression-related behavior regulated by the increment of noradrenaline in the brain.

POSTER (P2-G28)

Behavioral and neurochemical abnormalities in MHCI-expressed mice

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Genome-wide association studies have implicated the major histocompatibility complex (MHC) gene region on chromosome 6 in schizophrenia. The MHC genomic region in the mouse, located on chromosome 17, is named H-2. The MHC class I (MHCI) genes, such as H-2K and H-2D in the mouse, are highly polymorphic, and the unique roles of MHCI molecules have been demonstrated in the CNS. Although recent studies have suggested the physiological significance in MHCI in neurodevelopment and synaptic plasticity, a pathophysiologic/etiologic function in schizophrenia and other neurodevelopmental disorders remain obscure. We have previously reported that polyI:C treatment in neonatal mice affects the neurodevelopment, leading to the development of schizophrenia-like behaviors in adulthood. Neonatal polyI:C treatment in mice increased the mRNA levels of MHCI including H-2K and H-2D in the prefrontal cortex (PFC). In vitro experiments revealed that polyI:C-treated astrocytes secreted exosomes containing the MHCI/H-2D and its truncated form (H-2D 1-894). To investigate the role of MHCI in astrocytes, H-2D full or H-2D 1-894 was expressed in the PFC of mice by using AAV vector under the control of GFAP promoter. Mice that had expressed H-2D full or H-2D 1-894 in astrocytes of the mPFC exhibited impairments in social interaction and novel object recognition tests. AAV-H-2D 1-894-expressed mice also showed an impairment in prepluse inhibition test. A significant increase in the number of microglial cells, and a decrease in the number of parvalbumin-positive cells as well as neuronal spine density were evident in the mPFC of H-2D full or H-2D 1-894-expressed mice. These results suggest that the expression of H-2D in astrocytes promotes the secretion via exosomes, which may lead to the proliferation of microglial cells and neuronal injury nearby, which may be associated with impairments of social and cognitive behaviors, and deficits in sensorimotor gating in mice.

POSTER (P2-G29)

Disruption of exons 2 and 3 of the Disc1 gene in the mouse is associated with elevated repetitive behavior

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INTRODUCTION : Disrupted-in-Schizophrenia 1 (DISC1) is a strong candidate gene for schizophrenia and other mental disorders that are accompanied by cognitive impairment. We previously generated mice lacking exons 2 and 3 of the Disc1 on a C57BL/6J genetic background (Disc1Δ2-3/Δ2-3 mice).
OBJECTIVE : The aim of present study is to see if mutation in Disc1 would produce impairments in visual discrimination learning and memory in mice.
METHOD : We investigated the cognitive function and effects of daily administration of an antipsychotic clozapine (1 mg/kg, intraperitoneally) in Disc1Δ2-3/Δ2-3 mice on performance in a touchscreen-based visual discrimination task. To further characterize repetitive and compulsive-like behaviors, marble-burying and nestlet shredding tests were conducted
RESULTS : Disc1Δ2-3/Δ2-3 mice exhibited deficits in the visual discrimination task, which was mainly due to high perseverative response compared to the controls. The daily treatment of clozapine ameliorated the impairment by normalizing the preservative behavior. Disc1Δ2-3/Δ2-3 mice exhibited a significant increase in the number of marbles buried in a marble bury test and shredded more nestlets in a nestlet shredding test compared with wild-type mice.
CONCLUSION : These results suggest that the Disc1 mutation in mice is associated with elevated repetitive and compulsive-like behaviors that could be ameliorated by treatment with clozapine.

POSTER (P2-G30)

Lower brain pH as a shared endophenotype of psychiatric disorders

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Objectives: Accumulating evidence indicates that a substantial part of genetic influences on schizophrenia, bipolar disorder (BD), and autism spectrum disorder (ASD), overlap, suggesting a common biological basis underlying the diseases. Lower pH is a well-replicated finding in the postmortem brain of patients with schizophrenia and BD. Interpretation of the data, however, is controversial as to whether it reflects a primary feature of the diseases or is a result of confounding factors such as medication, postmortem interval, and agonal state.
Methods: We first reevaluated the pH of the postmortem brains of patients with schizophrenia and BD by conducting a meta-analysis of existing datasets from nine studies. Then, by using animal models of psychiatric disorders, we tested the hypothesis that lower brain pH exists in these brains compared to controls to provide support for the proposal that lower pH is part of the pathophysiology or is an endophenotype of these brains disorders. We used three mouse models of schizophrenia (Schnurri-2 knockout [KO], forebrain-specific calcineurin KO, and Neurogranin KO mice) and one of BD (Camk2a heterozygous KO [HKO] mice), as well as an ASD model (Chd8 HKO mice) to measure the pH, lactate, and the related metabolite levels in brain homogenates. All mice were drug-naïve with the same postmortem interval and agonal state at death.
Results: Two-way ANOVA revealed that the brain pH was significantly lower in patients with schizophrenia and BD as compared to control subjects (n = 240, 147, 280, respectively). In the animal studies, all mice used to model psychiatric disease showed significantly lower pH in the postmortem brains as compared to the corresponding controls. These mouse strains also had a significantly higher lactate level in their brains.
Conclusions: Our results suggest that lower pH and increased lactate level are a pathophysiology of the diseases rather than artifacts.

POSTER (P2-H1)

Pharmacometabolomic changes following antidepressants in patients with major depressive disorder

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Objectives : The main purpose of the present study is to characterize metabolomic changes induced by 8 weeks treatments with antidepressants in patients with major depressive disorder (MDD).
Method s: We conducted a non-targeted metabolomic profiling in a cohort of 33 drug-naïveMDD patients and 33 non-psychiatric controls using capillary electrophoresis time-of-flight mass spectrometry (CE-TOFMS). Among the 33 MDD patients, 10 patients provided blood samples not only at baseline but also after 8 week-treatment. The institutional ethics committee of the University of Tokushima Graduate School approved the current study and all subjects signed written, informed consent forms.
Results : Among 263 metabolites, 43 metabolites showed significant differences between MDD patients and controls. Of these 43 metabolites,significant pharmacometabolomicalterationsfollowing 8 week-treatment were observed in 3 metabolites.
Conclusions : Our results may provide further insight into the molecular mechanisms of drug treatments and the pathophysiologyof MDD.

POSTER (P2-H2)

Dentate gyrus cells count and impulsivity in Sprague Dawley rats post *vascular cognitive impairment* induction and after treatment with haloperidol and olanzapine

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Objectives : The objective of this study was to measure cell count the hippocampus post *vascular cognitive* impairment (VCI) and after treatment with haloperidol and olanzapine.
Methods : This study was a quasi experimental study with a post test only control group design. Subjects were male Sprague Dawley rats weighing 200-250 grams. VCI was induced with bilateral carotid ligation method. Each group received intramuscular injection of haloperidol (1mg/kgBW), olanzapine (2mg/kgBW) and aquabidest injection (sham) for three days. After treatment, the rats were tested for impulsive behavior using cliff jumping tests. The brains were then evacuated and analyzed histopathologically for cell counts in dentate gyrus.
Results : Analyses results showed that there were no significant differences in the cell counts of granule cells in the dentate gyrus in all groups. Impulsivity was lower in the group treated with haloperidol (0.43) and relatively similar for olanzapine and sham (0.57 and 0.56), suggesting behavioral inhibition in group treated with haloperidol. These differences were not statistically significant.
Conclusions : The benefit of atypical antipsychotic over typical antipsychotic in term of safety was not shown in our study as both have similar effect on cell survivability after VCI induction. Typical have small advantage over atypical antipsychotics in term of impulsivity control.

POSTER (P2-H3)

The ubiquitination of serotonin transporter in lymphoblasts derived from fluvoxamine-resistant depression patients

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Objectives : There is insufficient serotonergic neuronal function in the pathophysiology of depression. The serotonin transporter (SERT) plays a critical role in terminating the function of serotoninergic neurons. This is linked to vulnerability to depression and is an important target for antidepressants. The expression of SERT in the lymphocytes and platelets is associated with their expression in central nervous system. Most of the clinical studies that have analyzed the role of SERT in depression have focused on absolute expression of SERT in the brain or peripheral tissue. Our study has shown that the SERT protein is ubiquitinated, which has been previously implicated through the observation of SERT stability and depressive behavior in mice.
Methods: We have used lymphoblasts derived from the peripheral blood lymphocytes to quantitatively examine SERT protein expression and ubiquitination in fluvoxamine-responsive and fluvoxamine-resistant depression patients.
Results: We found that the SERT protein increased in the fluvoxamine-resistant depression patients. Ubiquitinated SERT protein decreased in the fluvoxamine-resistant depression patients. The proteasome inhibitor failed to increase the expression of the SERT protein in both fluvoxamine-responsive and resistant depression patients.
Conclusions: These findings suggest that the downregulation of the ubiquitination of SERT protein induces insufficient degradation of SERT by proteasome, which resulted in the upregulation of SERT protein in fluvoxamine-resistant depression patients. Although further studies with various populations will be required to generalize results, SERT protein expression, ubiquitination, and the responsiveness of SERT expression to proteasome inhibitor are potential biomarkers for the diagnosis of depression and antidepressant efficacy.

POSTER (P2-H4)

On the importance of emergency intervention : A case series of Neuroleptic Malignant Syndrome in Sanglah General Hospital, Denpasar, Bali

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Objectives : Outcomes of the patients with neuroleptic malignant syndrome (NMS) have varied but determinants of this outcome have not been clearly understood. This study was therefore conducted to provide a descriptive account on aspects that might play role in determining the outcomes among patients with NMS.
Methods : Case series.
Results : Three cases of NMS were defined: 1) 39 year old male diagnosed with delirium et causa intracranial process DD impending NMS with a medication history of three days 5 milligrams haloperidol given every 12 hours; 2) 40year old female diagnosed with delirium et causa meningoencephalitis DD NMS with a medication history of fifteen days 2.5 milligrams haloperidol given every 12 hours;. 3). 19 year old male diagnosed with organic catatonic disorder DD NMS with a medication history of twice 5mg intramuscular injection of haloperidol. On case 1 and 3, early interventions included the cessation of antipsychotics, supportive measures, and the administration of diazepam, and both patients survived. On case 2, however, the confusion of NMS with meningoencephalitis had led to delayed recognition and therapy that led to patient's death.
Discussions : On cases 1 and 3, the patients had favorable outcomes due to early recognition which led to immediate cessation of antipsychotic medications followed by concordant intervention for the diagnosis of NMS. On case 2, however, delayed recognition and therapy have led to poor outcome.This emphasizes the importance ofimmediate cessation of antipsychotic medications followed by supportive measures for the management of NMS.
Conclusions : Early recognition followed by appropriate emergency intervention might lead to favorable prognosis among patients with NMS.

