Methods: We studied 20 healthy volunteers who were tested on two occasions receiving either ebselen (3600mg over 24 hours) or identical placebo in a double-blind, random-order, cross-over design. Two hours after the final dose of ebselen/placebo, participants underwent proton magnetic resonance spectroscopy (1H MRS) at 7 tesla (7T) with voxels placed in anterior cingulate and occipital cortex (Figure 1). Neumetabolite levels were calculated using an unsuppressed water signal as a reference and corrected for individual cerebrospinal fluid content in the voxel.

Results: Ebselen produced no effect on neurometabolite levels in the occipital cortex. In the anterior cingulate cortex, ebselen lowered concentrations of inositol as well as those of glutathione, glutamine, glutamate and Glx (Table 1).

Conclusions: The study suggests that at the dosage used, ebselen produces a functional inhibition of IMPase in the human brain. The ability of ebselen to lower indices of glutamate activity are consistent with its action, reported in animal experimental work, to inhibit the enzyme, glutaminase. Ebselen appears to have potential as a repurposed treatment for bipolar disorder and it would be of interest to see if similar biochemical alterations are produced by ebselen treatment in this patient group.

PS55
Parkinsonism induced by valproic acid: a case report and review of literature
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Abstract
Valproic acid (VPA) is a drug commonly used as an antiepileptic and mood stabilizer. We describe a patient who presented with particularly severe, but reversible parkinsonism during VPA treatment. We also provide a literature review on VPA-induced parkinsonism. The case was a 75-year-old woman who was diagnosed with bipolar disorder and was stabilized on lithium since the age of 50. At the age of 74, she started complaining of freezing of gait, which did not improve with L-DOPA administration. She became depressed and was admitted to a psychiatric ward. The patient complained of finger tremors, which improved after lithium was switched to 1000-mg/day VPA. The change in medication ameliorated both the tremors and the depressive symptoms. She was discharged from the hospital after 2 months. However, her parkinsonism worsened 4 months after discharge. The subsequent exacerbation of parkinsonism left her bedridden and unable to walk by herself. Her Unified Parkinson’s Disease Rating Scale score was 98. Because drug-induced parkinsonism was suspected, VPA was gradually withdrawn thereafter. Forty-five days later, she was able to walk by herself with a cane. The Unified Parkinson’s Disease Rating Scale score improved to 11. Improvement of parkinsonism after withdrawal of the medication led us to diagnose her as age-related vascular parkinsonism exacerbated by medication. Previous studies showed that approximately 20% of patients on chronic VPA therapy developed tremor (Aleksandar J et al., 2006). In majority of the previously reported VPA-induced parkinsonism cases, the parkinsonism was improved after discontinuation of the drug (Mahmoud F et al., 2011). Although drug-induced parkinsonism is a frequent side-effect of VPA, severe cases such as the present case are uncommon. The recognition of VPA-induced parkinsonism is of great clinical significance, because appropriate treatment results in significant improvement of symptoms.

PS56
A smaller percentage of unipolar depression patients with manic or hypomanic switch during acute antidepressant treatment convert to bipolar disorder
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Abstract
Objective: To investigate 3-year outcomes of unipolar depression patients with manic or hypomanic switch during acute antidepressant treatment.

Methods: A review of medical records revealed 37 consecutive patients admitted from 1997 to 2002 who underwent an antidepressant-induced manic or hypomanic switch fulfilling DSM-IV criteria. Their clinical courses were retrospectively investigated after discharge.

Results: Of the 37 patients, 29 (78.4%) were followed for 3 year after discharge. None developed a manic episode, while 10 developed a hypomanic episode, including 2 patient who were lost after emerging from a hypomanic episode during the observation
period. Only 2 of those 10 patients developed hypomania during acute antidepressant treatment for a recurrent depressive episode under maintenance mood stabilizer treatment. Furthermore, bipolar conversion occurred in 6 patients within the first 1 year, including 1 with rapid cycling, and in another 2 patients over the subsequent 1 year after discharge. Of these 29 patients, 23 (79.3%) received continuous maintenance treatment with mood stabilizers for the 3-year period after discharge.

Conclusions: A smaller percentage of unipolar depression patients with manic or hypomanic switch during acute antidepressant treatment converted to bipolar disorder. Bipolar conversion subsequently decreased and did not occur from 2 to 3 years after discharge. Longer follow-up studies appear warranted to determine the diagnostic issues of antidepressant-induced switch in unipolar depression.

