

Welcome to the 16th Annual Conference of the International Society for Bipolar Disorders.

On behalf of the Scientific Program, Steering and Local Organizing Committees of the 16th Annual Conference of the International Society for Bipolar Disorders (ISBD), we would like to welcome you to Seoul for what has over the past 20 years become the premier international conference on bipolar disorders.

The origin of the conference began in 1994 when Dr. David Kupfer and Dr. Ellen Frank from the University of Pittsburgh organized the *International Conference on Bipolar Disorder* (ICBD), the first international meeting entirely focused on bipolar disorder. Since then, the ICBD had built its reputation as an excellent conference for clinicians, researchers, patients and family members through its 9 biennial conferences in Pittsburgh, with the last one being held in Miami in 2013.

Overview

The Scientific Program Committee tried to keep the traditions from both conferences, which include Key-note Lectures, Concurrent Parallel Symposia, Rapid Oral Communications, Poster sessions and Industry Sponsored Satellite Symposia. In addition, we have continued the relatively new format of the last two meetings (Istanbul and Miami) with early morning Brainstorming Sessions and Pre-conference Courses.

The program includes all aspects of clinical and research activities on bipolar disorders, from diagnosis to treatment, from basic research to psychosocial rehabilitation, from children to late life, in order to meet the interests of all participants and to enhance discussion. The core of the program, the concurrent parallel symposia, is divided and designated into tracks (clinical manifestation, treatment, neurobiology, imaging, cultural, and advocacy) to allow participants to follow all symposia meeting their specific different interests.

ISBD has a tradition of working with patients and their families to overcome the burden of bipolar disorder. This will be highlighted in the program of the last day, when advocacy sessions and lessons from the West will enhance supportive activities in the Asian regions, which still suffer from strong stigma against bipolar disorder.

The meeting in Seoul was planned to promote bipolar disorders in Asia, and to facilitate mutual under-

In 1999, together with Dr. Samuel Gershon, Drs. Kupfer and Frank also founded the *International Society for Bipolar Disorders* (ISBD), which has subsequently organized 5 biennial meetings around the world, from Sydney to Edinburgh, Delhi, Sao Paulo and Istanbul. The ISBD meetings have now gained recognition as the representative international conference on bipolar disorder.

In 2013, the biennial ICBD and the biennial conference of the ISBD have merged into the Annual Conference of the International Society for Bipolar Disorders, and collectively we now have the *16th Annual Conference of the International Society for Bipolar Disorders*.

standing of the psychosocial environment surrounding bipolar disorders between the East and the West. The Scientific Program Committee worked with the Regional Organizing Committee to develop a Regional Satellite Symposium and a Regional Poster Session to promote bipolar disorder among Asian clinicians and researchers.

We hope all of you enjoy the diversity and inspiration of the program. Also, we recommend that you explore the dynamic cultural diversities of Seoul and Korea beyond Seoul, including sites that offer opportunities for breathtaking scenery as well as quiet contemplation. These experiences will extend your understanding of yin and yang, harmony and balance, which is also essential for understanding of bipolar disorder.

We thank all members of the committees, all our chapter chairs, our ISBD Staff, and our PCO, Kenes International.

Kyooseob Ha, MD, PhD
VP for Education, ISBD Chair
Scientific Program Committee

Willem Nolen, MD, PhD
President, ISBD Co-chair
Scientific Program Committee

Poster Session I

Lateral hypothalamic kindling induces manic-like behavior in rats: a novel animal model

O Abulseoud^a, UM Camsari^a, CL Ruby^a, K Mohamed^a, N Abdel Gawad^a, A Kasabeh^a, MY Yuksele^a, DS Choi^b

^aPsychiatry and Psychology, Mayo Clinic, Rochester, NY, USA,

^bDepartment of Molecular Pharmacology & Experimental Therapeutics, Mayo Clinic, Rochester, NY, USA

The lateral hypothalamus is the epicenter for integrating critical physiological functions such as the sleep-wake cycle, energy expenditure, and sexual behaviors. Many of these functions are disrupted during mania. In this study, we were able to successfully induce manic-like behavioral phenotypes in wild-type, adult, male Wistar rats through bilateral lateral hypothalamic area kindling (LHK). Compared with pre-kindling behaviors, LHK rats showed significantly more sexual self-stimulation, excessive rearing, feeding, and more grooming in addition to increased ethanol consumption during the kindling process. Moreover, markedly increased total locomotor activity and reduced rest interval during the kindling and post-kindling days were documented. This collective phenotype was not observed in non-kindled rats or in rats that were kindled at other brain regions: the nucleus accumbens shell or the infralimbic cortex. To test the validity of the model, we studied the effect of standard anti-manic medications in attenuating manic-like behaviors in the LHK rat. Compared with saline treatment, lithium 47.5mg/kg or valproic acid 200mg/kg administered IP twice/day for 15 days significantly attenuated manic-like behaviors. Furthermore, real-time polymerase chain reaction was utilized to measure the mRNA concentration of circadian genes known to be dysregulated in humans with bipolar disorder. Significant long-term upregulation of *Per1* and *CLOCK* gene mRNA in the dorsal striatum and medial prefrontal cortex was found with lithium and valproic acid treatment. Given the behavioral phenotype, the response to standard anti-manic medications, and the associated upregulation in certain circadian genes with treatment, the LHK rat may provide a model for studying critical aspects of manic psychopathology in humans.

Neuromodulation of the DLPFC induced by rTMS assessed with oculomotricity and cortical excitability in bipolar disorder

L Beynel^a, A Chauvin^a, N Guyader^b, S Harquel^a, T Bougerol^c, C Marendaz^d

^aPsychology Univ. Grenoble Alpes LPNC, UMR 5105 CNRS, Grenoble, France, ^bImages and Signal Univ. Grenoble Alpes GIPSA-lab, UMR 5216 CNRS, Grenoble, France, ^cPsychiatry and Neurology department Univ. Grenoble Alpes University Hospital of Grenoble LPNC, UMR 5105 CNRS, Grenoble, France, ^dPsychology Univ. Grenoble Alpes LPNC, UMR 5105 CNRS, Grenoble, France

Aim: Finding biomarkers of the neuromodulation induced by repetitive transcranial magnetic stimulation (rTMS) during depressive episode is a critical clinical issue as it might contribute to optimize the rTMS treatment. This study aims to assess rTMS-induced phasic and tonic neuromodulations of the dorsolateral prefrontal cortex (DLPFC) through the evaluation of cortical excitability (CE) and saccadic control (Malsert et al., 2013).

Method: Ten drug-resistant bipolar patients suffering from depression received sham (N = 5) or active excitatory rTMS (N = 5) 5 days per week during 3 weeks over the left DLPFC. Once a week, patients performed a saccadic task, mixing anti-, pro- and no-saccades, before (session 1) and just after (session 2) the rTMS treatment. Saccadic control was compared between sessions 1 and 2 (phasic neuromodulation) and, with CE, between the first and the last days of the rTMS treatment (tonic neuromodulation).

Results: Saccadic control (error rate) between sessions 1 and 2 was improved only for the active group showing a phasic neuromodulation. Between the first and the last days of the rTMS treatment no difference was found. Indeed, both groups improved their performances. This is consistent with the enhancement of the mood in 80% of patients in each group. CE also failed to reveal any difference due to the tonic neuromodulation between both groups.

Conclusion: This study evidences the rTMS-induced phasic neuromodulation of DLPFC, confirming that, for its assessment, saccadic control is a reliable tool. However, it fails to evidence the tonic neuromodulation. Four non exclusive hypotheses might be discussed: (1) lack of power; (2) similar mood improvement that masks neuromodulation effect; (3) lack of relevance of CE and saccadic control as biomarkers and (4) no tonic neuromodulation induced by rTMS over the DLPFC. The final assumption could explain that only 30% of depressed patients respond to rTMS treatment (Berlim et al., 2013). Finally, the improvement of performance in saccadic control is consistent with mood enhancement. Hence, we suggest that, in addition to being a useful tool to assess rTMS-induced phasic neuromodulation of DLPFC, the saccadic control seems to be a reliable indicator of mood variation.

Keywords: repetitive transcranial magnetic stimulation (rTMS), DLPFC neuromodulation, biomarkers, oculomotricity, cortical excitability

Saccadic inhibition—a trait biomarker of bipolar disorder

A Chauvin^a, N Guyader^b, L Beynel^a, S Harquel^a, B Fredembach^c, T Bougerol^d, C Marendaz^a, M Polosan^e

^aPsychology, Univ. Grenoble Alpes LPNC, UMR 5105 CNRS, Grenoble, France, ^bImages and Signal, Univ. Grenoble Alpes GIPSA-lab, UMR 5216 CNRS, Grenoble, France, ^cPsychiatry and Neurology Department, University Hospital of Grenoble, Grenoble, France, ^dPsychiatry and Neurology Department, Univ. Grenoble Alpes University Hospital of Grenoble LPNCUMR 5105 CNRS, Grenoble, France, ^ePsychiatry and Neurology Department, Univ. Grenoble Alpes University Hospital of Grenoble Institute of Neurosciences INSERM U836, Grenoble, France

Introduction: Identification of trait abnormalities in the bipolar disorder (BD), which persist in the euthymic phase, is particularly important as it may contribute to an early diagnosis, thus reducing the latency to adequate treatment and improving outcome (Cusin et al., 2000; Altamura et al., 2010). The present study aims to assess saccadic tasks as neuropsychophysical biomarker of euthymic BD.

Method: Thirty two euthymic BD patients and 27 healthy subjects performed an oculomotor task mixing antisaccade (64 AS), prosaccade 64 (PS) and no saccade (32 NS) (Malsert et al., 2012a). On each trial, a white central fixation dot appeared and changed its color either to red (AS), green (PS) or blue (NS), followed by

a cue on the right or on the left. Participants had to look as quickly as possible either to the cue (PS) or to the mirror position of the cue (AS). When the eye reached the correct position a target (6 or 9) appeared (gaze contingent display) and the subject had to identify the number (oral response). Saccadic reaction time (SRT) and accuracy (ACC) were recorded as well as inhibition errors.