POSTER (P2-H5)

Bradycardia: an adverse effect caused by administration olanzapine

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BACKGROUND:
Olanzapine, an atypical antipsychotic, is often regarded as a safe choice for psychosis management. Olanzapine with complex pharmacological actions on different receptors (dopamine, serotonin, muscarinic) and moreover with additional inhibitory effects on Na+, Ca2+ channels may exert various antiarrhythmic/proarrhytmic actions and their effects on the QT interval *in vivo* may be quite variable depending on the animal species and experimental model. We hereby report a case that presented with catatonia, bradycardia, and hypotension.

CASE:

A 21-year-old male presented to psychiatry ward at Sanglah Hospital with chief complaints bradycardia and hypotension since 2 days before admitted. Patient has been diagnosed with schizophrenia catatonic dan taking olanzapine 10 mg orally once a day for last 8 days. Patient experiencing hypotension and ECG result was sinus bradycardia (51 times per minute). Routine blood analysis, EEG, CT Scan, lipid profile within normal limit. Olanzapine was suspected drug causing bradycardia, so it was replaced with Risperidone 2 mg twice a day orally. Patient showed recovery of symptoms within 2 days after stopping olanzapine.

CONCLUSIONS:
Olanzapine should be consider as one of suspected drug causing bradycardia in treatment psychotic patients. It is very important to monitor the cardiac side-effects in the patients who are using Olanzapine and ECG monitorization is equally important. Although further similar evidence from observational studies and/or reports are needed to establish the causal relationship

POSTER (P2-H6)

Rapamycin treatment of impaired social behavior in adolescent *Tsc2*$^{+/-}$ mice

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Tuberous sclerosis complex (TSC) is an autosomal dominant neurocutaneous disorder caused by a mutation in either *TSC1* or *TSC2*. Patients with TSC present neurologically early-onset epilepsy and tuberous-sclerosis-associated neuropsychiatric disorders (TAND) such as autism spectrum disorder (ASD) and intellectual disability from the childhood. We previously reported adult *Tsc2* heterozygous knockout (*Tsc2*$^{+/-}$) mice display ASD-like social deficits which were recovered by mTOR inhibitor, rapamycin. In the present study, we examined the seizure susceptibility and effects of rapamycin on ASD-like behaviorsin *Tsc2*$^{+/-}$ mice in the young period to establish an early intervention model of TAND.

We administered *N*-methyl-D-asparate (NMDA), kainic acid (KA), or pentylenetetrazole (PTZ) to *Tsc2*$^{+/-}$ mice on postnatal day (P) 13 and evaluated seizure severity. Developmental milestones were also analyzed between P4-28 in *Tsc2*$^{+/-}$ mice. Reciprocal social interaction test was conducted in P31-35 and three-month-old *Tsc2*$^{+/-}$ mice with rapamycin treatment.

No spontaneous seizures were identified in *Tsc2*$^{+/-}$ mice. Administration of NMDA, KA, or PTZ induced seizures specific to each drug with no significant difference in seizure severity between the wild type and *Tsc2*$^{+/-}$. *Tsc2*$^{+/-}$ mice exhibited no developmental delay of physical landmarks, reflexes, and motor skills, but showed a reduction in reciprocal social interaction time on P31-35 which continued till three months. This social impairment was improved by rapamycin treatment both on P31-35 and in the adulthood.

Our findings suggested *Tsc2*$^{+/-}$mice had social impairment without increased seizure susceptibility from the young period in the mTOR dependent manner. *Tsc2*$^{+/-}$ mice can be useful for investigating early intervention for TAND and other types of ASD related to mTOR signaling.

POSTER (P2-H7)

Psychosis induced by Corticosteroid (Methylprednisolone) Use : a case report

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Background : Psychiatric symptoms are not uncommon complications of the corticosteroid treatment. The prevalence of corticosteroid-induced psychotic disorders varies around 5–6%. Despite its relatively common occurrence, studies about clinical features of corticosteroid use have been limited in Indonesian patients. This study was therefore conducted.
Method : Case Report
Results& Discussion : The patient was female, 55 years old, who was hospitalized due to auditory hallucination, persecutory delusion, and increased psychomotor activity since one week prior to admission. No previous nor family history and no known stressor was found. Her medical history revealed a diagnosis of bullous pemphigus two months before admission with current treatment of 32 miligrams methylprednisolone per day. Her psychotic symptoms were then attributed to this medication use, and she was treated with haloperidol 10 miligrams/day.
Higher risk of psychotic symptoms has been found in patients using more than 30 miligrams/day, and this might be case with the patient. However, most corticosteroid-induced symptoms start during the first few weeks after treatment initiation but in this patient, the symptoms appeared much later. Quite likely, this is due to the relatively low dose used compared to the dose used by the subjects in the literature.
Conclusion : The use of more than 30 miligrams/day methylprednisolone might put the patient at risk of experiencing psychotic symptoms and the onset of these symptoms might be dose-dependent.

POSTER (P2-H8)

Inhibition of mTOR improves autism-like behaviors in mice *in utero*exposed to valproic acid

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The mammalian target of rapamycin (mTOR) signaling pathway has a crucial role in cell metabolism, growth and proliferation.Overactivationof mTOR has been reportedly implicatedin the pathogenesis of particular forms of syndromic autism spectrum disorder (ASD), such as tuberous sclerosis complex (TSC). Treatment with rapamycin, an mTOR inhibitor, improved social deficits in mouse models of TSC. Prenatal exposure of valproic acid (VPA), an anticonvulsant drug,causes increased incidence of ASD. Rodent pups exposed *in utero* to VPA have been used as an animal model of ASD. Recently, enhanced mTOR signaling pathway was shown in rodents exposed *in utero* to VPA. In the present study, we investigated the effect of rapamycin on social deficits of mice exposed *in utero* to VPA (VPA-exposed mice). We subcutaneously injected pregnant mice on gestational day 12.5 with a dose of 600 mg/kg of VPA, and used the pups as ASD model mice. The mice were injected rapamycin (10 mg/kg) or vehicle (10 ml/kg) intraperitoneallyfor 2 consecutive days. Social interaction test was conducted both in adolescence and adult. The VPA-exposed mice treated with vehicle showed decreased social interaction time compared to control mice, and the VPA-exposed mice treated with rapamycin showed improvement in their social deficits in both adolescence and adult. Furthermore, we analyzed expression of mRNA and phosphorylation of proteinsin the brains of adult mice. The VPA-exposed mice treated with vehicle showed decreased expression of *Tsc1*, a causal gene of TSC, and elevated S6 phosphorylation levels compared to control mice. Rapamycin treatment suppressed S6 phosphorylation in VPA-exposed mice. These results suggest that mTOR signaling pathway is associated with autism-like behaviors in the VPA-exposed mice and rapamycin has potential to provide an effective treatment for ASD patients with mTOR signaling pathway impairment.

POSTER (P2-H9)

Immediate Versus Gradual Discontinuation in Antipsychotic Switching : A Systematic Review and Meta-analysis

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Background : Antipsychotic switching is routine in clinical practice, although it remains unclear which is a safer switching method: immediate discontinuation of the current antipsychotic or a gradual tapering approach.The first strategyhas been implicated in rebound/withdrawal symptoms and emergence/exacerbation of symptoms whereas the gradual approach is thought to pose a risk of additive or synergistic side effects if employed in the context of a crossover approach. In order to address this clinically important question, we conducted a systematic review and meta-analysis of randomized controlled trials examining immediate vs. gradual antipsychotic discontinuation in patients with schizophrenia undergoing a switch.
Methods : MEDLINE, Embase, and Cochrane Central Register of Controlled Trials were systematically searched (last search: August 30, 2016). Randomized controlled trials including patients with schizophrenia and/or schizoaffective disorder, as well as both immediate and gradual discontinuation arms were selected.Data on clinical outcomes, including study discontinuation, psychopathology, extrapyramidal symptoms, and treatment-emergent adverse events, were extracted.
Results : A total of 9 studies involving 1,416 patients that met eligibility criteria were included in the meta-analysis. No significant differences in any clinical outcomes were found between the 2 approaches (all *Ps*>0.05). Sensitivity analyses revealed that the findings remained unchanged in the studies whereswitching to aripiprazole was performed or where immediate initiation of the next antipsychotic was adopted.
Conclusions : In practice, it is commonplace to see clinicians employ gradual discontinuation of the existing antipsychotic as part of switching when transitioning to a new agent. Intuitively, this would seem the preferred strategy and it has made its way into teaching as a strategy that will reduce risk of symptom exacerbation and/or withdrawal side effects. Current evidence, however, fails to support this line of thinking.

