Abstract
Translational researches in schizophrenia have revealed the many aspects of biological evidence for schizophrenia. To find the intracellular signaling pathway responsible for antipsychotic medications, metabolic adverse events induced by atypical antipsychotics can provide a window to look for the novel molecular target mediating the therapeutic action of antipsychotics. Mammalian target of rapamycin (mTOR) is master switch regulating protein translation through sensing cellular energy state. Akt and mitogen activated protein kinase (MAPK) pathways cooperatively regulate mTOR signal pathway. In addition, AMP-activated protein kinase (AMPK), another major metabolic sensor maintaining metabolic homeostasis, interacts with mTOR to regulate the cellular response to various stimuli. Recent studies have suggested that mTOR signal pathway is involved in mood and psychotic mimetic behavioral changes as well as epileptogenesis. In this talk, involvement of mTOR and AMPK signal pathways in the therapeutic and pathogenetic mechanisms of psychotic disorders will be reviewed and discussed based on the recent findings.

Speaker 2: Tae Young Lee, Republic of Korea
Title: Transcranial direct current stimulation in schizophrenia: a systemic review and meta-analysis

Abstract
Transcranial direct current stimulation (tDCS) has been proposed as a novel treatment options for in patients with schizophrenia. Several studies have investigate regarding the efficacy of tDCS intervention, but results were inconsistent. Therefore, meta-analytic conclusion is needed to evaluate the prospectives of this new intervention. Online literature retrieval was conducted using Pubmed, Web of Science and Cochrane Central Register of Controlled Trials databases from January 2003 to October 2015. Key words were “tDCS”, “transcranial direct current stimulation”, and “schizophrenia”. Eighteen studies addressing tDCS for treatment of schizophrenia were screened. We will investigate the pooled effect size of tDCS in schizophrenia and elaborate the effectiveness of tDCS as a novel treatment option.

Speaker 3: Se Hyun Kim, Republic of Korea
Title: Targeted profiling for the metabolic syndrome

Abstract
Translational researches in schizophrenia have revealed the many aspects of biological evidence for schizophrenia. To find the intracellular signaling pathway responsible for antipsychotic medications, metabolic adverse events induced by atypical antipsychotics can provide a window to look for the novel molecular target mediating the therapeutic action of antipsychotics. Mammalian target of rapamycin (mTOR) is master switch regulating protein translation through sensing cellular energy state. Akt and mitogen activated protein kinase (MAPK) pathways cooperatively regulate mTOR signal pathway. In addition, AMP-activated protein kinase (AMPK), another major metabolic sensor maintaining metabolic homeostasis, interacts with mTOR to regulate the cellular response to various stimuli. Recent studies have suggested that mTOR signal pathway is involved in mood and psychotic mimetic behavioral changes as well as epileptogenesis. In this talk, involvement of mTOR and AMPK signal pathways in the therapeutic and pathogenetic mechanisms of psychotic disorders will be reviewed and discussed based on the recent findings.

Speaker 4: Hans-Jürgen Möller, Germany
Title: Signatures from neuroimaging studies predict transition to psychosis
Möller HJ, Koutsouleris N, Meisenzahl EM, Falkai P

Abstract
Currently in the field of schizophrenia research the early detection of at risk mental states for psychosis is an important topic of clinical research. Beside clinical and neuropsychological parameters structural MRI related parameters in focus.

Using support vector machine learning and pattern detection analysis, we demonstrate that the different kinds of at risk states (early at risk state, versus late at risk state) are associated with different kinds of brain alterations. It is possible to predict the risk of transition to psychosis on an individual level with high sensitivity and specificity. This pattern recognition analyses proved also to be useful to differentiate between schizophrenia and depression (MDD) using brain aging as intermediate parameter.

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S9: Novel neuromodulation-based approaches for neuropsychiatric disorders

Chair: Daniel Javitt, USA
Co-Chair: Chan-Hyung Kim, Republic of Korea

Speaker 1: Andre Brunoni, Brazil
Title: Perspectives of tDCS in the treatment of affective disorders

Abstract
Major Depressive Disorder (MDD) is an incapacitating condition associated with significant personal, social and economic impairment. Nearly 30% of patients present drug refractoriness, reinforcing the need to develop novel therapeutic strategies for MDD. Transcranial direct current stimulation (tDCS) might be an alternative for these patients considering its tolerability, portability and ease of use. The tDCS technique alters neuronal resting membrane potentials to facilitate (anodal) and inhibit (cathodal) neuronal firing rates. The antidepressant effects of tDCS are based on neuroimaging studies, which have shown that, in depression, the left dorsolateral prefrontal cortex (DLPFC) is hypoactive and the right DLPFC is hyperactive. To achieve antidepressant effects, anodal tDCS is delivered over the left region for depolarization and cathodal tDCS is delivered over the right DLPFC for hyperpolarization. In this presentation, we review putative tDCS antidepressant mechanisms as well as clinical evidence based on recent controlled studies and meta-analyses evaluating tDCS efficacy and predictors of response for MDD. Present evidence indicates that tDCS may be an effective treatment strategy for MDD. There are no studies specifically examining the efficacy of tDCS in bipolar depression and mania, which are urgently needed in order to address tDCS effectiveness for bipolar disorder. In addition, there are reports of hypomania/mania after or during tDCS treatment; this risk should be prospectively investigated in further studies.
First, we examined the effects of applying transcranial direct-current stimulation (tDCS) to the frontal cortex, and found improved error-monitoring and adaptive control behaviors in schizophrenia patients that were accompanied by normalized error-related negativity.