Results: ANOVA shows that patients were faster but less accurate during AS than controls. Patients also produced more saccades during NS. Neither reaction time nor accuracy were different between patients and controls for PS. Logistic regression with AS SRT, AS ACC and NS fixation time predictive variables and groups (Patient, Control) as output predicts a sensibility of 85% correct classification for controls ($IC_{95\%}$ (P) = [70.4 % 98.5%] and predict a specificity of 91.9% ($IC_{95\%}$ (P) = [83.1% 100%] correct classification for patients. A bootstrap analysis gives similar results and similar confidence intervals.

Conclusion: This study shows that a saccadic task coupling AS with PS and NS is a reliable tool to identify euthymic bipolar disorder. Specifically, AS and NS performance were affected in euthymic bipolar patients, while PS was unaffected, suggesting a specific alteration of the prefrontal inhibition. Specificity of this biomarker will be further tested in major depression disorder.

Keywords: biomarker, inhibition, saccades, euthymic, prefrontal

Epigenetic regulation of EAAT2 (SLC1A2) in bipolar disorder patients

J Ayers Ringler^a, N Kang^b, Y Choi^b, D Choi^c, M Veldic^d

^aNeurobiology of Disease Program, Mayo Clinic, Rochester, NY, USA, ^bMolecular Pharmacology, Mayo Clinic, Rochester, NY, USA, ^cMolecular Pharmacology and Psychiatry, Mayo Clinic, Rochester, NY, USA, ^dPsychiatry and Psychology, Mayo Clinic, Rochester, NY, USA

Introduction: Glutamate is the main excitatory neurotransmitter in the brain and precursor for glutamine, GABA, and glutathione. Glutamatergic abnormalities are a prominent feature of bipolar disorders, but mechanisms responsible for synaptic glutamate levels remain unknown in humans. Epigenetic mechanisms provide an example of environmental regulation of gene expression and can explain how identical twins can be discordant for major mental disorders. Several lines of research suggest that hypo-functional cortical activity is mediated by promoter hypermethylation of candidate genes. Recently, our findings showed that differences in *in vivo* anterior cingulate glutamate between phenotypical subgroups of bipolar depressed patients as measured by MR spectroscopy are associated with variants of the *SLC1A2* gene. *SLC1A2* encodes excitatory amino transporter 2 (EAAT2), the principal transporter responsible for removal of 95% of glutamate from the synaptic cleft into astrocytes. In this study we used methylation-sensitive high resolution melting (HRM) PCR to compare promoter methylation of the *SLC1A2* gene from peripheral blood samples obtained from 240 nonpsychiatric subjects from the Mayo Clinic Community Biobank and 238 bipolar disorder patients from the Mayo Clinic Individualized Medicine Biobank for Bipolar Disorder. Our preliminary findings show a trend of increased DNA methylation of the *SLC1A2* promoter in bipolar patients in comparison to matched normal controls.

Serum myelin oligodendrocyte glycoprotein levels are stable in depressed females with bipolar disorder

M Sehmbi^a, L Cudney^a, RB Sassi^b, M Steiner^b, BN Frey^b

^aMinDS Neuroscience Graduate Program, McMaster University, Hamilton, Canada, ^bPsychiatry & Behavioural Neurosciences, McMaster University, Hamilton, Canada

Background/Aims: White matter abnormalities are being increasingly implicated in the pathophysiology of Bipolar Disorder (BD). Studies have revealed compromised white matter in frontal and prefrontal regions of the brain, along with projection, associative, and commissural fibres in patients with BD. There is also evidence that following myelin damage, free-floating myelin proteins can activate immune responses in the central nervous system (CNS) and activate peripheral T cells, potentially exacerbating myelin-related damage and the inflammatory response associated with BD. Here we investigated a peripheral biomarker of myelin integrity. Myelin Oligodendrocyte Glycoprotein (MOG) is expressed exclusively in myelinating oligodendrocytes of the CNS, and has been implicated as a target antigen in autoimmune demyelination.

Methods: We measured levels of serum MOG via ELISA in a total of 72 female participants: 24 patients with BD currently depressed, 24 patients with unipolar Major Depressive Disorder (MDD) currently depressed, and 24 age-matched healthy controls. Participants' psychiatric status was confirmed with the Structured Clinical Interview for DSM-IV (SCID-I). The severity of depressive symptoms was assessed via the Montgomery-Asberg Depression Rating Scale (MADRS), and the Hamilton Depression Rating Scale (HDRS).

Results: Serum MOG levels were not different between depressed BD, MDD or controls ($F_{2,67} = 0.26$, $p = 0.77$, one-way ANOVA). Serum MOG levels did not correlate with MADRS (r_s (46) = -0.009, $p = 0.94$) or HDRS scores (r_s (46) = -0.14, $p = 0.33$).

Conclusions: Previous studies have found altered levels of MOG expression in the CNS of patients with BD in comparison to healthy controls. Our results indicate that these differences are not detectable at the protein level in serum.

Exome sequencing in bipolar disorder: family and case-control results implicate a set of ten interacting genes

F Goes^a, J Parla^b, M Pirooznia^c, M Kramer^d, P Zandi^e, WR McCombie^f, J Potash^g

^aPsychiatry, Johns Hopkins University School of Medicine, Baltimore, MD, USA, ^bPsychiatry, Cold Spring Harbor Laboratory, Cold Spring Harbor, USA, ^cPsychiatry, Johns Hopkins University, Baltimore, MD, USA, ^dCold Spring Harbor, Cold Spring Harbor Laboratory, Baltimore, MD, USA, ^eDepartment of Mental Health, Johns Hopkins School of Public Health, Baltimore, MD, USA, ^fCenter for Cognitive Genomics, Cold Spring Harbor Laboratory, Cold Spring Harbor, USA, ^gPsychiatry, University of Iowa, Iowa City, IA, USA

Complex disorders such as bipolar disorder (BD) are likely to harbor both common and rare susceptibility alleles. While common variation has been widely studied in the last decade, identification of rare variants has only recently become feasible with next-generation sequencing. In this study, we employed whole-exome sequencing to identify rare coding variants that segregate in eight multiplex families with BD. We found 100 rare (MAF < 1%), damaging segregating variants in 98 genes, including 26 novel variants. We performed association testing in an independent case-control sample of 937 cases and 912 controls in a parallel, ongoing exome sequencing study. We used the case-control samples to filter out variants

that, despite full segregation, are unlikely to be associated with BD, resulting in a final “candidate” list of 52 variants in 50 genes. Several genes (*SLC4A1*, *THAP7*, *PRKAG2*, *SF3B3*, *TIGD7*) had evidence for overall enrichment of rare damaging variants with gene burden ORs > 2, although none met stringent statistical thresholds for multiple testing. However, among these genes were ten whose products participated in two protein–protein interaction networks, including one large network reflecting eight brain-expressed genes with prominent involvement in stress-related (*HSP90AA1* and *HYOU1*) and intracellular signaling pathways (*ANHAK* and *PRKCZ*). Our results show that a sequential strategy of family-based exome analysis followed by pruning using case-control results can successfully identify a relatively small number of potentially biologically related candidate genes. However, our results also point to the presence of prominent locus and allelic heterogeneity in BD, and suggest that very large samples will be required to definitively confirm individual rare variants or genes conferring risk for this disorder.

Staging bipolar disorder: clinical, biochemical, and functional correlates

I Grande^a, PV Magalhães^b, I Chendo^c, L Stertz^b, B Panizutti^b, G Colpo^b, AR Rosa^b, CS Gama^b, F Kapczinski^b, E Vieta^a

^aPsychiatry, Bipolar Disorders Unit Clinical Institute of Neurosciences Hospital Clinic University of Barcelona IDIBAPS CIBERSAM, Barcelona, Spain, ^bPsychiatry, Bipolar Disorder Program and Laboratory of Molecular Psychiatry National Institute for Translational Medicine INCTM Hospital de Clínicas de Porto Alegre Federal University of Rio Grande do Sul, Porto Alegre, Brazil, ^cPsychiatry, Hospital de Santa Maria, Lisbon, Portugal

Aims: There are several models of staging in bipolar disorder (BD), but none has been validated. The aims of this study were to investigate empirically if there are clinical variable that may be useful to classify patients in different cluster according to stage and study the association with biomarkers as biological validators.

Methods: This was a case-control study matched for age and gender performed in the Bipolar Disorders Program of Hospital de Clínicas de Porto Alegre from April 2009 to September 2011. Patients (n = 115) were diagnosed with BD and had not had an acute episode during the previous month. Exclusion criteria included neuropsychiatric or medical disorders. Controls (n = 25) were first degree relatives of patients diagnosed with BD and never diagnosed with a psychiatric disorder. Socio-demographic, clinical and functional data were collected. Serum cytokines, brain-derived neurotrophic factor and biomarkers of lipid and protein oxidation were assessed. Cluster analysis was carried out to build a model of staging and a logistic regression was conducted to study any associations between the model and biomarkers.

Results: Cluster analysis divided the sample into two equitable groups, denominated early- and late-stage, with empirical cut-offs for the Functioning Assessment Short Test score, number of episodes, age at onset of the disorder and time elapsed since first episode. In the logistic regression, IL-6 was associated with late-stage (p = 0.029).

Conclusions: The present study supports the distinction between two clusters in bipolar patients, namely early- and late-stage, in terms of clinical, functional and biochemical correlates.

Keywords: staging; early-stage; late-stage; bipolar disorder; interleukin 6; functional outcome

Mood and cognition in bipolar disorder—the association with glycogen synthase kinase-3 beta

AS Jacoby, M Vinberg, K Munkholm, L Kessing

Department of Affective Disorders, Psychiatric Centre Copenhagen, Copenhagen, Denmark

Objectives: Glycogen synthase kinase-3β (GSK-3β) is a promising biomarker involved in the mechanism of action of lithium and in mood and cognition in bipolar disorder. The aim of the present study is to investigate whether the activity of GSK-3β varies with longitudinal alterations in mood in patients with bipolar disorder. Furthermore we wish to investigate cognitive function and activity of GSK-3β in patients in remission compared to healthy individuals. We hypothesise that: (1) The activity of GSK-3β in peripheral blood varies with mood states in patients with bipolar disorder, (2) The activity of GSK-3β is slightly increased in the remitted state of individuals with bipolar disease compared to healthy control individuals and (3) The activity of GSK-3β is associated with cognitive function in patients with bipolar disorder and in healthy controls.