POSTER (P2-H10)

Association study of metabolic syndrome andpolymorphism of serotonin receptor genes in schizophrenic patients using atypical antipsychotics

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Objectives: Metabolic syndrome (MetS) is recognized as a cluster of risk factors for cardiovascular diseases (CVD). People with MetS are more likely to develop cardiac vascular diseases and type-2 diabetes. Studies on Caucasians revealed that the prevalence of MetS was higher in schizophrenic patients and the risk of MetS was implicated with the use of atypical antipsychotics. Further studies found an association between MetS and serotonin receptor gene polymorphisms, suggesting that the genes corresponding to serotonin receptors are good candidates for pharmacogenetic studies of MetS associated with atypical antipsychotics. The relationship between the risk of MetS and serotonin receptor gene polymorphisms remains obscure in Taiwanese schizophrenic patients receiving atypical antipsychotics treatment. This study aims to determine the variation of serotonin receptors genes (HTR2A, HTR2B and HTR2C) in Taiwanese schizophrenic patients and to investigate whether the genetic differences of serotonin receptors relate to the risk of MetS that is associated with atypical antipsychotics treatment.
Methods: This study enrolled 181hospitalized schirophrenic patients who had taken clozapine, quetiapine or risperidone for more than 3 months. A cross-sectional assessment of anthropometric and metabolic parameters has been performed in accordance with the criteria of 2005 International Diabetes Federation (IDF) Asia. Single nucleotide polymorphism analysis was carried out by TaqManR SNP genotyping assays using the genomic DNA isolated from buccal swab. Differences in the means of continuous variables were evaluated using Student's t-test or one-way ANOVA. The categorical data were analyzed using the chi-square test. Likelihood ratio forward stepwise logistic regression analyses were conducted in genetic analysis.
Results: The rs2316100 SNP showed a significant association with MetS and homozygosity of T allele was associated with an increased risk of MetS. Whereas, the A-A type of rs6313 in the HTR2A gene significantly decrease the risk of MetS.
Conclusions: We have demonstrated a correlation between the HTR2A and HTR2C gene polymorphisms and the susceptibility of Taiwanese schizophrenic patients to MetS when they were treated with atypical antipsychotics. It is anticipated that the genetic variations of the serotonin receptors can help us tellwho are vulnerable to MetS following atypical antipsychotics treatment. These information may improve the efficacy and safety of atypical antipsychotics in clinical practice. Large population-based prospective studies are required to validate our findings.

POSTER (P2-H11)

Simvastatin as Adjuvant Therapy to Fluoxetine in Patients with Depression

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Background: Fluoxetine is one of the most prescribed and used antidepressant worldwide. Despite of that fact around 30% patients drops out within the first week of the medication due to the lack of progress and unwanted side effect. This highlights the need of new and more effective strategies. Among various methods proposed by researchers in effort to address to this issue, augmentation medication has gained popularity in the recent years. Studies have shown that statins decrease depressive symptoms in certain groups of patients, an effect that mostly attributed to their anti-inflammatory and neurotransmitter modulatory potential. We aimed to investigate the antidepressant effects of simvastatin as adjuvant therapy in patient with depression.
Method: In this double-blind-placebo-controlled clinical trial 20 patients were randomly allocated to recieve simvastatin 10mg or placebo as an adjunct to fluoxetine 20mg for 2 weeks. Patients are evaluated with Hamilton Depression Rating Scale (HDRS) at baseline and 2 weeks after. The data will be compared between the two groups.
Results: Both groups showed a significant decrease of depression score on Hamilton Depression Scale after 2 weeks. However the treatment group decreased depresion score more than placebo group [8.2(±3.22) vs 5.3(±1.41) p<0.01].
Conclusions: Simvastatin seems to be an effective adjuvant therapy for patients suffering from depression. However , more confirmatory studies are warranted.

POSTER (P2-H12)

Is there any difference of incidence of the Restless Leg Syndrome between antipsychotics?

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Introduction : It has been reported that schizophrenics experience the restless leg syndrome (RLS) more frequently than healthy people. Antipsychotics may be one possible cause of this frequent RLS in patients. Authors investigated the prevalence and characteristics of RLS in schizophrenics, and whether frequency of RLS in schizophrenics varies in different antipsychotics.
Method : 244 patients with schizophrenia (male = 87, female = 157) were included in this study. The International Restless Leg Syndrome Study Group (IRLSSG) diagnostic criteria and IRLSS rating scale were used for diagnosis and evaluation of severity of the RLS. We assessed psychopathology using the positive and negative scale for schizophrenia (PANSS), and evaluated sleep disturbance using the Athens insomnia scale (AIS).
Results : Among 244 patients, 45(18.4%) met the IRLSSG diagnostic criteria. Also, 79(32.4%) met at least one of the IRLSSG diagnostic criteria. Most of patients having RLS experienced less than once per week. RLS lasted less than 1 hour per day in 58.2% of patients experiencing RLS. The incidence of the RLS in each medication was as follows; aripiprzole 4(13.3%), risperidone 9(14.5%), amisulpiride 9(31.0%) olanzapine 6(14.3%), clozapine 3(12.5%), quetiapine 3(11.1%) and haloperidol 11(35.7%) (P<0.05). Each medication showed different severity of RLS (P<0.05). Amisulpirode and haloperidol tended to be higher in severity of RLS than other antipsychotics. The patients experiencing RLS scored higher in PANSS and in the AIS than the patients with no RLS symptoms(P<0.05).
Conclusions : Different antipsychotics showed different incidence of RLS. The severity of RLS varied in different antipsychotics. Drugs with higher antidopaminergic effect revealed the tendency of higher incidence and higher severity of RLS. This finding indirectly supports dopamine depletion hypothesis of RLS. Further study with experimental design for the causal relationship between the kind of antipsychotics and RLS is necessary.

POSTER (P2-H13)

Pharmacokinetics of mirtazapine included glucuronidated metabolites in Japanese psychiatric patients

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Objectives: This study evaluated the factors including*CYP2D6* polymorphismon the steady-state plasma concentrations of mirtazapine (MIR) and its metabolite N-desmethylmirtazapine (DMIR), 8-OH-MIR and their glucuronidated metabolites in Japanese psychiatric patients.
Patients and Methods: The subjects were 82 Japanese patients treated with racemic MIR. The steady-state plasma concentrations of MIR and DMIR 8-OH-MIR were measured using high perfgormance liquid chromatography. The plasma concentrations of glucuronidated metaboliteswere by their concentrations after hydrolysis with beta glucrunonidase minus their concentrations without hydrolysis.The CYP2D6 genotypes were determined by polymerase chain reaction.
Results: Plasma concentrations of 8-OH-MIR, 8-OH-MIR glucuronide (8-OH-MIR-G), DMIR, MIR, MIR glucuronide (MIR-G) were as follows (nmol/L/mg/kg; corrected for dose and body weight; mean±SD, range).8-OH-MIR; 3.50±5.61 (3.50-39.10), 8-OH-MIR-G; 165.55±197.29 (3.20-1234.41), DMIR; 62.84±50.99 (1.99-217.64), MIR; 113.08±85.50 (6.03-437.54), MIR-G; 111.42±128.56 (4.52-722.82). Multiple regression analysis (stepwise method) was performed to analyze the relationship between subject-independent variables (sex, age, smoking status and number of mutated CYP2D6 alleles) and subject-dependent variables such as plasma concentrations of MIR, DMIR, 8-OH-MIR andMIR-G, 8-OH-MIR-G. Multiple regression analysis revealed that smoking had a significant factor correlated to plasma concentration of MIR (corrected for dose and body weight) (p=0.040). The final model was described by the following equation: Plasma concentration of MIR (corrected for dose and body weight) = 291.17 - 92.71 × smoking (smoking=1, smoking=0) (R= 0.23, p=0.040, R^2=0.054).
Multiple regression analysis also revealed that age (year old) had a significant factor correlated to plasma concentration of DMIR (corrected for dose and body weight) (p=0.018). There were no significant factors correlated to in plasma concentrations of glucuronide metabolites in the multiple regression analysis.
Conclusion: Glucuronidation is supposed to be important pathway for excretion of 8-OH-MIR.Smoking habit might affect pharmacokinetics of racemic MIR in Japanese patients.

POSTER (P2-H14)

The association between demographic and disease treatmentcharacteristics of Multi Drugs Resistant Tuberculosis (MDR TB) patient with cycloserine induced psychosis

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Objective: Psychiatric problems are common to those treated with cycloserine. The objective of this study was to determined the association between demographic and disease treatment characteristics with cycloserine induced psychosis in MDR-TB patients.
Method: This study was a descriptive analytic study with a cross sectional design. Data were taken secondary from medical record of MDR-TB patients admitted to Sardjito Hospital from 2013 to 2016. The sampling method used was whole sampling. The association between cycloserin induced psychosis and demographic and disease treatment variables such as age group, sex, marital status, education, weight, dose of cycloserin, was statistically analyzed. Significance level was defined at $p < 0,05$.
Result: Demographic and disease treatment characteristics might be an important variables associated with the development of cycloserine induced psychosis. Associations between these variables and cycloserine induced psychosis will be analyzed and presented as the results of this study. This study is still in progress and results will be reported later.
Conclusion: Understanding the variable associated with the development of cycloserine induced psychosis is important in order to provide a better preventive measure as well as to reduce morbidity and mortality.

POSTER (P2-H15)

A case of sibutramine causing acute psychosis

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Background/Objective : Sibutramine, a sympathomimetic drug, exerts its effects on weight loss through the blocking of norepinephrine & serotonin reuptake. Case reports on psychiatric symptoms secondary to sibutramine use have been published. There have also been reports on slimming products adulterated with sibutramine, causing psychosis. We report a case of catatonia, likely recurrent, caused by ingestion of herbal slimming products purchased over the internet.
Case report : A 30-year-old Malay lady was admitted for sudden onset of odd behaviour over 3 days consisting of staring blankly into space, mutism, neglecting self-care, and purposeless motor activity. There was a significant history of two similar episodes in 2011 and 2013, with acute onset of mutism, avolition and disorganised behaviour. She was diagnosed as having a Psychotic Disorder Not otherwise Specified (NOS) both times, with complete resolution of symptoms after 3 days of Risperidone 0.5mg per day. She was completely well prior this episode, with no identifiable stressors, family history of psychiatric illness, or history of alcohol or illicit substance use. Mental state examination showed an overweight lady who was mute and perplexed. Brain imaging and blood work were unremarkable. She was commenced on Risperidone 0.5mg daily and her symptoms resolved completely in 3 days. She reported taking herbal weight loss supplements purchased online, a week prior to her admission. She had complete amnesia for the whole episode. Toxicology testing of the herbal supplement found Sibutramine to be the only active ingredient.
Ms N admitted to also taking slimming pills purchased online over the past few years, which was likely to have precipitated her psychosis on both occasions.
Discussion : This case highlights psychosis caused by taking unregulated herbal slimming products, which did not list sibutramine as an active ingredient. Physicians need to be aware of unregulated slimming product use as a possible cause of acute catatonia.