PS57
P600 alteration of syntactic language processing in patients with bipolar mania: comparison to schizophrenic patients and healthy subjects
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Abstract
Background: Disturbances in thought, speech, and linguistic processing are frequently observed in bipolar manic patients, but the underlying neurophysiological mechanisms are not well understood. P600 is a distinct, positive event-related potential component elicited by syntactic violations. Using the P600 ERP, we examined neural processing of syntactic language comprehension in patients with bipolar mania compared to patients with schizophrenia and healthy people.

Method: P600s were recorded from 21 manic patients with bipolar disorder, 26 patients with schizophrenia, and 29 healthy subjects during the presentation of 120 sentences with syntactic violations or non-violations. Subjects were asked to judge whether each sentence was correct or incorrect.

Results: Patients with mania and schizophrenia had significantly smaller P600 amplitudes associated with syntactic violations compared with healthy subjects. There was no difference in P600 amplitude between patient groups. For behavioral performance, patients with schizophrenia were significantly less accurate compared with healthy subjects, whereas manic patients were not significantly different from healthy subjects.

Conclusion: Despite having normal behavioral judgment of syntax, patients with bipolar mania have reduced P600 amplitude, comparable to patients with schizophrenia. Our findings may represent the first neurophysiological evidence of abnormal syntactic linguistic processing in bipolar mania.

PS58
Time perception with auditory stimulus and manic symptoms in bipolar patients
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Abstract
Objectives: The purpose of this study was to investigate 1) whether there would be significant changes in time perception between acute manic and euthymic states and 2) whether changes in time perception with auditory stimulus in bipolar patients would be consistent with changes in time perception with visual stimulus.

Methods: The thirty-eight patients who were diagnosed as manic episode of bipolar disorder by DSM-IV participated in this study. They were presented with a time reproduction task at two states – acute manic state and euthymic state. Participants were asked to listen for “beep” sound on a portable sound equipment for a certain length of time. After that, they were asked to reproduce the same length of time. The psychopathology was measured using Young Mania Rating Scale (YMRS) and Hamilton Depression Rating Scale (HDRS) by a trained psychologist. After 6 weeks of drug treatment, the psychopathology were retested by the same psychologist.

Results: Time reproduction for 11 seconds, 36 seconds in acute manic state were shorter than in euthymic state and time reproduction in acute manic state were correlated with YMRS score.

Conclusions: Time reproduction is shorter in acute manic state than in euthymic state. And the severity of manic symptom is correlated with time perception. This result is consistent with previous studies with visual stimulus and suggests that the difference between cognitive process of visual stimulus and auditory stimulus does not affect time perception.

PS59
The Sex-Related Differences of EEG Coherences between Patients with Bipolar Disorder and Controls
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Objectives: Sex hormones exposure during the prenatal period has an effect on cerebral lateralization. Male brains are thought to be more lateralized than female brains. Bipolar disorder was known to show abnormalities in cerebral laterality whose characteristics could be estimated by electroencephalography (EEG) coherences. We studied sex-related differences of EEG coherences between healthy controls and patients with bipolar disorder to examine the sex effects in the genesis of bipolar disorder.

Methods: Participants were 25 patients with bipolar disorder (11 male, 14 female) and 46 healthy controls (23 male, 23 female). EEG was recorded in the eyes closed resting state. To examine dominant EEG coherence associated with sex differences in both groups within five frequency bands (delta, theta, alpha, beta, and gamma) across several brain regions, statistical analyses were performed using analysis of covariance.

Results: Though statistically meaningful results were not found, some remarkable findings were noted. Healthy control females showed more increased interhemispheric coherences than control males in gamma frequency band. There were no differences in the intrahemispheric coherences between the healthy control males and females. In patients with bipolar disorder, female dominant pattern in interhemispheric coherences was attenuated compared with healthy control.

Conclusions: Sex differences of EEG coherences, which could be a marker for cerebral laterality, were attenuated in patients with bipolar disorder compared with healthy controls. These results imply that abnormal sex hormone exposure during early development might play some role in the pathogenesis of bipolar disorder.

PS60
Associations between Pro-inflammatory cytokines and grey matter/ cortical thickness in patients with bipolar disorder
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