Methods: The study will include a total of 60 patients with bipolar disorder aged 18–60 years and currently hospitalised with a manic or mixed episode at a psychiatric ward in the Capital Region of Denmark. Forty healthy age and gender matched control individuals will be recruited via the Blood Bank of the Capital Region of Denmark. Patients are followed prospectively during the hospitalisation period and in a six-month period following discharge from hospital with assessment during mood episodes and remitted phase. Blood testing and ratings are performed during the initial manic/mixed episode, during remission and during subsequent depressive and new manic or mixed episodes. Patients' cognitive function is tested twice during the study (in remitted phase). In healthy control individuals, similar tests are performed at the initial interview and after 3 months.

Results: The study is ongoing and so far 36 patients and 40 controls have been included.

Perspectives: This is the first study using a prospective design with assessment of GSK-3β in manic, depressive and remitted states of bipolar disorder in this way taking intraindividual as well as inter-individual differences into account. The results of the study are expected to contribute to the understanding of the neurobiological mechanisms underlying bipolar disorder and the observed disturbances in cognitive function in the disorder.

Strong evidence for an association between electrodermal hyporeactivity and suicide propensity in bipolar disorder

W Kaschka^a, LH Thorell^b, S Hodgkinson^a, J Steyer^a, R Straub^a, M Wolfersdorf^c, M Jandi^a

^aPsychiatry I, University of Ulm, Ravensburg, Germany, ^bResearch, Emotra AB, Linköping, Sweden, ^cPsychiatry, District Hospital, Bayreuth, Germany

In a meta-analysis electrodermal hyporeactivity was strongly associated with suicide in depression. Its sensitivity and specificity for suicide were high. The present study was designed to confirm earlier results and to explore electrodermal hyporeactivity in relation to diagnosis (unipolar or bipolar depression), severity of depression, trait anxiety, and its stability over several episodes of depression. Depressed inpatients (n = 783), 18–65 years of age, were investigated for habituation of electrodermal response and by Beck's Depression Inventory (BDI) and STAI-Trait scale. The high sensitivity and specificity of electrodermal hyporeactivity for suicide risk were confirmed. Its prevalence was highest in bipolar disorders and was independent of severity of depression, trait anxiety, gender, and age. Hyporeactivity was stable over several depressive

episodes, while reactivity changed into hyporeactivity. Present and previous findings strongly support the hypothesis that electrodermal hyporeactivity represents a central disorder, which is independent of the clinical severity of depression, but closely related to suicide propensity.

Metabolic parameters in first episode mania

S Kesebir, E Tatlidil Yaylaci, N Atgüden, M Altintas

Psychiatry, Erenköy Mental and Neurological Disease Training and Research Hospital, Istanbul, Turkey

Objective: Increasing number of evidence shows that there is a bidirectional connection between mood disorders and some medical diseases. Glucocorticoid/insulin signal mechanisms and immunoenflammatory effector systems are junction points that show pathophysiology between bipolar disorder and general medical situations susceptible to stress. A subgroup of mood disorder patients are under risk of developing obesity and diabetes. Their habits and life styles, genetic predisposition and treatment options are parameters that define this subgroup. The aim of this study was to compare metabolic parameters at first manic episode and healthy individuals.

Methods: Fifty patients diagnosed with mania according to DSM IV-TR criteria in Erenköy Mental and Neurological Diseases Training and Research Hospital and who had their first episode and did not previously receive antipsychotic treatment and 50 controls composed of healthy volunteers were evaluated in the study. In both groups BMI, fasting blood glucose, HbA1c, total cholesterol, triglyceride, HDL cholesterol and, LDL cholesterol levels were measured and compared. For the confirmation of mania Young Mania Rating Scale were used.

Results: In first manic episode, HDL cholesterol level was found to be lower than those in healthy individuals. For only women patients, BMI, triglyceride and LDL cholesterol levels were found to be higher than those in healthy individuals. A weak correlation was found between triglyceride and YMRS score.

Conclusion: These findings should be considered as to question if the bipolar disorder itself acts like metabolic syndrome related to gender.

Keywords: first episode, mania, metabolic syndrome

Thyroid functioning in first episode mania

S Kesebir, E Tatlidil Yaylaci, N Atgüden, M Altintas

Psychiatry, Erenköy Mental and Neurological Disease Training and Research Hospital, Istanbul, Turkey

Objective: Nevertheless the effects of lithium and carbamazepine do not fully explain the association between Bipolar Disorder and thyroid dysfunction. In a sample of bipolar patients who had never been treated with either lithium or carbamazepine the rate of thyroid hypofunction was 9%. Primary hypothyroidism was diagnosed in 3% of a general population. The aim of this study was to compare thyroid function tests at first manic episode and healthy individuals.

Methods: Fifty patients diagnosed with mania according to DSM IV-TR criteria in Erenköy Mental and Neurological Diseases Training and Research Hospital and who had their first episode and did not previously receive antipsychotic treatment and 50 controls composed of healthy volunteers were evaluated in the study. In both groups TSH, FT3, and FT4 levels were measured and compared. For the confirmation of mania Young Mania Rating Scale were used.

Results: In first manic episode, TSH level was found to be higher than those in healthy individuals.

Conclusion: First episode manic patients showed significantly lower levels of thyroid functioning than those in healthy individuals, as measured by higher TSH levels.

Keywords: first episode, mania, thyroid functioning

Are ICAM, VCAM and E-Selectin levels different in first manic episode and subsequent remission?

S Kesebir, C Turan

Psychiatry, Erenköy Mental and Neurological Disease Training and Research Hospital, Istanbul, Turkey

Objective: In bipolar patients, the rate of mortality from cardiovascular diseases is two fold higher than that in other psychiatric disorders. The risk of atherosclerosis and cardiovascular diseases was found to be associated with some cellular adhesion molecules: Intracellular adhesion molecule (ICAM), vascular cell adhesion molecule (VCAM) and E-Selectin. The aim of this study was to compare ICAM, VCAM and E-selectin levels at first manic episode and subsequent remission period and to determine whether they are different from those in healthy individuals.

Methods: Fifty patients diagnosed with mania according to DSM IV-TR criteria in Erenköy Mental and Neurological Diseases Training and Research Hospital and who had their first episode and did not previously receive psychotropic medication and 50 controls composed of healthy volunteers were evaluated in the study. In both groups and in remission period following mania (n = 40) plasma ICAM, VCAM and E-Selectin, fasting blood glucose, total cholesterol, LDL cholesterol, HDL cholesterol and triglyceride levels were measured and compared. For the confirmation of remission period, Young Mania Rating Scale and Hamilton Depression Rating Scale were used.

Results: In first manic episode, ICAM and VCAM values were found to be higher than those in subsequent remission and in healthy individuals. A weak correlation was found between first manic episode ICAM levels and YMRS scores. In mania, a weak correlation was found between ICAM and total cholesterol and LDL cholesterol levels and between ICAM, VCAM and E-Selectin levels and BMI.

Conclusion: In the study, which is the first investigation of proinflammatory and prothrombotic state, which is defined as a risk for metabolic syndrome and cardiovascular disease, ICAM and VCAM levels were found to be higher in mania than subsequent remission and healthy individuals. As the study group included first episode cases, there was no effect of chronic psychotropic use. Probable risk of cardiovascular disease, reflected by increased ICAM and VCAM levels is already present in bipolar patients at the onset of the disease.

Keywords: bipolar disorder, ICAM, VCAM, E-Selectin, atherosclerosis

Serotonergic dysfunction in patients with bipolar disorder assessed by the loudness dependence of the auditory evoked potential (LDAEP)

S Lee

Psychiatry, Inje University Ilsan Paik Hospital, Gyeonggi-do, Korea

Background: The loudness dependence of the auditory evoked potential (LDAEP) is suggested to be a marker of serotonin system function. This study explored the LDAEP of multiple mood statuses (depression, mania, and euthymia) and its clinical implication in bipolar disorder patients.

Methods: A total of 89 subjects, comprising 35 patients with bipolar disorder, 32 patients with schizophrenia, and 22 healthy controls were evaluated. The bipolar disorder cases comprised 10 depressed patients, 15 patients with mania, and 10 euthymic patients. The N1/P2 peak-to-peak amplitudes were measured at five stimulus intensities, and the LDAEP was calculated as the

slope of the linear regression. Both cortical and source LDAEP values were calculated.

Results: LDAEP varied according to mood statuses, and was significantly stronger in cases of euthymia, depression, and mania. Cortical LDAEP was significantly stronger in patients with bipolar euthymia compared with schizophrenia, stronger in bipolar depression than in schizophrenia, stronger in healthy controls than in schizophrenia patients, and stronger in healthy controls relative to bipolar mania. Source LDAEP was significantly stronger in patients with bipolar euthymia, bipolar depression, and bipolar mania compared with schizophrenia. Psychotic features weakened the source LDAEP relative to nonpsychotic features. The severity of the depressive symptom was negatively correlated with source LDAEP.

Keywords: LDAEP, serotonin, bipolar disorder, ERP

Immune and neurotrophic factors in bipolar offspring: followed from adolescence into adulthood

E Mesman^a, MHJ Hillegers^a, O Ambree^b, V Arolt^b, WA Nolen^c, HA Drexhage^d

^aPsychiatry, UMC Utrecht, Utrecht, Netherlands, ^bPsychiatry, University of Muenster, Muenster, Germany, ^cPsychiatry, University of Groningen, Groningen, Netherlands, ^dImmunology, Erasmus Medical Center, Rotterdam, Netherlands

Background: There is increasing evidence that both immune and neurochemical alterations are involved in the pathogenesis of bipolar disorder; however, their precise role remains unclear. In this study, we examine immune and neurotrophic factors in a prospective study on children of patients with bipolar disorder (bipolar offspring).

Methods: Bipolar offspring, originating from the Dutch bipolar offspring study (n = 140), were evaluated at adolescence, young adulthood and adulthood. We examined the expression of 44 inflammation-related genes in monocytes, and the cytokines PTX3, CCL2 and IL-1 β and the neurotrophins BDNF and S100B in the serum of bipolar offspring and healthy controls.

Results: During adolescence, bipolar offspring showed an increased inflammatory gene expression in monocytes, high serum PTX3 levels, but normal CCL2 levels. BDNF levels were decreased, while S100B levels were normal. During young adulthood monocyte activation remained, although to a lesser degree. Serum PTX3 levels remained high, CCL2 levels were increasing. BDNF and S100B levels were not measured. At adulthood, circulating monocytes had lost their activation state, but signs of monocyte migration into the tissues became apparent through raised CCL2 levels. BDNF was decreased, whereas S100B increased. Abnormalities were independent of psychopathology state at all stages.