POSTER (P2-H16)

Comparison of cell counts in hippocampus of Sprague Dawley rats post VCI induction after treatment with haloperidol and olanzapine

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Aims The objective of this study was to measure cell count the hippocampus post VCI and after treatment with haloperidol and olanzapine.
Methodology This study was a quasi experimental study with a post test only control group design. Subjects were male Sprague Dawley rats weighing 200-250 grams. VCI was induced with bilateral carotid ligation method. Each group received intramuscular injection of haloperidol (1mg/kgBW), olanzapine (2mg/kgBW) and aquabidest injection (sham and control) for three days. The brains were then evacuated and analyzed histopathologically for cell counts in the CA1, CA3, and dentate gyrus.
Results Analyses results showed that the cell counts in CA1 was higher in haloperidol group (60.94 vs 59.44), in CA3 was higher in the olanzapine group (37.50 vs 35.13), and in dentate gyrus was higher in haloperidol group (133.38 vs 122.19). But these differences were not statistically significant.
Conclusion Although atypical antipsychotics have a better safety profile compared to typical antipsychotics, but their effects on cell survivability after VCI induction was not significantly different.

POSTER (P2-H17)

Effect of fluvocamine on plasma interleukin-6 in major depression

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Objectives
The etiology of depression remains unknown.There is,however, a growing body of evidence that cytokines are involved in the pathophysiology of depression. The aim of the present study is to investigate the effects of fluvoxamine on plasma interleukin-6 (IL-6) levels and on clinical improvement of the depressive state.
Methods
Thirty patients who met the DSM-IV criteria for major depressive disorder (MDD) were enrolled in the study. Thirteen were male and 17 were female, and their ages ranged from 26to 70(mean ± SD = 45.0 ± 14.2) years. The patients were treated with fluvoxamine for 8 weeks. The dosages offluvoxaminevaried among the patients and, based on ethical considerations, were not fixed.
Results
The fluvoxamine doses were positively related to plasma fluvoxamine levels ($r=0.8798$, $p<0.001$). A significant correlation was observed between the patients' plasma IL-6 levels and their HAMD17 scores ($r = .4555$, $p = 0.0010$) . A positive correlation was found between the delta plasma IL-6 (0W-8W) and the delta HAMD17 (0W-8W) ($r=0.5226$, $p=0.002$).
Conclusions
Effect of fluvoxamine on IL-6 is partially associated with its clinical efficacy.

POSTER (P2-H18)

Breastfeeding Cessation during Antipsychotic Treatment in Postpartum Women: Is It A Must?

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Objectives: To provide empirical evidence for the continuation of antipsychotic treatment in breastfeeding mothers.

Methods: We searched for publications in Pubmed and Springer databases with keywords antipsychotics, breastfeeding and postpartum. The selection criteria were published within ten years, using human subjects, and we are able to retrieve full text.
Results: We found 238 publications and 15 journals fulfilled selection criteria. If a breastfeeding mother needs antipsychotic prescription, the choice of medication should be guided primarily by its safety profile. The publication state that some antipsychotic drugs such as haloperidol and olanzapine categorized as L2 in lactation risk category (safer).[1] Breastfeeding of infants by a mother using quetiapine, at therapeutic levels, results in low quetiapine serum levels in the infants, with no clinical adverse events reported.[2] Women who take clozapine should not breastfeed their infants, as there has been one case report of a baby developing agranulocytosis.[3]
Conclusion: Based on this review we concluded that continuation of antipsychotic treatment for breastfeeding mother should consider the risk and benefits for both the mother and infant. Although it is relatively safe, but careful precaution should be educated to the mother along with collaboration with the obstetrician and paediatrician.
Keywords: antipsychotic, breastfeeding, postpartum

POSTER (P2-H19)

Adjunctive brexpiprazole, a novel effective strategy for treating Major depressive disorder? : Systematic review and Meta-analysis

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Objectives: Brexpiprazole was approved for adjunctive treatment in major depressive disorder (MDD) in 2015. Because only a small number of randomized controlled trials have investigated the use of brexpiprazole in MDD, we performed a meta-analysis.
Methods: We systematically searched literatures in PubMed, Cochrane library database, EMBASE, Google scholar, and clinicaltrials.gov up to Jan 2016. The primary efficacy measure was the mean change in total Montgomery-Åsberg Depression Rating Scale (MADRS) score from baseline. Secondary efficacy measures were the mean change in total Hamilton Rating Scale for Depression (17 items) (HAM-D-17) score from baseline and the response (≥50% reduction in MADRS total score) and remission (MADRS total score ≤ 10 with ≥50% reduction) rates.
Results: Four studies fulfilled the inclusion criteria and were included in the analysis. Brexpiprazole showed superior efficacy over placebo with effect sizes (mean differences) of -1.76 (95% CI=-2.45 – -1.07) for MADRS and -1.21 (95% CI=-1.71 – -0.72) for HAM-D-17. The risk ratios (RRs) for response and remission were 1.57 (95% CI=1.29–1.91) and 1.55 (95% CI=1.22–1.96), respectively. The incidences of discontinuation due to adverse events, akathisia, and weight increase were higher in the brexpiprazole group than in the placebo group, with RR of 3.44 (95% CI=1.52–7.80), 3.39 (95% CI=2.08–5.51), and 4.36 (95% CI=2.45–7.77), respectively, and the incidence of akathisia was related to the brexpiprazole dose.
Conclusions: Although our results suggest that brexpiprazole could be an effective adjunctive agent for MDD, they should be cautiously translated into clinical practice because the meta-analysis was based on only a handful of RCTs.

POSTER (P2-H20)

Zinc Efficacy as Adjuvant Therapy to Fluoxetine in Improving Depressive Symptoms

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Objectives : Depression is a serious psychiatric illness that affects million of people worldwide. Zinc inhibits the NMDA receptor via its binding site located on one of its subunits. Studies show zinc as an adjunct therapy can help improve clinical symptoms of unipolar depression by lowering the score of HDRS after administration of antidepressant with zinc adjuvant.
Methods : A prospective cohort experimental approach, with 20 subjects which were divided into 2 groups. Each group consists of 10 subjects. The first group was treated by fluoxetine 20 mg plus zinc 20 mg once daily in the morning, and the second group was treated by fluoxetine 20 mg only once daily in the morning. HDRS score were measured in both groups before treatment and the 2nd, the 4th and the 6th week after therapy. We analyze the data using SPSS 22 with Repeated ANOVA for each groups and Independent sample T-test to compare between 2 groups.
Results : Both groups showed significantly decrease of HDRS score after at the 2nd, the 4th, and the 6th week therapy. With p=0.005 In the first group and p=0.001 in the second group. However, we found that the mean score of HDRS of the first group significantly decreased in the 2nd to 4th week of therapy compared to the second group. But there is no significant difference between the two groups after the 6th week therapy with p=0.187.
Conclusions : Supplementation of zinc to fluoxetine improves depression symptoms more effectively in the early weeks of therapy compared to fluoxetine only, however more confirmatory study are warranted.

POSTER (P2-H21)

Case report serotonin syndrome due to drug interactions sanglah hospital, Bali

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Background: Serotonin syndrome (serotonin syndrome (SS)) caused by excessive serotonergic activity in the central and peripheral nervous system. SS often characterized by three clinical manifestations of the change in mental status, autonomic hyperactivity, and neuromuscular abnormalities. SS is an important clinical problem due to the discovery of many new anti-depressant. SS arising after an increase in the dose of medication or taking a new medication. Some medications associated with SS is monoamine oxidase inhibitors (MAOIs), tricyclic antidepresans (TCAs), selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), there are several other types of drugs can also trigger serotonin syndrome. **Methods**: Female, 31 years consulted for feeling sad, dispirited and complained to quickly tired it felt since being diagnosed with a malignant tomor buttocks area. Complaints perceived been experienced since 1 month before consulted. Patients diagnosed with episodes of major depression without psychotic symptoms and get treatment Fluoxetine 10 mg @ 24 hours and clobazam 10 mg @ 24 hours after the treatment and suspected infection patients were cultured with the results of sensitive patients with Linezolid 600 mg intravenously after 1 day of administration of patients experience agitation , increased blood pressure, fever and stiffness in the lower extremity. **Results**: The combination of Fluoxetine as the antidepressant class selective serotonin reuptake inhibitors (SSRIs) with antibiotic Linezolid that have pharmacokinetic mechanism works on monoamine oxidase (MOA) increase the risk of serotonin syndrome. **Conclusion**: Serotonin syndrome (serotonin syndrome (SS)) caused by excessive serotonergic activity in the central and peripheral nervous system. SS often characterized by three clinical picture that changes in mental status, autonomic hyperactivity, and neuromuscular abnormalities. The combination of SSRIs and MAO increase the risk of serotonin syndrome.

POSTER (P2-H22)

Antipsychotic dose reduction in schizophrenia: a systematic review

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Objectives: Minimizing the dose of antipsychotics in the maintenance treatment of schizophrenia is critically important in light of their dose-dependent side effects, including extrapyramidal symptoms, cognitive impairment, and cardiac sudden death. However, it is unclear regarding factors associated with successful antipsychotic dose reduction, which was addressed in this study. **Methods**: A systematic literature search for studies examining antipsychotic dose reduction in schizophrenia was conducted in September 2016, using PubMed. Successful dose reduction was defined as any significant superiority or no significant difference in relapse rate in the dose reduction versus maintenance group, or any significant improvement or no significant change in symptom severity between pre- and post-reduction. In case all included studies identified a certain factor for successful dose reduction while a majority of unsuccessful studies did not show the factor for unsuccessful dose reduction, the factor was considered to be associated with successful dose reduction**. Results**: Thirty studies were identified. Sixteen studies (53%) were randomized controlled trials, and 19 studies (63%) targeted first generation antipsychotics. Relapse rates or symptom changes were compared between the dose reduction and maintenance groups in 16 studies, and between pre- and post-reduction in 5 studies. Among those 21 studies, dose reduction was successful in 16 studies (76%). Age of >40 years, duration of illness of >10 years, and post-reduction chlorpromazine equivalent (CPZE) dose of >200 mg/day were found to be associated with successful dose reduction. Subjects who had experienced a clinical deterioration were stabilized by increasing the doses back to the baseline doses in all of 9 studies that used this strategy. **Conclusions**: Antipsychotic dose reduction was successfully performed in a majority of the previous studies while target doses may need to be set conservatively (e.g. >200 CPZE mg/day). Special caution should be exercised especially for younger patients with a relatively short illness duration.