Second, we combined deep brain stimulation (DBS) with functional near-infrared spectroscopy (fNIRS) to observe the potential cortical and behavioral effects of DBS of the subthalamic nucleus (STN) in early stage of Parkinson’s disease. We found that frontal cortical activity increased during a working memory task with STN-DBS. However, there was no addition behavioral benefit above and beyond the dopaminergic medication in this group.

Third, we used a neuroplasticity-based brain fitness training to boost cognitive function in pediatric survivors of brain tumor and documented changes in frontal activity using fNIRS before and after training. Working memory and frontal cortical activity improved after 6-week brain fitness training.

Lastly, we demonstrate that the most effective, high-compliance and safe solution for improving cognitive, social and affective functioning in people with schizophrenia might lie in music. Music-making is a complex and multisensory, cognitive and social activity that promotes pro-social behavior and leads to brain reorganization. Hence, music-training is a readily available cognitive remediation strategy. Furthermore, singing (or speaking) inhibits auditory hallucinations that originate from inner-speech. We found beneficial effects of music training on working memory and social cognition across old and young participants.

In sum, these strategies provide excellent options for adjunct therapies in addition to traditional pharmacotherapy and suggest that there is a need for a more integrative and innovative treatment approaches to remediate and enhance human cognition at all levels of performance.

Speaker 4: Daniel Javitt, USA
Title: Transcranial electrical stimulation (tES) for enhancement of neuroplasticity in schizophrenia

Abstract
Treatments for brain dysfunction have relied traditionally on medication-based approaches. Non-invasive transcranial electric stimulation (tES) approaches such as transcranial direct current stimulation (tDCS) and transcranial alternating current stimulation (tACS) offer an alternative approach for psychiatric treatment. In this approach, low level (1–2 mA) currents are applied over appropriate brain regions to target specific symptoms of neuropsychiatric illness.

This presentation will discuss use of tDCS/tACS approaches in combination with neurophysiological measures such as EEG or event-related potentials (ERP) to target persistent cognitive deficits of schizophrenia, including impairments in learning, social cognition and reading ability related to basic auditory and visual impairments. Human and animal data will be compared to highlight underlying mechanisms. Finally, we will discuss use of tDCS to treat specific symptoms of schizophrenia, including persistent auditory hallucinations.

Overall, studies will demonstrate potential opportunities arising from tES-based treatment, as well as current challenges to widespread application.

CPO1: Bipolar Disorders

Speaker: Lakshmi N. Yatham, Canada
Title: Contemporary challenges in the management of bipolar disorder

Abstract
Bipolar disorder is a complex condition with different mood episodes, varied course, and increased incidence of comorbidity. Further, there are many areas of treatment where the data are inconsistent. Thus, it is not surprising that the management presents challenges for clinicians. This presentation will review some of the controversies in the management of bipolar disorder. For instance, whether antidepressants should be used for treating bipolar depression or not is a major area of controversy. Similarly, when manic patients improve on the combination of a mood stabilizer and an atypical antipsychotic, how long should the atypical antipsychotic be continued given their propensity to cause weight gain and metabolic side effects? These and other controversies in management will be addressed in this presentation.

Speaker: Tadafumi Kato, Japan
Title: Diagnosis of bipolar disorder

Abstract
Bipolar disorder is characterized by recurrent episodes of depression and (hypo)manic. Bipolar I disorder is diagnosed by the presence of mania in the course of illness, whereas bipolar II disorder is defined by the presence of depression and hypomania. Currently, the diagnosis of bipolar disorder is based solely on the clinical course, and therefore when the first episode is depression, it is diagnosed as major depression. Because some of antidepressants can cause manic switch and worsen the course of illness, earlier diagnosis is indispensable to improve the prognosis of bipolar disorder.

To enable biological diagnosis of bipolar disorder, numerous studies have been performed. Several lines of blood biomarkers have been proposed in mood disorders; serum/plasma brain derived neurotrophic factor, inflammatory cytokines including interleukin-6 and tumor necrosis factor alpha, and dexamethasone suppression test, among others. However, none of them can robustly discriminate bipolar disorder from unipolar depression. Recent neuroimaging studies suggest that structural magnetic resonance imaging (MRI) or functional MRI can potentially differentiate between bipolar disorder and unipolar depression.

To discriminate bipolar depression from unipolar depression, Mitchell and colleagues proposed a probabilistic approach. In this approach, features more common in bipolar depression were several clinical features such as earlier age of onset, more prior depressive episodes, shorter depressive episodes, and a family history of bipolar disorder are more common in bipolar depression. Several symptomatic features such as atypical features, and pathological guilt and lability of mood, may be more common in bipolar disorder. These features may be useful to discriminate bipolar depression from unipolar depression.

The presentation, clinical diagnosis of bipolar disorder and future directions toward biological diagnosis bipolar disorder will be discussed.

Reference
Mitchell PB, Goodwin GM, Johnson GF, Hirschfeld RM. Diagnostic guidelines for bipolar depression: a probabilistic approach. Bipolar Disord. 10:144–152, 2008.