Conclusions: This study demonstrates an aberrant immune and neurotrophic state in bipolar offspring, which followed a dynamic course from adolescence into adulthood and was present irrespective of lifetime or future mood disorders. We therefore assume that the aberrant immunoneurotrophic state rather reflects a general state of vulnerability for mood disorders than being of direct predictive value.

Influence of AHI1 variants on diagnosis and treatment outcome in mood disorders

C Pae^a, S Porcelli^b, B Balzarro^b, O Bianchini^b, C Han^c, S Lee^a, S Lee^d, PS Masand^e, A Serretti^b

^aPsychiatry, Bucheon St. Mary's Hospital, The Catholic University of Korea, Bucheon, Korea, ^bPsychiatry, Institute of Psychiatry, Department of Biomedical and NeuroMotor Sciences, University of Bologna, Bologna, Italy, ^cPsychiatry, Korea University, Seoul, Korea, ^dPsychiatry, Duke University, Durham, NC, USA, ^eCEO, Global Medical Education, New York, NY, USA

Objective: The present study aimed to explore whether four single nucleotide polymorphisms (SNPs) within the AHI1 gene could be associated with major depression (MD) and bipolar disorder (BD), and whether they could predict clinical outcomes in such psychiatric disorders.

Methods: 184 in-patients suffering from MD and 170 in-patients with BD, and 170 psychiatrically healthy controls were genotyped for four AHI1 SNPs (rs11154801, rs7750586, rs9647635 and rs9321501). Baseline and final clinical measures for MD and BD patients were assessed through the Hamilton Rating Scale for Depression (HAM-D). Allelic and genotypic frequencies in subjects suffering from each disorder were compared with those of other groups together using the χ^2 statistics. Repeated measure ANOVA was performed to test possible influences of SNPs on treatment efficacy.

Results: The rs9647635 A/A was more represented in subjects with BD as compared with MD and healthy subjects together. The rs9647635 A allele was more represented in subjects with BD and rs7750586 C allele frequency was higher in subjects suffering from BD and MD as compared with healthy subjects.

Conclusion: Our findings provide potential evidence of an association between AHI1 and mood disorders susceptibility. However, further research is needed to draw more definitive conclusions.

Keywords: pharmacogenetics, mood disorders, AHI1, mood stabilisers, antidepressants

Quantitative electroencephalogram (QEEG) findings suggesting bipolarity in patients with depressive episode : a preliminary report

S Ryu, H Jeon, B Lee, Y Cho, Y Kim, E Lee, S Yoon, K Hong, B Yu

Department of Psychiatry, Samsung Medical Center Sungkyunkwan University School of Medicine, Seoul, Korea

Objective: The identification of objective biomarkers for detecting bipolarity in depressed patients will contribute to differentiation of bipolar spectrum disorder from unipolar depression. This study aimed to investigate neurophysiologic characteristics related to bipolarity in depressed patients using quantitative analysis of electroencephalogram (qEEG).

Methods: The study subjects were 22 hospitalized patients with depressive episode (age 20–49 years). We used the Korean versions of the Mood Disorder Questionnaire (K-MDQ) to assess their bipolarity. Diagnoses were evaluated via the Korean version of Mini-International Neuropsychiatric Interview (M.I.N.I.)–14 patients with major depressive disorder (MDD) and eight patients with bipolar II disorder. Resting state eye-closed EEG signals were recorded from 19 scalp locations according to the international 10/20 system. Relative qEEG powers were calculated for delta (1–4 Hz), theta (4–8 Hz), alpha (8–12 Hz) and beta (12–25 Hz) bands.

Results: In the partial correlation test adjusted for sex, age, diagnosis and Hamilton Depression rating scale (HAM-D) score, relative beta powers at the frontal area (Fp2, F3, F7, F8) were positively correlated with K-MDQ scores. In the comparison between patients group with bipolarity (K-MDQ score ≥ 7) and without

bipolarity (K-MDQ score < 7), the former group showed higher relative beta power at the left frontal area (F3, F7). The correlation between K-MDQ score and relative beta power at the frontal area was also significant in the subgroup analysis of patients with MDD ($r = 0.670$, $p = 0.024$ at F3; $r = 0.657$, $p = 0.028$ at F8).

Conclusion: These findings suggest that increased frontal beta activity could be a biomarker of bipolarity in patients with depressive episodes.

Lithium ameliorates rotenone-induced methylation and hydroxymethylation of dna in cortical primary neurons

G Scola^a, HH Kim^a, M Salvador^b, LT Young^a, AC Andreazza^a

^aPsychiatry, University of Toronto, Toronto, Canada,

^bBiotechnology, University of Caxias do Sul, Caxias do Sul, Brazil

Background and objective: Mitochondrial complex I dysfunction is consistently reported in bipolar disorder (BD). Alterations in methylation levels have also been reported in BD, and lithium was found to cause modifications in epigenetic factors in patients and in cells. One of the mechanisms by which lithium may exert its effects in BD is by improving mitochondrial function. Therefore, in order to examine the link between complex I activity and methylation and hydroxymethylation of DNA, we treated rat primary cortical neurons with rotenone, which is an inhibitor of complex I.

Methods: Rat E18 cortical neurons were grown for 7 days and treated with 0.75 mM lithium for another 7 days and rotenone (5 nM, 10 nM, and 50 nM) for 30 min. Complex I activity, ATP production, cellular death and apoptotic cells and the levels of 5-methylcytosine (5mc) and 5-hydroxymethylcytosine (5hmc) were examined.

Results: Rotenone was found to decrease complex I activity, ATP production and increase apoptotic cells. Moreover, rotenone increased levels of 5mc and 5hmc, suggesting a possible association between complex I dysfunction and epigenetic changes. Importantly, lithium was able to ameliorate rotenone-induced damage to mitochondrial function, cell viability and prevent hypermethylation and hydroxymethylation of DNA, demonstrating its ability to maintain cellular homeostasis.

Conclusions: Although preliminary, the findings of this study implicate the involvement of complex I in epigenetic alterations found in patients with BD, and the ability of lithium to ameliorate such modifications. Future studies using different models and techniques may further elucidate the relationship between complex I function and epigenetic factors in BD.

Correlation between peripheral BDNF levels and hippocampus volume in children and adolescents with bipolar disorder

TL Peruzzolo, M Anes, GLCL Motta, LS Motta, AC Louredo,

JB Brun, R Rodrigues^a, F Kapczinski, S Tramontina, CP Zeni

^aPsiquiatria, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil

Abstract: Pediatric bipolar disorder is a serious mental disorder that affects the development and emotional growth of patients. BDNF is known to be one of the etiological factors involved. This neurotrophin has recognized role in survival, differentiation, and neuronal growth during childhood and adulthood. Furthermore, BDNF seems to affect neurogenesis in the hippocampus, one of the brain regions involved in the pathogenesis of mood disorders.

Aims: The study of possible correlations between serum BDNF and hippocampal volumetric changes in patients with bipolar disorder by magnetic resonance may bring important contributions to the understanding of the disorder neurobiology. Thus, our aim

with this study is to evaluate possible changes in hippocampal volume in children and adolescents with BD, and associate them to serum BDNF.

Methods: Subjects included 30 patients aged 6 to 18 years from the ProCAB (Program for Children and Adolescents with Bipolar Disorder).

Evaluation process: Patients undergo screening in which are applied the DSM-IV criteria for BD by a child and adolescent psychiatrist. When BD was suspected, patients were submitted primarily to a semi-structured interview with K-SADS-PL, performed by assistant researchers. A second clinical evaluation was performed by a child and adolescent psychiatrist, followed by the application of scales for measurement of mood symptoms (Brazilian version of YMRS and CDRS). Patients with confirmed diagnosis of BD collected blood samples for genetic evaluation and biochemistry, and performed neuroimaging studies.

Results: Blood samples for peripheral BDNF assessment, as well as neuroimaging, are being processed at this time. We expect to find reductions in hippocampal volumes, as well as low levels of BDNF, in accordance with that found in most previous studies.

Conclusions: Despite the devastating effect of BD on child development, little is known about the causes of this disorder. With our study, we expect to contribute to the advancement of research of the BD pathophysiological mechanisms.

Amygdalar volumetric correlates of social anxiety in bipolar offspring with subthreshold mood symptoms and high social anxiety

MH Park, A Garrett, S Boucher, M Howe, EM Sanders, JG Pearlstein, MK Singh, KD Chang

Pediatric Bipolar Disorders Program, Stanford University School of Medicine, Stanford, CA, USA

Objective & Background: The prevalence of social anxiety disorder is remarkably high in bipolar offspring and social anxiety disorder may be a significant risk factor for developing bipolar disorder (BD). We compared social anxiety symptoms between BD offspring with subthreshold mood symptoms (high-risk group: HR) and healthy controls (HC). We also explored the correlations between amygdalar volumes and social anxiety symptoms in the HR group with high social anxiety scores (HRHA).

Methods: Youth participating in the study included 29 HR and 17 HC of comparable age and gender. To assess social anxiety symptoms, we used the Multidimensional Anxiety Scale for Children (MASC) social anxiety scale.

Results: The HR group's MASC social anxiety score was significantly higher than that of the HC group ($p < 0.0001$). Among the 29 HR, 17 subjects (58.6 %) showed high social anxiety and they were classified as the HRHA. There were significant negative correlations between amygdalar volumes and MASC social anxiety score in the HRHA group (total: $\beta = -0.742$, $p = 0.004$, left: $\beta = -0.727$, $p = 0.016$, right: $\beta = -0.672$, $p = 0.002$).

Conclusions: Taking the results of this study and previous studies into consideration, the HRHA group and pediatric BD patients may share similar neural phenomena: decreased amygdalar volume and amygdalar hyperactivity. These results support the suggestion from previous studies that social anxiety symptoms in high-risk youth may increase the risk for developing BD.

Lamotrigine treatment of adolescents with unipolar and bipolar depression: a retrospective chart review

SH Shon, HW Kim, YH Joo, JS Lee

Psychiatry, Asan Medical Center Seoul, Seoul, Korea

Objectives: To investigate the preliminary effectiveness and safety of lamotrigine for the treatment of depressive episodes in adolescents.