POSTER (P2-H23)

Differences in schizophrenic patients cognitive function againts granting risperidone and haloperidol based on duration of illness

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Objective : Schizophrenia is a clinical syndrome that is varied, but very annoying, psychopathology involve cognition, emotion, perception, and other aspects of behavior. Manifestations of this expression varies on all patients and from time to time, but the effects of this disease are always severe and usually have a longer period of time. Therapy for the treatment of schizophrenia consist of somatic and psychosocial therapy. Ie somatic therapy using antipsychotics. Atypical antipsychotics such as risperidone may improve cognitive function in schizophrenic patients when compared with typical antipsychotic. There are differences in how the drugs haloperidol and risperidone in influencing cognitive function. Mechanism of action of the drug associated with neurotrophin compound. Haloperidol may decrease neurothropin while conversely, risperidone may increase neurothropin. Neurothropin compound that can improve cognitive function. Based on that we want to know the differences in cognitive function to the administration of haloperidol and risperidone and the effect of a long illness in patients skizorenik.
Methods : This study is an analytic study with cross-sectional design of the study conducted in RSJ Prof. Dr. M. Ildrem field during the months of June to November 2016. How sampling taken with non-probability sampling method types consecutive sampling, 80 patients with schizophrenia. To see any difference in cognitive function used chi-square test.
Result : in progress
Conclusion : in progress.

POSTER (P2-H24)

The Role of Olanzapine as Augmentation Therapy in Generalized Anxiety Disorder: A Case Report

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Introduction: Based on evidence suggesting anxiolytic properties of the atypical antipsychotic olanzapine. This case report was presented to demonstrated whether olanzapine may be efficacious in treating Generalized Anxiety Disorder.
Method: Case Presentation: A 40 years old woman, has an excessive worrying. She was also difficulty in concentrating and disturbed sleep. She reported physical anxiety simptoms such as tachycardian and tremor. The symptoms limited her daily activities. She did not responded to combination of fluoksetine and alprazolam. She was also afraid of dependency on alprazolam.
Result: patient remaining symptomatic after 6 weeks of combination Olanzapine (2mg) and Fluoksetine (20mg). There were a 50% reduction in Hamilton Anxiety Scale (HAM-A) score.
Discussion: several research have demonstrated the efficacy of olanzapine as augmentation therapy on generalized anxiety disorder. Olanzapine might be considered as an add-on treatment for patient who fail to respond to one or more SSRI trials. Olanzapine with its 5-HT2 antagonists may represent an effective treatment and does not possess the dependency.
Conclusion: Olanzapine augmentation of Fluoksetine may have a greater effect on improving anxiety for refractory generalized anxiety disorder.

POSTER (P2-H25)

A Comparison of Coercive and Voluntary Long-Acting Injectable Antipsychotic Use and Patient Outcomes

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OBJECTIVES: The use of Community Treatment Orders (CTOs) or similar coercive community based care is continuing to rise worldwide despite contradictory empirical findings and their impact upon patient autonomy. Numerous reviews have indicated that CTOs have limited or no effectiveness. While other studies have shown positive results particularly in regards to service use indices. Despite the plethora of studies in the area the effectiveness of CTOs on patient outcomes remains unclear. In particular outcomes associated with levels of functioning and well-being have not received a great deal of attention in previous studies. Therefore this study aims to investigate and compare the functioning and wellbeing of patients using long-acting injectable antipsychotics either voluntarily or under the direction of a CTO.
METHODS: This study is currently being conducted in a regional area of NSW Australia in collaboration with the local health authority. Patients from both groups (CTO or voluntary) completed a questionnaire with the assistance of the researcher; the questionnaire included the Subjective Well-being Under Neuroleptics Scale, the WHO Disability Assessment Schedule 2.0 and the Beck Insight Scale. In addition to this questionnaire the researcher completed the Clinical Global Impression Scale - Improvement, Personal and Social Performance Scale, The Negative Symptom Assessment Schedule and the Health of the Nation Outcome Scale.
RESULTS: As data collection for this study is still in progress there are no results at this time. Very preliminary results are indicating that levels of functioning and well-being may be similar between the two groups. Further statistical analyses will be conducted at the completion of data collection.
CONCLUSIONS: The results of this research will assist in elucidating the effect of CTOs on patient's levels of functioning and well-being. The implications of this research will be discussed with reference to the importance of clinician decision making, patient autonomy and the recovery model

POSTER (P2-H26)

Risk of Venous Thromboembolism during Treatment with Clozapine : Case Report

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Preliminary : Based on theadverse reaction reports, the Food and Drug Administration found the overall risk of death in association with pulmonary embolism during the therapy with clozapine to be 1 in 3450 patients per year. The evidence to date on the relation between the risk of venous thromboembolic disease (VTE) and antipsychotic agents derives primarily from observational and case history studies. While an increased risk of VTE has been associated with antipsychotic agents, particularly clozapine, there appears to be a growing number of reports on the occurrence of this adverse reaction during the use of second-generation antipsychotics. Potential etiopathogenetic factors leading to VTE during treatment with antipsychotic agents include sedation, obesity, elevation of antiphospholipid antibodies, increased platelet activation and aggregation, hyperhomocysteinemia, and hyperprolactinemia.
Method : Case Report
Result and Discussion
A 36 Years Old Woman, inpatient of Sanglah General Hospital, was refered by Bali Mental Health Hospital with Paranoid Schizophrenia and VTE. Patient was inpatient in Bali Mental Health Hospital for 1 month and administered by clozapine 2 x 50 mg. Complain of VTE was 1 week before referred to Mental Hospital. Patient had lack of mobilisation and lot of sleep. In Sanglah General Hospital, patient was bandaged and had active mobilisation, and was optimalized by Internist. VTE recovered, oedem reduced, and had better mobilisation after 2 weeks hospitalitazion.
Conclusion
Case Report show an increased risk for the development of thromboembolic complication in patients treated with antipsychotics. When selecting the product, phychiatrist should screen for risk factors of VTE.
Key Word : VTE, treatment, antipsychotic.

POSTER (P2-H27)

Effect of Zinc Supplementation as Adjuvant Therapy of Alprazolam to Improvement The Clinical Symptoms of Anxiety

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Objectives : In Indonesia, the prevalence of anxiety disorders estimated to range between 9-12% of the general population. Alprazolam is an anti-anxiety drug and anti panic, it's effectively used to reduce abnormal excitability in the brain, inhibiting the neurotransmitter GABA receptors. Zinc can be used for adjunctive therapy that can improve the symptoms of anxiety. The purpose of this study was to determined the effect of zinc as an adjunctive therapy to improvement of clinical symptoms of anxiety.
Methods : This study is an experimental type, samples were taken by consecutive sampling, totally 20 persons. This study devided into two groups, the first group was treated with alprazolam combined with zinc and the second group was treated only with alprazolam, each group consists of 10 persons. We used HARS score to assess the improvement of clinical symptoms of anxiety which measured before treatment and during the second, fourth and sixth weeks therapy. We analyse the datas by using SPSS 22 with Repeated ANOVA for each groups and Independent samples T-tes to compare between two groups.
Results : Both groups shows significant decrease in HARS Score from base line to week sixth (p=0.000). However there are no significant difference between two groups in decreasing HARS Score from base line, week 2, week 4 and week 6 (P0 = 0.095, P2 = 0.218, P4 = 0.928, P6 = 0.65). But we found there are better improvement in the first group rather than second group (Mean Value Ratio 26.40 vs 21.90, 21.30 vs 18.50, 16.40 vs 16.20, 12.50 vs 13.40)
Conclusions : Zinc could be effective as an adjunctive therapy to Alprazolam in improving the symptoms of anxiety, however more confirmatory study is needed.

POSTER (P2-H28)

Higher serotonin transporter availability in early onset obsessive-compulsive disorder patients under escitalopram treatment: A [11C]DASB PET study

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Objectives : Whilst obsessive-compulsive disorder (OCD) patients have low serotonintransporter (SERT) availability, drug-naïve early-onset OCD (EOCD)patients have higher SERT availability than late-onset OCD (LOCD)patients, suggesting less degree of serotonergic pathology in EOCD.
Nonetheless, EOCD and LOCD are treated with serotonin reuptakeinhibitors but there is no report regarding the effect of serotonin reuptakeinhibitors on the serotonergic system according to the age of onset.
Methods : Six medicated EOCD patients and six medicated LOCD patients were enrolled.They underwent serial [11C]DASB PET scans during maintenance therapywith escitalopram and its plasma concentration was measured with thescan. Drug-free binding potential (BP) of SERT was calculated frompharmacokinetic-pharmacodynamic modelling.
Results : In comparison with LOCDpatients, SERT availability was significantly higher in putamen of EOCDpatients (U=4, p=0.026), but not in caudate nucleus, thalamus and dorsalraphe nucleus. BP of putamen showed a negative correlation (r=-0.580,p=0.048) with age of onset of the disease.
Conclusions : These findings indicate thatearlier the age of onset of OCD the less serotonergic pathology there is,and that this difference remains even after long-term SRI treatment.Clinically it might suggest that non-SRI treatments such as cognitivebehavioural therapy or non-serotonergic pharmacotherapy would be a better option for EOCD patients.

POSTER (P2-H29)

Clinical outcomes with long acting injection (LAI) in schizophrenia treatment in Japan

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objective
Many schizophrenia patients tend to stop their medication and relapse repeatedly. Long-acting injection (LAI) is useful for such patients. There are few studies on LAI in schizophrenia treatment. We investigated clinical outcomes with LAI at our hospital.
methods
We investigated 45 schizophrenia outpatients prescribed with LAIs on retrospective observational study.
results
Haloperidol decanoate (HD), fulphenazine decanoate (FD), risperidone long acting injection (RLAI) and paliperidone palmitate (PP) were prescribed. Prescription of HD and RLAI accounted for 80%. The mean age of LAI initiation was 51.6yo. The duration from disease onset was 23.4 years. Delusional schizophrenia was more prescribed than Hebephrenia (60% and 29.8% respectively). Reasons to start LAI were ineffectiveness (33.3%) and nonadherence (60%). No obvious adverse reaction were observed.
conclusions
LAIs might be useful and safety medication for refractory schizophrenia. Further investigations are necessary to elucidate it.