Methods: This was a 12-week retrospective chart review of lamotrigine treatment among 37 adolescents (mean age 16.3 ± 1.3 years) suffering from depressive episodes (15 with bipolar disorder and 22 with major depressive disorder). Illness severity at the 4th, 8th, and 12th weeks were retrospectively scored using Clinical Global Impression of Severity (CGI-S) and Clinical Global Impression of Improvement (CGI-I).

Results: The mean dose of lamotrigine was 65.4 ± 37.5 mg/day (range 12.5–181.7 mg/day) for a mean duration of 199.9 ± 217.4 days (range 14–879 days). The CGI-S scores were significantly decreased over 12 weeks ($F = 39.611$, $p < 0.001$, partial $\eta^2 = 0.531$). Seventeen subjects (45.9%) showed a treatment response at 12-week follow up (defined by a CGI-I score ≤ 2). There were no differences in treatment effectiveness between the bipolar and unipolar groups. Overall, lamotrigine was well tolerated. The most common adverse event was skin rash ($n = 5$, 13.5%) which resolved spontaneously after drug discontinuation.

Conclusion: Our results provide preliminary evidence of the effectiveness and safety of lamotrigine in adolescents with bipolar and depressive disorders. Large, prospective, placebo-controlled studies are needed to confirm these findings.

Keywords: adolescent; bipolar disorder; depression; lamotrigine

Early signs of anomalous neural functional connectivity in healthy offspring of parents with bipolar disorder

M Singh^a, KD Chang^a, RG Kelley^a, M Sagar^a, A Reiss^a, IH Gotlib^b

^aPsychiatry and Behavioral Sciences, Stanford University, Stanford, CA, USA, ^bPsychology, Stanford University, Stanford, CA, USA

Objective: Bipolar disorder (BD) is associated with aberrant functional connectivity between frontal and subcortical brain regions involved in emotion regulation. It is unknown whether these connectivity patterns occur before the onset of illness representing a vulnerability for developing BD. This study aimed to use resting state functional magnetic resonance imaging (rs-fMRI) to examine underlying neural network vulnerabilities for cognitive and affective dysfunction in healthy offspring of parents with BD and matched control participants.

Methods: Using two complementary methodologies (data-driven independent component analyses (ICA) and hypothesis-driven region-of-interest (ROI)-based functional connectivity), we examined rs-fMRI data in 8–18 years old healthy offspring with at least one parent with BD ($N = 24$, “high-risk”) and age-matched healthy comparison youth without any personal or family history of psychopathology ($N = 25$, “low-risk”).

Results: ICA revealed that relative to low-risk youth, high-risk youth showed significantly increased functional connectivity between the left ventrolateral prefrontal cortex (VLPFC) and the left executive control network. ROI-based analyses revealed decreased functional connectivity of cortico-subcortical connections in high-risk youth. Older and higher functioning high-risk youth showed stronger connections between the left VLPFC and executive control network, suggesting a potential neuroprotective mechanism for high-risk youth as they age. High-risk youth with more chaotic family settings showed decreased connectivity between the left VLPFC and caudate, suggesting an environmental influence on frontostriatal connectivity.

Conclusions: Healthy offspring of parents with BD show atypical patterns of prefrontal-subcortical intrinsic connectivity that may be candidate BD endophenotypes. Longitudinal studies are needed to determine whether these patterns are associated with poor clinical outcome.

Circadian rhythm disruption in women with bipolar and premenstrual dysphoric disorder during remission: preliminary results

SK Syan^a, M Smith^b, N Snelgrove^b, M Sehmbi^a, O Allegra^b, L Minuzzi^b, BN Frey^b

^aMcMinds Neuroscience Graduate Program, McMaster University, Hamilton, Canada, ^bPsychiatry & Behavioural Neurosciences, McMaster University, Hamilton, Canada

Background/Aims: Women with bipolar disorder (BD) and premenstrual worsening of symptoms display shorter time to relapse, more frequent hospitalization and greater symptom severity. Moreover, abnormalities in sleep often precede the occurrence of manic and depressive episodes. We hypothesize that women with BD and co-morbid premenstrual dysphoric disorder (PMDD) will display greater disruptions in sleep and circadian rhythms. Here we measured circadian rhythm disruption in women with BD (with and without PMDD), women with PMDD only and matched controls using the Biological Rhythms Interview of Assessment in Neuropsychiatry (BRIAN) scale.

Methods: Women between 18 and 45 years of age, with regular menstrual cycles, not using any form of hormonal contraceptive were studied. Psychiatric diagnoses were assessed with the SCID-IV and PMDD was confirmed with 2 month prospective charting. All BD subjects were euthymic for at least 2 months. BRIAN was administered during the follicular phase of the menstrual cycle.

Results: Bipolar subjects with co-morbid PMDD scored highest on the BRIAN (BD+/PMDD+, $n = 4$, mean \pm SD = 54.0 ± 3.1) followed by patients with PMDD only (BD-/PMDD+, $n = 4$, mean = 41.7 ± 8.1), BD only (BD+/PMDD-, $n = 5$, mean = 41.2 ± 6.2), and healthy controls (BD-/PMDD-, $n = 9$, mean = 31.8 ± 4.8). One-way ANOVA ($F = 14.5$, $p = 0.00004$) followed by Tukey's HSD revealed that BRIAN scores were higher in BD + PMDD+ than BD+PMDD- ($p = 0.016$), BD-/PMDD+ ($p = 0.03$) and controls ($p = 0.00002$). In addition, both BD+/PMDD- ($p = 0.03$) and BD-/PMDD+ ($p = 0.04$) had higher BRIAN scores than controls. No differences in BRIAN scores were found between BD+/PMDD- and BD-/PMDD+ ($p = 0.99$).

Conclusions: These preliminary results suggest greater circadian rhythm instability in patients with BD and co-morbid PMDD. Unexpectedly, participants with PMDD only displayed a comparable level of circadian disruption during the follicular phase of the menstrual cycle with bipolar subjects without co-morbid PMDD. This finding might suggest that these psychiatric conditions may carry the same level of impact on circadian rhythms during inter-episodic periods (remission). These preliminary findings support the hypothesis that individuals with BD and co-morbid PMDD display worse quality of life and course of illness than women without co-morbid PMDD.

Does pregnancy affect circadian rhythms in women with mood disorders during remission?

E Krawczak^a, M Sehmbi^a, BN Frey^b

^aMcMinds Neuroscience Graduate Program, McMaster University, Hamilton, Canada, ^bPsychiatry & Behavioural Neurosciences, McMaster University, Hamilton, Canada

Background/Aims: Disruptions in circadian/biological rhythms are a hallmark of mood disorders such as bipolar disorder (BD) and

major depressive disorder (MDD). A significant proportion of BD and MDD subjects display abnormal circadian rhythms even during inter-episodic periods. Pregnancy is often marked with changes in circadian rhythms, but no previous studies have compared circadian rhythms in pregnant and non-pregnant women with mood disorders. The objective of this ongoing study is to determine if circadian rhythm disruptions are exacerbated in late pregnancy in women with BD and MDD. Because both manic and depressive episodes are associated with marked changes in circadian rhythms we studied only women during sustained euthymia.

Methods: 46 women were included in this preliminary analysis (26 Controls, 10 with BD, 10 with MDD). All groups were age-matched. Half of the participants were pregnant and half were non-pregnant experiencing regular menstrual cycles and not on hormonal contraceptives. Clinical assessments were carried out during the third trimester of pregnancy (>26 weeks) for the pregnant group and during the follicular phase of the menstrual cycle in non-pregnant women. Psychiatric diagnoses were confirmed with the MINI-International Neuropsychiatric Interview. Circadian rhythms were assessed through the Biological Rhythms Interview of Assessment in Neuropsychiatry (BRIAN). Severity of mood symptoms was assessed with the Montgomery-Asberg Depression Rating Scale (MADRS) and Young Mania Rating Scale (YMRS). All BD and MDD participants were currently euthymic for at least 3 months (Mean \pm SD MADRS = 7.3 ± 4.1 ; YMRS = 2.1 ± 1.7).

Results: No significant differences were found in BRIAN scores between pregnant and non-pregnant groups in either the controls or mood groups (both $p > 0.05$). However, comparisons of BRIAN scores between mood and control subjects revealed higher BRIAN scores in the mood group, despite pregnancy status ($p = 0.0003$).

Conclusions: These preliminary results show that pregnancy does not seem to affect circadian rhythms in women with or without history of BD/MDD during remission. Rather, our findings are consistent with previous literature suggesting that circadian irregularities are phenotypic characteristics of mood disorders and may have a genetic basis.

Irregularity in sleep and mealtime in the patients with bipolar disorders: a preliminary study

E Joo, E Kim, K Lee, CW Yeom

Psychiatry, Eulji General Hospital Eulji University School of Medicine, Seoul, Korea

It has been noticed that there are rhythm disturbances in bipolar disorders, macroscopically and microscopically. Circadian rhythm disturbance and more evening preference in bipolar disorder have been reported. In addition, social rhythm disturbance could precipitate the occurrence of bipolar disorders. Sleep and mealtime are essential components of circadian rhythm and social rhythm. They are the result of combination biological circadian rhythm and social circumstances. And also, sleep and mealtime provide the cues for biological and social rhythm. We hypothesized that the subjects with BPD II has more irregularity in sleep and mealtime than the subjects with BPD I, because BPD II has poorer course of illness and longer duration of episodes. Information on sleep and mealtime regularity has been collected using 3 points scale with the question: how much irregular are your sleep and mealtime. More score indicates more irregularity. We included 64 patients with BPD I and 21 patients with BPD II. For the comparison, we also included 112 recurrent MDD. Three groups were compared with ANOVA test. No statistically significant difference was found among three groups. However, there is a tendency of more irregularity in BPD II for both sleep and mealtime. We found a significant correlation between sleep regularity and mealtime regularity. More irregularities for both sleep and mealtime were correlated

with younger age, more history of suicidal attempt, more alcohol problem, and more family history of psychiatric illness. No correlation was found with sex. The sample size was not enough to conclude anything. Further studies on regularity of sleep and mealtime would be necessary.

Seasonality and its distinct clinical correlates in bipolar ii disorder: a comparison study with bipolar I disorder and major depressive disorder

J Kim, TH Ha, YS Park, JS Chang, J Kim, KS Hong, KS Ha

Psychiatry, Seoul National University Bundang Hospital, Gyeonggi-do, Korea

Objective: Seasonality is an important clinical presentation of mood disorders. More than 20% of patients with bipolar disorder and 11% with major depressive disorder may present a seasonal pattern. However, clinical phenomenology related to seasonality in bipolar disorders has been less explored. This study aimed to investigate distinct expressions and clinical correlates of seasonality between bipolar I disorder, bipolar II disorder and major depressive disorder.

Method: The subjects consisted of 204 patients with bipolar I disorder, 308 patients with bipolar II disorder and 106 patients with major depressive disorder. Seasonality was measured by using the Seasonal Pattern Assessment Questionnaire and clinical variables were obtained from structural clinical interview. The patients with and without seasonality were compared regarding sociodemographic, clinical variables and lifetime comorbid diagnoses. A stepwise logistic regression was performed.

Results: The group of bipolar II disorder has the highest Global Seasonality Score of Seasonal Pattern Assessment Questionnaire. However, the severity of seasonality was not different between the bipolar I disorder and major depressive disorder groups. In the bipolar II disorder group, the presence of seasonality was associated with female gender, depressive predominant polarity and premenstrual dysphoric disorder. The group of bipolar I disorder with seasonality showed more lifetime history of suicide attempts.

Conclusions: Our findings suggest that seasonality, as a maker of vulnerability to cyclic worsening by changes in the internal milieu, may differentiate bipolar II disorder from other subtypes of mood disorder.

Late-onset mania: white matter integrity and cognitive implications

J Ramírez-Bermúdez^a, C Berlanga^a, A Guadamuz^b, O Marrufo-Melendez^b, P Alvarado^b, C Atriano^c, R Favila^d, J Taboada^b, R Carrillo-Meza^b

^aNeuropsychiatry, Instituto Nacional de Neurología y Neurocirugía "Manuel Velasco Suárez", Mexico City, Mexico, ^bNeuroradiology, Instituto Nacional de Neurología y Neurocirugía "Manuel Velasco Suárez", Mexico City, Mexico, ^cNeuropsychology, Instituto Nacional de Neurología y Neurocirugía "Manuel Velasco Suárez", Mexico City, Mexico, ^dExperimental Neuroscience, Instituto Nacional de Neurología y Neurocirugía "Manuel Velasco Suárez", Mexico City, Mexico

Objective: To assess the integrity of white matter and cognition of patients with late-onset mania and compare the results with healthy subjects.

Background: Late-onset mania, it is known as a heterogeneous disorder, frequently related to neurological comorbidities. Neurodegenerative disease and cerebrovascular disease have been proposed as its etiological basis.

Methods: Twenty two patients with first episode mania in late life (>40), and a group of 22 healthy subjects (HS), were included in a case-control study at the National Institute of Neurology and Neurosurgery (NINN), Mexico City. Patients fulfilled criteria for

mania with or without psychotic symptoms (ICD-10: F30.1, F30.2; Bipolar I Disorder, single manic episode, in DSM-IV-TR Criteria: 296.01–296.06). HS were evaluated to discard previous or current neurological or psychiatric disease. Following data was collected from the whole sample: performance in Cognitive Status Examination (COGNISTAT), Trail Making Test A and B (TMT-A/TMT-B), as well as in the Frontal Assessment Battery (FAB). Fractional anisotropy (FA), obtained by a 3 tesla GE MRI system at the Neuroradiology Unit of NINN was obtained per participant. Correlation between participants FA, as white matter integrity marker, along with scores in cognitive performance is reported with inferential statistics analysis.

Results: We report no significant differences regarding age ($p = 0.307$), sex ($p = 1.00$) or scholastic level ($p = 0.503$) in patients group and HS group. Patients present alterations in integrity in these fascicles: right and left corpus callosum, right and left uncinate fasciculus (both, their frontal portion); left uncinate fasciculus (insular portion); left and right corpus callosum (minor forceps), and left cingulum, posterior portion. In FAB, executive motor function, showed significant difference in between groups ($p = 0.006$) and so did in inhibition tests ($p = 0.010$), HS performed better; also in COGNISTAT calculus score, $p = 0.081$.

Conclusions: Correlation between the scores in cognitive tasks and alterations in tract integrity in late-onset mania patients, showed statistical significance demonstrating the role of disruption in bilateral connectivity between ventral-prefrontal networks and temporal lobe amygdala, with cognitive diminished performance.

Changes in sleep architecture and quality in minimal hepatic encephalopathy patients and relationship to psychological dysfunction

C Liu, J Zhou

Mental Health, No. 411 Hospital of CPLA, Shanghai, China

Abstract Objectives: We investigated the characteristic changes in sleep architecture and quality in minimal hepatic encephalopathy (MHE) patients and assessed the relationship between these changes.

Methods: We conducted polysomnography (PSG) and used the Pittsburgh Sleep Quality Index (PSQI) to assess sleep architecture and quality in 98 MHE patients. We also evaluated multiple psychological dimensions and symptoms of dysfunction using the SAS, SDS, and SCL-90 inventories.

Results: The proportions of Stage 1 and Stage 2 sleep, sleep latency, microarousal frequency, total sleep time (TST), and total monitoring time were higher in the MHE group compared to the healthy control group ($p < 0.05$). In contrast, the SWS duration, REM stage duration, REM latency, sleep maintenance rate, and sleep efficiency were all reduced in MHE patients compared to the healthy group ($p < 0.01$). Except for the hours of sleep and use of hypnotic medications reported on the PSQI, all inventory item scores and total scores were significantly higher in the MHE group ($p < 0.05$). Correlation analysis revealed that there were strong correlations between many aspects of sleep architecture revealed by PSG, indices of subjective sleep dysfunction (PSQI), and self-reported psychological symptoms.

Conclusions: MHE patients suffer from multiple subjective dyssomnias, and show characteristic changes in sleep architecture. MHE is related to psychological factors.

Ultra-brief right unilateral ECT is rapidly effective in ameliorating severe mania-a case series

P Mayur^a, A Sidorov^b, A Harris^a

^aPsychiatry, University of Sydney, Sydney, Australia, ^bPsychiatry, Cumberland Hospital, Sydney, Australia

Ultra-brief right unilateral electroconvulsive therapy (ECT) in which, the pulse width of stimulation is reduced to 0.3 ms, is a novel technique that has an excellent antidepressant effect and causes only minimal cognitive impact. However its use, as an anti-manic treatment is unexplored unlike other forms of brief-pulse (≥ 0.5 ms) bilateral or unilateral ECT. Three consecutive patients who had a severe manic episode (DSM-IV) received high dose (6 times threshold) ultra-brief right unilateral ECT in the past 6 months due to inadequate response to lithium and oral and injectable anti-psychotic medications. All three patients had a complete remission from symptoms (as evaluated by clinical global impression and Young Mania Rating Scale) in less than six treatment sessions. Details of the clinical scenarios, the process of ECT and the clinical progress will be detailed during the presentation. This preliminary report of rapid amelioration of mania with ultra-brief right unilateral ECT in a small case series is promising but requires validation in larger controlled trials.

Osteoporosis: a neglected medical co-morbidity in mood disorders

M Berk^a, JA Pasco^a, FN Jacka^a, JM Hodge^b, A Stuart^a, A Torpy^a, S Dodd^a, L Williams^a, Y Gilbert^c

^aSchool of Medicine IMPACT Strategic Research Centre, Deakin University and University of Melbourne, Geelong, Australia,

^bDepartment of Medicine, Barwon Health, Geelong, Australia,

^cSchool of Medicine, Deakin University, Geelong, Australia

Background: Mood disorders are a potential risk factor for low bone mass, falls and fragility fracture as a result of disease and/or medication-related processes. However this process, its extent and the processes involved are poorly understood. The aim of this presentation is to review the extant literature on the epidemiology of bone health in mood disorders, and the effects of treatment.

Methods: A literature review was conducted and details of epidemiological and laboratory studies will be presented.

Results: Mood disorders are associated with lowered bone mineral density, and an increased risk of falls and fractures. Indeed, the presence of mood disorder is a robust risk factors for osteoporosis. Complicating this, many, but not all medications have adverse effects on bone health in addition to and independent of the impact of mood. Interestingly, there are major within-class differences in the effects of bone among antidepressants and antipsychotics. Mood disorders are also associated with an increased risk for falls and fracture.

Conclusion: Given that osteoporosis develops at a glacial pace, that these disorders are chronic and treatment is often lifelong, and that many of the pharmacological agents of concern have only been in use in recent decades, bone health is a major hidden health burden whose impact will likely emerge in coming decades. Considering the growing coalescence of basic and clinical evidence, it may be appropriate for safety monitoring guidelines to incorporate recommendations for prevention and treatment of bone disease in psychiatric patients.

Circadian genes and risk of the metabolic syndrome in patients with bipolar disorders

EY Kim^a, YM Ahn^a, SH Kim^b

^aDepartment of Psychiatry, Seoul National University Hospital, Seoul, Korea, ^bMedical Research Institute, Seoul National University, Seoul, Korea

Objective: Bipolar disorder is associated with an increased risk of metabolic syndrome (MetS). Accumulating evidence raises the hypothesis that dysregulation of circadian clock mechanisms are involved in the development of the metabolic syndrome and in the pathophysiology of bipolar disorder. The aim of the present study was to investigate the relationship between polymorphisms in selected circadian genes and features of the metabolic syndrome in bipolar and schizophrenia subjects.

Methods: A total of 150 subjects with bipolar disorder and 125 subjects with schizophrenia were included in this cross-sectional analysis. Subjects were screened for the metabolic syndrome (National Cholesterol Education Program Adult Treatment Panel III criteria) and Vitamin D-binding protein (DBP) gene (rs3848543), Period 2 genes (PER2, rs2304669), Period 3 (PER3, rs228669) genotypes.

Results: In patients with bipolar disorder, the minor alleles of rs3848543 in DBP gene, were associated with a lower risk of metabolic syndrome ($p = 0.008$), lower waist circumference ($p = 0.014$) and lower triglyceride levels ($p = 0.040$). The minor alleles of rs2304669 and rs228669 in PER genes were related with higher HDL level in bipolar subjects (both $p = 0.006$). However, there association were not significant in patients with schizophrenia.