POSTER (P2-H30)

Therapeutic Drug Monitoring of paliperidone palmitate in patients with schizophrenia or Bipolar disorder

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Background: Blood level of antipsychotics impact on the clinical response, and it is influenced by several individual factors. There were seldom studies investigating the blood drug level of second generation antipsychotics in Han Chinese. Aim of our study was to analysis the therapeutic plasma concentration (Cps) of paliperidone palmitate in Taiwanese clinical samples.
Methods: Total sample included 30 patients receiving paliperidone palmitate. All of the patients have received paliperidone palmitate monthly for at least 5 months, and the trough plasma concentrations before the next injection were monitored. Clinical Global Impression of Severity (CGI-S) and Drug-Induced Extrapyramidal Symptoms Scale (DIEPSS) were used for clinical assessment.
Results: 18 males and 12 females, with mean age of 44.1±13.5 years were studied. In 18 patients receiving monotherapy of 100mg/month paliperidone palmitate, the mean Cps was 30.1±12.9 ng/ml (0.47±0.25 ng/ml/Kg); in 8 patients receiving monotherapy of 150mg/month paliperidone palmitate, the mean Cps was 48.1±24.4 ng/ml (0.71±0.42 ng/ml/Kg), with a mean of 35.6±18.7 ng/ml (0.55±0.33 ng/ml/Kg) in total subjects. The mean CGI-S and DIEPSS were 2.9±0.4 and 1.6±1.8, respectively.
Conclusions: There exists a wide variety in the Cps of studied individuals, and dose/Cps correlation was noticed. The mental conditions of most patients were stable and side effects were mild and tolerable when received paliperidone palmitate maintenance therapy.

POSTER (P2-H31)

Improvement Of Negative Symptoms In Schizophrenic Patients Treated With Risperidone and Fluoxetine Compared With Risperidone and Amitriptyline

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Objectives : Negative symptoms of schizophrenia are the key elements and affect the ability of patients everyday and has a negative impact on their quality of life. Antidepressants becomes a natural choice and common for the treatment of negative symptoms given the closeness conceptual and etiologic hypotheses involving the neurotransmitter. The aim of this study is to compare the improvement of negative symptoms in schizophrenic patients that were treated by risperidone and fluoxetine compared with risperidone and amitriptyline
Methods : A prospective cohort experimental approach, with 20 subjects with chronic schizophrenia based on PPDGJ III who received risperidone 4 mg therapy for 6 months or more which were divided into 2 groups, each group consists of 10 subjects. The first group was treated by fluoxetine 10 mg once daily in the morning, the second group was treated by amitriptyline 25 mg once daily in the evening. Entire subjects are measured negative symptoms by the PANSS score before and at the 2nd, the 4th, and the 6th weeks after therapy with antidepressants. We analyze the data using SPSS 22 with Repeated ANOVA for each groups and Independent sample T-test to compare between 2 groups.
Results :
- In the fluoxetine group, p=0.001, statistically significant differences between the PANSS Score at all time measurements. Decreased of negative symptoms on the N3 (poor rapport), N4 (passive social withdrawal), N5 (difficulty in abstract thinking), N6 (lack of spontaneity and flow of conversation), and N7 (stereotyped thinking)
- In the amitriptyline group, statistically significant differences between the PANSS Score only at the 2nd weeks of therapy with p=0.005. Decreased of negative symptoms on the N2 (emotional withdrawal) only.
- From the comparative analysis between the two groups, the value of p= 0.564, not statistically significant difference. However, we found that the mean rank of PANSS score of the amitriptyline group significantly decreased at the 2nd weeks of therapy and the fluoxetine group significantly decreased at the 4th to the 6th weeks of therapy
Conclusions :
- Fluoxetine and amitriptyline therapy can help reduce the negative symptoms in schizophrenic patients
- Fluoxetine is more effective as maintenance therapy in reducing the negative symptoms in schizophrenic patients compared with amitriptyline

POSTER (P2-H32)

Psychiatric Problems Profile Among Patients Being Treated For Multi Drugs Resistant Tuberculosis At Dr.Sardjito Hospital, Yogyakarta

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Objectives : The aim of this study was to assess psychiatric problems profile among patients being treated for multi drug resistant tuberculosis at Dr.Sardjito Hospital, Yogyakarta.
Methods : This study was a descriptive analytic study with cross sectional design. The sampling method used was purposive sampling. Data's were taken secondary from medical record, included all multi drug resistant tuberculosis patients admitted at Dr.Sardjito Hospital during the period from January 2014 to July 2016. The exclusion criteria were there present of other organic mental disorders and brain infections. Data will be analyzed statistically using descriptive measures.
Results : Multi drug resistant tuberculosis patients were resistant to at least Rifampicin and being treated with Cycloserine. Data will be analyzed in terms of sosio-demografic character, clinical history, comorbidities, profile of psychiatric problems, and psychopharmacotherapy were used to treat patients. This study is still in progress and result will be reported later.
Conclusion : Psychiatric problems are common in patients with multi drug resistant tuberculosis.[1,2] Providing data and reports on the profile of psychiatric problems among multi drug resistant tuberculosis patients will provide useful information for preventive measures to reduce morbidity and mortality.

POSTER (P2-H33)

Neuroleptic Malignant Syndrome Following High Potency And Polypharmacy Administration Of Antipyschotics in Patient with Chronic Schizophrenia : Case Report

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Objectives : To report and discuss a case of neuroleptic malignant syndrome following high potency and polypharmacy administration of antipyschotics in patient with chronic schizophrenia.
Methods : Systematic assessment and management of neuroleptic malignant syndrome was retrieved and reviewed together with relevant literatures.
Results : A 38 years old Javanese female with chronic schizophrenia presented with severe muscle rigidity, elevated temperature, diaphoresis, confusion, disorientation, mutism, tremors, and haemodinamic dysregulation on hospital day 3'rd. Laboratories results include elevation of creatine kinase level (913 U/L), leukocytosis (23.500/µL) and elevated hepatic enzymes (AST 75 U/L) and ALT (35 U/L). This patient met diagnostic criteria for neuroleptic malignant syndrome, with the cardinal symptoms of fever and muscle rigidity were shown on her episode, escalate over on 48 hours after restarting antipsychotic injection. An objective causality assessment suggests that this case of neuroleptic malignant syndrome was probably related to high potency drug, multiple neuroleptics administration, and intramuscular injection of neuroleptic drugs.[1] Haloperidol and olanzapine intramuscular were injected to control her schizophrenia symptoms. The management of this case is reviewed. She was not successfully treated with diazepam, bromocriptine and dymenhidrinate. After 3 days treatment her condition worsened. Patient death was caused by respiratory failure.
Conclusions : Because of the life threatening nature of this syndrome, clinicians should always apply caution fully in using high potency, polypharmacy and intramuscular depot forms of antipsychotic.[1] This will help to reduce mortality risk for neuroleptic malignant syndrome, no do harm and guarantee the patient optimal care.[2]

POSTER (P2-H34)

Hypoprolactinemia in male patients treated with risperidone or aripiprazole

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Aim: It is widely known that hyperprolatinemia is induced by dopamine blockers, antipsychotics such as risperidone. However, several reports that aripiprazole decrease prolactin concentration although clinical relevant of hypoprolactinemia in schizophrenia is still unknown. Serum prolactin concentration in patients treated with risperidone or aripiprazole was investigated.
Methods: Subjects were 94 male schizophrenia out patients receiving risperidone or paliperidone and 83 male schizophrenia out patients receiving aripiprazole. Mean age was 42.2±11.8 years for risperidone or paliperidone group, and 37.3±10.7 years for aripiprazole group. Serum prolactin concentrations were measured. This study was approved by ethics committee of Hirosaki University School.
Results: Serum prolactin concentration is 27.5±13.1ng/ml for risperidone or paliperidone group and 3.9±3.5ng/ml for aripiprazole group, which was significantly different. While frequency of serum prolactin level less than 5ng/ml was 0 of 94 (0%) in the risperidone or paliperidone group, it was 62 of 83 (75%) in aripiprazole group. On the contrary, frequency of serum prolactin level more than 20ng/ml was 61 of 94 (65%) for risperidone or paliperidone, whereas it was 0 of 83 (0%) for aripiprazole.
Conclusions: Serum prolactin concentration is significantly lower in aripiprazole group than the risperidone group, and hypoprolactinemia at high frequency in aripiprazole group was observed

POSTER (P2-H35)

Novel strategies of treatment of schizophrenia and Alzheimer's disease besed on D-cell hypothesis

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Due to complexity of the human central nervous system (CNS), there is an urgent necessity to elucidate pathophysiology of disorders in the human CNS. The anatomical subgroups of D-neurons (trace amine (TA) neurons) were specified in the human CNS, and D-neuron decrease was shown in the nucleus accumbens (Acc, D16) of postmortem brains with schizophrenia (Ikemoto et al. 2003), leading to establishment of “D-cell hypothesis (TA hypothesis) of schizophrenia” by using a Patent Cooperation Treaty (PCT) patent-required method (Ikemoto et al.2016). Interestingly, the human D-neuron system is far developed in the forebrain in comparison with that of other species, including non-human primates. The TAAR1 (TA-associated receptor, type 1), exclusive receptor of TAs in humans, has a large number of ligands including tyramine, β-phenylethylamine and methamphetamine, which affect on human mental states. "D-cell hypothesis" is that accumbal D-neuron decrease in schizophrenia and consequent TAAR1 stimulation decrease to terminals of midbrain ventral tegmental area DA neurons induces mesolimbic DA hyperactivity of schizophrenia. Subventricular neural stem cells (NSC) dysfunction in Acc is the cause of D-neuron decrease in Acc (Ikemoto 2012). DA hyperactivity inhibiting NSC proliferation (Kippin et al. 2005) causes disease progression of schizophrenia. The rational is that “D-cell hypothesis of schizophrenia” is a pivotal theory to link NSC dysfunction hypothesis to DA hypothesis. (1) TAAR1 agonists or TAAR1 partial agonists, (2) DA D2 antagonists, and (3) neurotropic substances (e.g., brain-derived neurotrophic factor (BDNF), lithium, anticonvulsants, and antidepressants) have potential to normalize mesolimbic DA hyperactivity. Intranasal administration of these substances and/or precursors to reach the neuroleptic acting site, such as subventricular-accumbal region by using nanotechnology, or by inplantation of iPSC-induced D-neuron is a possible prospective therapeutic strategy, which is devoid of gastrointestinal side effects, for neuropsychiatric disorders, including degenerative disorders such as dementia, as well as developmental disorders.