Conclusions: Our study suggested the utility of circadian rhythm genes as a candidate genetic marker for metabolic risk in patients with bipolar disorder. Further studies are needed to uncover the exact molecular basis for this association, which could provide novel treatment targets for the metabolic syndrome in bipolar disorder.

Could metabolic syndrome comorbidity in bipolar disorder be overrated?: a study of metabolic syndrome in young subpopulation of bipolar disorder patients

N Yalin^a, OU Agdani^a, G Ergör^b, Z Tunca^a, S Vitoratou^c, A Ozerdem^a

^aDepartment of Adult Psychiatry, Dokuz Eylul University, Izmir, Turkey, ^bDepartment of Public Health, Dokuz Eylul University, Izmir, Turkey, ^cDepartment of Biostatistics, King's College of London Institute of Psychiatry, London, UK

Background & aims: The clustering of risk factors for cardiovascular disease has been described as metabolic syndrome. Bipolar patients tend to have higher rates of metabolic syndrome compared to general population. This study aimed to search for metabolic syndrome rates and associated clinical features in a young subpopulation of bipolar disorder patients.

Methods: Consecutive outpatients aging 18–45 years with a diagnosis of bipolar disorder type I were recruited in this cross sectional, naturalistic study. Patients had to be euthymic or in a subsyndromal depression/mania state (HAM-D and YMRS scores ≤ 12) with no medication change for at least 3 months preceding the time of enrollment. Patients using typical antipsychotics, sulpiride, amisulpride, clozapine, antidepressants (except for venlafaxine, escitalopram, sertraline, citalopram) or combination of two mood stabilizers except when one of them was lamotrigine and patients with a diagnosis or treatment not mentioned in metabolic syndrome criteria but influencing metabolic parameters were excluded. Metabolic syndrome was evaluated according to National Cholesterol Education Program Adult Treatment Protocol (NCEP ATP-III) criteria. Chi-square, independent

samples t-test and binary logistic regression analysis were used where needed.

Results: Eighty nine (female = 59) outpatients (mean age: 34.93 ± 7.20 years) met the inclusion criteria. The prevalence of metabolic syndrome was 32.6%. Groups with (38.34 ± 6.25 years) and without (33.28 ± 7.09 years) metabolic syndrome differed significantly with regard to age ($p = 0.002$), but not to gender. Among several clinical features that were studied, only the duration of illness was significantly different between patients with and without metabolic syndrome ($p = 0.009$). Ongoing treatments were grouped as mood stabilizer monotherapy and combination of a mood stabilizer plus an antipsychotic. There was no significant interaction between treatment groups and the presence of metabolic syndrome ($p = 1.000$). Regression model for metabolic syndrome which included duration of illness and age as covariates revealed a significant interaction only for age ($p = 0.003$) (Exp (B): 1.125 (CI: 1.042–1.215)).

Conclusion: The rate of metabolic syndrome in this young to middle age group of bipolar patients was comparable to previously reported rates (26.9% to 33.9%) in general population in Turkey. Among several clinical parameters that were assessed, age was the only predictor of metabolic syndrome.

Are EEG spectral power density of BD I and II different?

S Kesebir^a, S Sayakçi Gürdal^a, RMDemirer^b

^aPsychiatry, Erenköy Mental and Neurological Disease Training and Research Hospital, Istanbul, Turkey, ^bBiomedical Engineering, Kültür University, Istanbul, Turkey

Objective: The aim of this study was to investigate EEG spectral power density in remission of bipolar disorder type I and II, and to determine their difference.

Methods: Twenty five bipolar type I cases and 19 bipolar type II cases following in our outpatient clinic, evaluated in the remission period as at least 8 week. Inclusion criteria were not having a neurological disease especially epilepsy, no history of head trauma and/or loss of consciousness and not using drugs which can influence electroencephalographic activity. Diagnostic interviews were made with SCID-I and information on disease was recorded with SKIP-TURK. The remission was established with HDRS and YMRS. EEG records were made with digital device in 16 channels and 23 surface electrodes were placed according to international 10–20 system. Spectral power density (PSD) of EEG signal give information on the power carried out by EEG waves in defined frequency range per unit frequency. PSD is defined as per Hz microvolt decibel (dbuV/Hz) in the present study. We used median, peak, logarithmic relative power values (Lg (RP)) of each band (delta, theta, alpha, beta 1, beta 2, other) for each patient. In other words we have 16-dimensional (attributes) 44 patients with mixed classes. We implemented Support Vector Machine (SVM) and RBF function based on Principal Component Analysis (PCA) on the data matrix is used. The vector size is reduced 2 from 16 elements for each patient.

Results: We implemented 33 patients for training and remaining 11 patients are used for testing. We obtained confusion matrix. Eight patients are correctly classified as Type I (5) and Type II (3), whereas three patients are mis-classified.

Conclusion: In remission period, peak power values of spectral power density distinguish 72.2% of cases correctly as bipolar disorder type I and II.

Keywords: EEG, spectral power density, bipolar disorder type I, bipolar disorder type II

Cannabis use in first episode bipolar disorder is associated with elevated mood after one year

L Kvittland, PA Ringen, SR Aminoff, OA Andreassen, C Demmo, TV Lagerberg, IS Melle

Clinical Medicine, Oslo University Hospital, Oslo, Norway

Aims: Few risk factors outside family history have been identified as central in the development of bipolar disorders. Substance use is common in bipolar disorder and epidemiological studies show a high prevalence at first treatment. Recent evidence indicates that cannabis use may affect the onset of bipolar disorder, and that it seems to be associated with poorer outcome. Knowledge of the influence of cannabis on different aspects of longitudinal outcome in bipolar disorder is scarce. The main aim of this study was to investigate the association between cannabis use and clinical outcome after one year in patients with first episode bipolar disorder.

Methods: Sixty patients with first episode bipolar disorder from the Thematically Organized Psychosis (TOP)-study were evaluated within one year of onset (baseline-T1), and re-assessed after one year (T2). The SCID-I was used for DSM-IV diagnosis. Concurrent manic symptomatology was measured by the YMRS. Manic and depressive episodes were rated based on the SCID-I. Any cannabis use within the six last months before T1 and any use between T1 and T2 was recorded. A group comparison between the users and no-users was performed.

Results: Mean age of participants was 31 (SD: 10.6), 60% were females. Cannabis use at T1 was reported in 13% of the females and 35% of the men. Cannabis use at T1 was associated with higher YMRS-scores at T2 ($p < 0.01$). Cannabis use between T1 and T2 was associated with more concurrent suicide attempts ($p = 0.01$) and a higher number of admissions to psychiatric hospitals ($p < 0.05$).

Discussion: The first main finding is an association between cannabis use within one year of onset of bipolar disorder and more manic symptoms 1 year later. The second main finding was that cannabis use in the first year after the initial assessment was associated with more suicide attempts and psychiatric hospital admissions. Identification of possible course modifiers for bipolar disorder is of great clinical importance.

Clinical and biological characterization of young people at high genetic risk for bipolar disorder

P Mitchell

Psychiatry, University of New South Wales, Sydney, Australia

With an increasing focus on staging models for conditions such as bipolar disorder, there is growing interest in characterizing young people at increased genetic risk of bipolar disorder (stage 0). Better definition of distinctive clinical and biological characteristics of stage 0 could potentially allow for implementation of preventive or early intervention programs for bipolar disorder. This presentation will outline a prospective longitudinal “at risk” study of young people (12–30 years of age) with a first degree relative with confirmed bipolar disorder which commenced in 2009. Currently we have recruited 150 at-risk subjects, 120 controls with no family history of severe mental illness, and 65 subjects with bipolar disorder in this same age group. Detailed baseline clinical assessments have found significantly higher rates of mental illness in the at-risk subjects compared to controls, particularly depression and anxiety disorders, with the rates intermediate between those in controls and those with established bipolar disorder. Consistent with several other reports, the rates of prior anxiety disorders in the at-risk and bipolar disorder groups are significantly higher than those observed in controls. Neuropsychological testing is indicating no differences in executive tasks or verbal memory, suggesting that

cognitive impairment in those with established bipolar disorder is a consequence of the illness, rather than antecedent to this. In terms of neuroimaging, we have demonstrated (in those at high risk for bipolar disorder) significantly attenuated inferior frontal gyrus (IFG) activation during a GoNoGo task examining inhibition of emotional stimuli (Roberts et al, 2013) and significantly impaired functional connectivity of the IFG to other limbic areas in both at-risk and bipolar disorder patients compared to controls. Concerning genetic studies, we have found a significant difference in the number of bipolar disorder risk alleles in those at risk to this condition compared to controls. The ultimate focus of this research will be the identification of clinical and biological predictors of “conversion” to bipolar disorder in the at-risk sample, which will facilitate the development of focused early intervention/preventive programs.

Longitudinal change of the state of metabolic syndrome in patients with bipolar disorder

NY Lee^a, SH Kim^b, YS Kim^c, YM Ahn^d

^aNeuropsychiatry, Dongguk University Ilsan Hospital, Goyang, Korea, ^bNeuropsychiatry, Institute of Human Behavioral Medicine Medical Research Center Seoul National University, Seoul, Korea, ^cNeuropsychiatry, Dongguk University Ilsan Hospital Dongguk University College of Medicine, Goyang, Korea, ^dNeuropsychiatry, Seoul National University Hospital, Seoul, Korea

Although Cross-sectional prevalences of metabolic syndrome (MetS) in patients with bipolar disorder have been reported widely and variously, the longitudinal changes of metabolic syndrome in these populations have rarely been reported. Therefore, longitudinal changes of metabolic syndrome in Korean patients with bipolar disorder were evaluated. The electronic medical record of patients with bipolar disorder of Seoul National University Hospital from June 2007 to October 2010 was reviewed and patients with repeated data for all MetS subcomponents were recruited. The American Heart Association and the National Heart, Lung and Blood Institute adaptation of National Cholesterol Education Program Adult Treatment Panel III's (ATP-III) definition of MetS and waist circumference criterion of the Korean Society for the Study of Obesity and continuous MetS risk score (cMetS) were used for analysis. A total of 105 patients with bipolar disorder were analyzed. The mean interval of measurement was 18.9 months and the rate of MetS changed from 24.8% to 23.8% without statistical significance. All subcomponents did not change significantly. The incidence of MetS during 18.9 months was 10% and the reversal rate of that was 34.6%. The rates of MetS and subcomponents in both genders did not change, though a statistically significant increase in TG levels in male patients was found. In patients with bipolar disorder with maintenance treatment, the rate of MetS did not change after 19 months. However, a considerable number of patients had newly developed and resolved MetS during the treatment. Therefore, careful evaluation of MetS is needed in the treatment of bipolar disorder.