POSTER (P2-H36)

Efficacy of Lurasidone in Schizophrenia: A Systematic Review and Meta-Analysis of RCTs with Active Comparators

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Background: The objective of this study was to evaluate the efficacy of lurasidone in patients with schizophrenia. Methods: Systematic review and meta-analysis of short-term (≤6 weeks) randomized controlled trials (RCTs) comparing lurasidone and other antipsychotics head-to-head in schizophrenia. Primary outcome was change from baseline in the Positive and Negative Symptoms of Schizophrenia (PANSS) total score to study endpoint in the intent-to-treat population. Secondary outcomes included change from baseline in PANSS subscale scores and CGI-S score to study endpoint and treatment response. Results: Across 4 RCTs (n=1,902), lurasidone had similar effect with regard to mean change in PANSS total score (N=4, n=1,609, WMD=1.477, 95%CI: -1.257 to 4.210, p=0.290). PANSS-subscale score (positive, negative, and general psychopathology) were also comparable to active comparators (N=3, n=1,001, WMD=0.777, 95%CI: -0.527 to 2.081, p=0.243, N=3, n=883, WMD=0.683, 95%CI: -1.200 to 2.567, p=0.477, N=3, n=1,001, N=4, n=1,610, WMD=0.100, 95%CI: -0.836 to 0.636, p=0.789, respectively). There was also no significant difference between lurasidone and active comparators in CGI-S (WMD=0.030, 95%CI: -0.073 to 0.133, p=0.571). Conclusions: These meta-analysis indicate that the efficacy of lurasidone for schizophrenia is comparable to several other antipsychotics.

POSTER (P2-H37)

Novel strategies of treatment of schizophrenia and Alzheimer's disease besed on D-cell hypothesis

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Due to complexity of the human central nervous system (CNS), there is an urgent necessity to elucidate pathophysiology of disorders in the human CNS. The anatomical subgroups of D-neurons (trace amine (TA) neurons) were specified in the human CNS, and D-neuron decrease was shown in the nucleus accumbens (Acc, D16) of postmortem brains with schizophrenia (Ikemoto et al. 2003), leading to establishment of “D-cell hypothesis (TA hypothesis) of schizophrenia” by using a Patent Cooperation Treaty (PCT) patent-required method (Ikemoto et al.2016). Interestingly, the human D-neuron system is far developed in the forebrain in comparison with that of other species, including non-human primates. The TAAR1 (TA-associated receptor, type 1), exclusive receptor of TAs in humans, has a large number of ligands including tyramine, β-phenylethylamine and methamphetamine, which affect on human mental states. "D-cell hypothesis" is that accumbal D-neuron decrease in schizophrenia and consequent TAAR1 stimulation decrease to terminals of midbrain ventral tegmental area DA neurons induces mesolimbic DA hyperactivity of schizophrenia. Subventricular neural stem cells (NSC) dysfunction in Acc is the cause of D-neuron decrease in Acc (Ikemoto 2012). DA hyperactivity inhibiting NSC proliferation (Kippin et al. 2005) causes disease progression of schizophrenia. The rational is that “D-cell hypothesis of schizophrenia” is a pivotal theory to link NSC dysfunction hypothesis to DA hypothesis. (1) TAAR1 agonists or TAAR1 partial agonists, (2) DA D2 antagonists, and (3) neurotropic substances (e.g., brain-derived neurotrophic factor (BDNF), lithium, anticonvulsants, and antidepressants) have potential to normalize mesolimbic DA hyperactivity. Intranasal administration of these substances and/or precursors to reach the neuroleptic acting site, such as subventricular-accumbal region by using nanotechnology, or by inplantation of iPSC-induced D-neuron is a possible prospective therapeutic strategy, which is devoid of gastrointestinal side effects, for neuropsychiatric disorders, including degenerative disorders such as dementia, as well as developmental disorders.

POSTER (P2-H38)

Case report on risperidone induced acute dystonia and management treatment

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Background: Signs of extrapyramidal symptoms such as dystonia, parkinsonism and akathisia were recognized occurred among schizophrenia patients due to antipsychotic drug treatment use. Second-generation antipsychotics (SGAs) have been known for having a low risk of extrapyramidal symptoms (EPS) compare to first-generation antypsycotic (FGAs). Among SGAs, Risperidone is the most frequent antipsychotic that can induce EPS.
Method : Case study
Results: Male, 20 yrs, diagnosed with first-episode of schizophrenia paranoid, given Risperidone therapy 2 mg twice daily. On second days of treatment, patient experienced acute dystonia with symptoms of torticollis and opisthotonus. Slowly intravenous Diazepam injection 10 mg was given to overcome acute dystonia and Risperidone medication was reduced to 2 mg once daily, Trihexyphenidyl 2 miligram once daily was added.
Discussions: Risperidone is one of atypical antipsychotic that has side effect of EPS such as dystonia, akathisia and parkinsonism. Acute dystonia are frequently occur during first or second day of Risperidone treatment, however it also can occur during treatment or when the dose of Risperidone was increased significantly. This side effect can be treated by given benzodiazepine injection or anticholinergic orally or injection, reduce the dose of Risperidone or change Risperidone to other atypical antipsychotics.
Conclusion : Risperidone as a atypical antipsychotic also have side effect EPS such as acute dystonia. Treatment of diazepam injection immediately and continue with anticholinergic such as trihexyphenidyl orally shows a satisfactory results. The development of acute dystonias relates to antipsychotic potency, to dosage and rates of dose increment.

POSTER (P2-H39)

The cognitive profile of antipsychotic monotherapy and polypharmacy in chronic schizophrenia patients

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Objectives: Antipsychotic polypharmacy and high doses of antipsychotics have been associated with poorer outcome, longer hospital stays, increased side effects, and cognitive impairment for long time treatment of schizophrenia. This study investigates the difference of cognitive function between antipsychotic monotherapy and polypharmacy in chronic schizophrenic patients.
Methods: The participants were 31 chronic schizophrenic patients; 18 were male, 51.9 ± 11.8 years old. Fourteen patients had received antipsychotic monotherapy for more than xx months. Average antipsychotic dosage was 946.8 ± 740.4 mg/day of chlorpromazine equivalent. The Brief Assessment of Cognition in Schizophrenia - Japanese Version (BACS-J), Positive and Negative Symptom Scale (PANSS), and the Schizophrenia Quality of Life Scale translated into Japanese (JSQLS) were used to evaluate neurocognitive functions, psychiatric symptoms and QOL. The Mann-Whitney test was used for statistical analyses.
Results: The BACS-J composite score was correlated with PANSS total, negative, and general psychopathology score. There were no correlations among the BACS-J composite score, the prescribed dosage of antipsychotics, and JSQLS scores. The score of motor function was significantly lower in the patients who were taking antipsychotic polypharmacy.
Conclusions: These findings suggest that antipsychotic polypharmacy is unfavorable for neurocognitive function with chronic schizophrenic patients.

POSTER (P2-H40)

The Effect of Folic Acid And Cyanocobalamin as Adjuvant Therapy To Improve The Cognitive Function of Vascular Dementia Patients

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OBJECTIVE : The main cause of vascular dementia is cerebral vascular disease which causes a pattern of multiple symptoms of dementia. Folic Acid and Cyanocobalamin is generally classified as a vitamin neurotrophic and especially necessary for the nerves, brain, and energy metabolisme. This study is aimed to find out the effect of folic acid and cyanocobalamin as adjuvant therapy in improving the cognitive function of Vascular Dementia Patients.
METHODS : An experimental study with 20 subjects who received Donepezil 5 mg once daily in the evening and piracetam 800 mg twice a daily. The subjects were devided into two groups, the first group was given folic acid 400 mcq and cyanocobalamin 1000 mcg once daily in the morning. The second group just Donepezil 5 mg once daily in the evening and piracetam 800 mg twice a daily. MMSE score were measured before and at the 8th week after therapy. We analyze the data using SPSS 22 with Samples T-test each group.
RESULT : The first group obtained significant difference between before and at the 8th week of therapy with value of p= 0,002, there were improvements in cognitive function with MMSE scores increase. The second group obtained no significant difference between before and the 8th week of therapy with p=0,317. The comparison of the two groups obstained no statistically significant difference at the 8th week after therapy with p=0,639 in the first group and p=0,548 in the second group.
CONCLUSION: Combination adjuvant therapy of folic acid and cyanocobalamin can help increase the MMSE score and improving the cognitive function in patients with vascular dementia.

POSTER OF YOUNG PSYCHIATRIST AWARD (P2-I1/YPA-1)

The cognitive effects of atypical antipsychotic monotherapy in patients with acute schizophrenia

Hikaru Hori
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Objective: Although the effects of atypical antipsychotics with regard to improving neurocognitive function still remain controversial. The present study applied an atypical antipsychotic monotherapy for patients with acute schizophrenia to examine the percentage of patients who respond well to this treatment.
Methods: We studied 40 patients with acute schizophrenia who had received atypical antipsychotic monotherapy for 24 weeks. The demographic information of these patients was collected before treatment began. The following parameters were evaluated at baseline and 24 weeks after the start of treatment: background information, psychotic symptoms and neurocognitive function (using BACS-J). The degree of neurocognitive functional improvement in individuals was calculated using the equation for the z-score in Week 24 minus the z-score in Week 0. The improvement was rated on a 6-category scale that ranged from “very much worse” (-3<degree of improvement≦-2) to “very much improved” (2<degree of improvement≦3).
Results: The overall effect size of neurocognitive functional improvement following atypical antipsychotic monotherapy for 24 weeks was 0.21-0.57. Marked improvements in neurocognitive function were noted in 7.5-25% of patients. The percentage of patients showing deterioration in response to atypical antipsychotic therapy was 2.5-10%.

POSTER OF YOUNG PSYCHIATRIST AWARD (P2-I2/YPA-2)

Plasma Levels and Estimated Dopamine D_2 Receptor Occupancy of Long-Acting Injectable Risperidone During Maintenance Treatment of Schizophrenia: A 3-year Follow-up Study

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Objective: Dopamine D_2 receptor occupancy levels needed for the maintenance treatment of schizophrenia remain to be elucidated. We examined 3-year clinical outcomes of patients with schizophrenia who received long-acting injectable risperidone (LAI Risperidone) at baseline and investigated their dopamine D_2 receptor occupancy levels, estimated from plasma drug concentrations.
Methods: A chart review of 52 outpatients with schizophrenia who participated in the original cross-sectional study was conducted to examine their 3-year clinical outcomes between April and September, 2015. Patients who continued outpatient treatment with LAI Risperidone without any usage of concomitant chlorpromazine equivalent antipsychotic dosage at >200mg/d for the 3-year period were asked to participate in the follow-up assessments that included the Brief Psychiatric Rating Scale (BPRS) and estimated dopamine D_2 receptor occupancy levels at trough, using plasma concentrations of risperidone plus 9-hydroxyrisperidone. Data in this study were compared to those collected 3 years earlier from the same patients.
Results: Among the original 52 participants, 14 participants (27%) continued outpatient treatment with LAI Risperidone. Ten participants (19%) provided plasma samples; mean±SD measured trough concentration of risperidone plus 9-hydroxyrisperidone significantly increased from 22.9±15.6 ng/mL to 31.8±17.5 ng/mL (P=0.02). Estimated dopamine D_2 receptor occupancynumerically increased from 63.0±10.9% to 69.0±11.0% (P=0.12). A significant worsening was observed in the BPRS total score among these patients (mean±SD, 34.3±12.7 to 46.5±16.9, P=0.003).
Conclusion: Paradoxically, the increased plasma concentration was found to be associated with a significant worsening of the clinical outcome. More investigations are indicated to shed further light on optimal levels of D_2 blockade in the maintenance treatment of schizophrenia.

POSTER OF YOUNG PSYCHIATRIST AWARD (P2-I3/YPA-3)

Effect of Escitalopram on anti-inflammatory markers in Obsessive Compulsive Disorder (OCD)

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Background/objective: Dysregulation of immunological system is a proposed hypothesis for OCD. Previous literature in this area has been characterised by inconsistent results. The current study aims to study the level of anti-inflammatory cytokines in psychotropic-naïve patients with OCD and to investigate if treatment with escitalopram modifies the level of these markers and if it is related to the treatment outcome.
Method:30 psychotropic-naïve patients with OCD (18-50 years old) with OCD without any other axis-1 comorbidity (ascertained by MINI-PLUS) or history of neurological and chronic medical illnesses were recruited. YBOCS, YBOCS-SCL were administered on the patient group. An equal number of age and gender matched healthy controls were also recruited. Patients with OCD underwent a 12 week trial of fixed dosage scheduling of Tab Escitalopram. Patient's blood sample (5 ml; 8-10 AM) was collected at baseline and after the drug trial. The sample was assayed for the following anti-inflammatory cytokines: IL-10 and IL-1 RA (receptor antagonist). Using ELISA technique (Siemens Immulite™).
Results: The levels of IL-10 and IL-1 RA were significantly higher in the patient group as compared to the controls at the baseline $p<0.05$; $p<0.01$). 50% of patients (n=15) responded to escitalopram (defined as 25% reduction in YBOCS score). On comparison of responders and non-responders, responders demonstrated a significant decrease in IL-10 ($P<0.05$) though not IL-1 RA.
Conclusions: The study results provide preliminary evidence for immune dysregulation in OCD. The increase in level of anti-inflammatory markers at baseline can be considered a compensatory response to the inflammatory state in OCD. The decrease in level of IL-10 provides putative evidence for immunomodulatory actions of SSRIs. Single point blood sampling without a concomitant ex-vivo assay of cytokines or CSF assays are potential limitations of this study. Similar studies on a larger sample size might shed further light in this area.

POSTER OF YOUNG PSYCHIATRIST AWARD (P2-I4/YPA-4)

Cognitive Function and Hippocampal Volume of Chronic Schizophrenic Patients Receiving Risperidone

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Introduction: The objective of this study was to find out cognitive function and hippocampal volume in schizophrenic patients who received risperidone. It has never been done by anyone in Medan, Indonesia.
Method: Chronic schizophrenic patients (n=21) who received risperidone treatment were undergoing treatment stabilization stage with the total PANSS score of ≤ 60. The assessment of cognitive function with Montreal Cognitive Assessment – Indonesian (MoCA-Ina) version at the value of cut-off point > 26 was normal. Magnetic Resonance Imaging (MRI) 1.5 Tesla was used to measure hippocampal volume. The correlation of MoCA-Ina score with hippocampal volume would be analyzed by using Pearson statistical test. This study was conducted from April until November, 2016 at the Mental Hospital of North Sumatera,Medan.
Result: It was found that of the 21 schizophrenic patients, 18 of them had their MRI analyzed. Their cognitive function had negative correlation with the right side of hippocampal volume at r-value = -0.127; p = 0.615. Cognitive function had negative correlation with the left side of hippocampal volume at r-value = -0.126; p = 0.619. The duration of illness had negative correlation with the right side of hippocampal volume at r-value = -0.566; p = 0.014. The duration of illness had negative correlation with the left side of hippocampal volume at r-value = 0.459; p = 0.055.
Conclusion: This study supported the previous studies which found that there was the decrease in cognitive function and hippocampal volume in schizophrenic patients.

POSTER OF YOUNG PSYCHIATRIST AWARD (P2-I5/YPA-5)

D-Amino Acid Oxidase Inhibition as a Novel Approach For Refractory Schizophrenia

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Objectives: The treatment of refractory schizophrenia is a great challenge. Clozapine is the only approved antipsychotics for refractory schizophrenia; however, its efficacy is unsatisfactory. Enhancing N-methyl-D-aspartate receptor(NMDAR) activation, including inhibition of D-amino acid oxidase (DAAO),has been reported to improve the clinical symptoms and cognitive function of patients with schizophrenia. This study examined the efficacy and safety of a DAAO inhibitor,sodium benzoate,for the treatment ofrefractory schizophrenia.
Methods: We conducted arandomized, double-blind, placebo-controlled trial in four major centers in Taiwan.Sixty patients with refractory schizophrenia treated with clozapine were randomly allocated to sodium benzoate 1-g/d, sodium benzoate 2-g/d or placebo for a 6-weeks add-on therapy. The primary outcome measures including Positive and Negative Syndrome Scale (PANSS) total score,Scales for the Assessment of Negative symptoms (SANS), Quality of Life Scale (QOL) and Global Assessment of Function were assessed every two weeks.
Results: Both sodium benzoate 1-g/d and 2-g/d produced better improvement than placebo inSANS (p = 0.024 and 0.027 at endpoint, respectively). Sodium benzoate 2-g/d also produced better improvement than placebo inPANSS total score and QOL (p = 0.005 and0.008 at endpoint, respectively). However, sodium benzoate 2-g/d was not significantly better than 1-g/d in all primary and secondary outcome measures. Sodium benzoate was well tolerated without evident side-effects.
Conclusions: Sodium benzoate adjuvant therapy, at both doses, significantly decreased the negative symptoms of patients with refractory schizophrenia. The 2-g/d dose also reduced overall symptomatology and improved QOL. This is the first study to demonstrate that an NMDA-enhancing agent can help clozapine-resistant patients.

POSTER OF YOUNG PSYCHIATRIST AWARD (P2-I6/YPA-6)

Variability of 128 Schizophrenia-Associated Gene Variants across Distinct Ethnic Populations

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Schizophrenia is a common polygenetic disease affecting 0.5-1% of individuals across distinct ethnic populations. PGC-II, the largest genome-wide association study investigating genetic risk factors for schizophrenia, previously identified 128 independent schizophrenia-associated gene variants (GVs). The current study examined the genetic variability of GVs across ethnic populations. To assess the genetic variability across populations, the “variability indices” (VIs) of the 128 schizophrenia-associated GVs were calculated. We used 2,504 genomes from the 1000 Genomes Project taken from 26 worldwide healthy samples comprising five major ethnicities: East Asian (EAS:*n*=504), European (EUR:*n*=503), African (AFR:*n*=661), American (AMR:*n*=347) and South Asian (SAS:*n*=489). The GV with the lowest variability was rs36068923 (VI=1.07). The minor allele frequencies (MAFs) were 0.189, 0.192, 0.256, 0.183 and 0.194 for EAS, EUR, AFR, AMR and SAS, respectively. The GV with the highest variability was rs7432375 (VI=9.46). The MAFs were 0.791, 0.435, 0.041, 0.594 and 0.508 for EAS, EUR, AFR, AMR and SAS, respectively. When we focused on the EAS and EUR population, the allele frequencies of 86 GVs significantly differed between the EAS and EUR ($P<3.91\times10^{-4}$). The GV with the highest variability was rs4330281 ($P=1.55\times10^{-138}$). The MAFs were 0.023 and 0.519 for the EAS and EUR, respectively. The GV with the lowest variability was rs2332700 ($P=9.80\times10^{-1}$). The MAFs were similar between these populations (i.e., 0.246 and 0.247 for the EAS and EUR, respectively). Interestingly, the mean allele frequencies of the GVs did not significantly differ between these populations ($P>0.05$). Although genetic heterogeneities were observed in the schizophrenia-associated GVs across ethnic groups, the combination of these GVs might increase the risk of schizophrenia.

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