Association of serum BDNF with verbal and visual memory deficit in subjects with bipolar disorder I

B Chatterjee^a, A Sahu^b, R Sagar^b, S Vivekanandan^c

^aDepartment of Psychiatry, All India Institute of Medical Sciences, Patna, India, ^bDepartment of Psychiatry, All India Institute of Medical Sciences, Delhi, India, ^cDepartment of Neurobiochemistry, All India Institute of Medical Sciences, Delhi, India

Background: Role of brain-derived neurotrophic factor (BDNF) has been suggested in memory via its effect on neuroplasticity in hippocampus. The same is also associated with pathophysiology of

Bipolar disorder and peripheral BDNF levels have been reported to vary during illness episodes, independent of the medication status. Neurocognitive deficits among subjects of Bipolar Disorder-I (BP-I) in symptomatic state are common which improve with resolution of clinical symptoms. However, deficits in verbal learning and memory and in some aspects of executive function are reported to persist even in euthymic state.

Aims and objective: To determine the association of serum BDNF level with verbal and visual memory in euthymic and manic Bipolar disorder-I subjects.

Methodology: Subjects were recruited by consecutive sampling from Psychiatry out-patient department of a tertiary care centre. Diagnosis of bipolar disorder-I was made using Structured Clinical Interview for DSM-IV Axis I Disorders-Clinician Version (SCID-CV). Subjects with Hamilton Depression Rating Scale (HAM-D) score <7 and Young Mania Rating Scale (YMRS) score <4 were classified as euthymic. Those subjects with Intelligence Quotient (measured by VAIS) below 80 or with poor attention span (Digit span test) were excluded and the rest were assessed for verbal learning and memory using Rey Verbal Learning Test (RVLT) and visual memory using Rey-Osterrieth complex figure test (RCFT). Serum BDNF was measured using an enzyme-linked immunosorbent assay (sandwich-ELISA). One-way ANOVA was used to compare variables between symptomatic and euthymic subjects and correlation analysis was used for the relationship between the neuropsychological tests and serum BDNF level.

Result: The trend result shows decreased serum BDNF level among manic subjects compared to euthymic. After controlling for attention and YMRS scores, an association could be seen between serum BDNF and the memory deficits. The details of the result will be discussed in the presentation.

Conclusion: Serum BDNF appears to be a marker of memory deficit in BPAD besides being a state marker of the symptomatic period of illness.

Keywords: brain-derived neurotrophic factor, verbal memory, visual memory, bipolar disorder-I

Study to determine appropriate time for serum level estimation for once a day administration of divalproex sodium extended release preparations

S Damegunta, MS Reddy

Psychiatry, Asha Hospital, Hyderabad, India

Background: Divalproex sodium extended release (ER) preparations received FDA approval as monotherapy for bipolar disorder in 2005, intended for once a day (OD) oral administration maintains a steady state plasma concentration for 24 hours. Therapeutic efficacy is associated with a trough level concentration between 50 and 100 $\mu\text{g/mL}$. There is no one consensus that we depend upon for an appropriate time to estimate the trough levels which impacts the proper interpretation of the valproic acid (VPA) concentration. Blood sample collected at 21–24 hours after OD dose of ER preparation is expected to have a concentration within 3% of the trough value. Conversely, a blood draw 12–15 hours after the last dosing will give a value that is 18% to 25% higher, than the actual trough value. The current study is undertaken to test this hypothesis.

Methods: This cross sectional study involves analyzing serum valproic acid levels in bipolar disorders patients compliant with extended release preparations of divalproex sodium. The dose was administered at 8 pm and blood samples were collected at 12 and 24 hours after the last dose (medication is obtained from a single manufacturer and analysis was done in a single lab). The results were analyzed using standard statistical techniques.

Results: Serum VPA levels after 12 hours ($\mu = 88.9$, $\sigma = 26.8$) was 1.3 times higher than the 24 hour levels ($\mu = 66$, $\sigma = 22.1$) after an OD dose.

Discussion and conclusion: It is observed that measuring serum VPA levels at 24 hours is recommended and provides a more accurate value for patients on OD dosage. Measuring it at 12 hours in case of OD dosing would give a 1.3 times higher value than the actual trough value.

Keywords: Divalproex sodium, 24 hour serum levels, once a day dosing

Study to determine appropriate time for serum level estimation for once a day administration of lithium

S Damegunta, MS Reddy

Psychiatry, Asha Hospital, Hyderabad, India

Background: The classical administration schedule is thrice daily for standard preparations of lithium and twice-daily schedule for sustained-release preparation. However, in practice once a day dose is being prescribed as it is associated with better compliance, and fewer side effects. Therapeutic efficacy of lithium demands maintenance of serum concentrations in the range of 0.6 and 1.2 mmol/L (trough level). The current practice is to measure serum lithium levels at 12 hours after the last dosing irrespective of frequency of administration. Common sense dictates that the trough levels for OD dosing will be at 24 hours after the last dose. Serum levels at 12 hours post dose may not represent the true trough levels and may lead to erroneous therapeutic judgment. The current study is undertaken to test this hypothesis.

Methods: This cross sectional study involves analyzing serum lithium levels in bipolar disorder patients compliant with sustained release preparation of lithium. The dose was administered at 8 pm and blood samples were collected at 12 and 24 hours after the last dose (medication is obtained from a single manufacturer and analysis was done in a single lab). The results were analyzed using standard statistical techniques.

Results: Serum lithium levels after 12 hours ($\mu = 0.82$, $\sigma = 0.29$) was 1.3 times higher than the 24 hour levels ($\mu = 0.6$, $\sigma = 0.20$) after an OD dose.

Discussion and conclusion: In contrast to the usual practice of measuring serum lithium levels at 12 hours irrespective of the dosing pattern, it is observed that measuring at 24 hours is recommended which provides an accurate trough value for patients on OD dosage. Measuring serum lithium levels at 12 hours in case of OD dosing would give a 1.3 times higher value than the actual trough value.

Keywords: Lithium, 24 hour serum levels, OD dose

Antipsychotic use and differential monitoring of cardiometabolic health in patients with bipolar disorder compared to patients with primary psychotic disorders

J Kamath, R Singh

Psychiatry, University of Connecticut, Farmington, USA

Background: Use of antipsychotic (AP) medications has been on the rise secondary to broader FDA approved indications which includes bipolar disorder (BD). Use of APs, however, has also been associated with higher risk of weight gain and metabolic syndrome with potentially serious medical consequences. Recent data suggest that patients with bipolar disorder are at high risk for metabolic syndrome and this risk is greater in patients receiving AP medications. In 2004, the American Psychiatric Association (APA) and the American Diabetes Association (ADA), in a joint statement, recommended specific guidelines for monitoring of metabolic syn-

drome associated with AP use. Adherence to APA/ADA monitoring guidelines remains limited. The present report describes AP use in patients with bipolar and other non-psychotic disorders in comparison with psychotic disorders in the outpatient psychiatry clinic at the University of Connecticut Health Center (UCHC). Monitoring of cardiometabolic health (per the APA/ADA guidelines) by patient's providers was also investigated.

Methods: The project was approved by the UCHC Institutional Review Board. A chart review form was used to gather following information: patient demographic factors, APs and indications for their use, comorbidities including cardiovascular issues and diabetes, familial risk factors, current monitoring of cardiometabolic health (as recommended by the APA/ADA consensus statement, 2004).

Results: A total of 95 randomly selected charts of patients receiving APs with primary psychotic disorders ($n = 50$) and non-psychotic disorders ($n = 45$) were reviewed using this form. The non-psychotic disorder group included a large number of patients with BD. Patients were primarily white with almost equal number of men and women in both groups. The two groups did not differ significantly in terms of demographic factors, medical/psychiatric comorbidities and familial risk factors. Preliminary analyses showed gaps in certain aspects of cardiometabolic monitoring. Notably, the gaps in monitoring were primarily seen in patients receiving APs for non-psychotic indications which included a large number of patients with BD.

Conclusion: The present study results showed that APs are being prescribed more often for non-psychotic indications including for bipolar disorder and found significant gaps in monitoring of cardiometabolic health in these patients compared to patients receiving APs for primary psychotic disorders.

Effect of meditation on reduce in girls with acute stress reaction in Tehran meditation society in 2013

SH Kavari, K Nourozi

Rehabilitation Management, University of Social Welfare & Rehabilitation Sciences, Tehran, Iran

Introduction: Influence lifestyle and aspects of patients and lead to depression and anxiety.

Objectives & Aim: The purpose of this study was to assess to the effects of meditation on Reduce in girls with acute stress reaction in Tehran stress Society in 2013.

Method: This was a quasi-experimental study which covered 40 girls with acute stress reaction in Tehran stress Society. The samples have been selected through purposive sampling and then Random assignment into intervention (20 Samples) and control group (20 Samples). Intervention was meditation classes for 4 months (16 weeks).

Conclusion: The results suggested that meditation could be an alternative exercise intervention to Reduce in women with acute stress reaction. Data analysis between the mean scores of meditation an alternative exercise and acute stress reaction samples before and after the intervention group showed significant difference ($P < 0/001$).

Keywords: meditation, acute stress reaction, Iranian girls

Comparison of brain white matter connectivity between panic disorder with and without comorbid bipolar disorder

K Se-Woong, MK Kim, B Kim, SH Lee

Department of Psychiatry, Bundang CHA Medical Center CHA University School of Medicine, Seongnam Kyonggi, Korea

Introduction: The patients of panic disorder (PD) suffered from several comorbid mental illness, especially bipolar disorder. Although

previous studies have used magnetic resonance imaging (MRI) to demonstrate structural abnormalities of brain in subjects with PD and bipolar disorder respectively, no study about the brain white matter (WM) connectivity differences between PD with and without comorbid bipolar disorder has been conducted. The objective of this study is to compare the brain WM connectivity between PD with (PD + B) and without comorbid bipolar disorder (PD-B).

Methods: 36 right-handed patients with PD (PD + B, $n = 18$; PD-B, $n = 18$) enrolled this study. All patients were interviewed and diagnosed with the diagnostic criteria in Structured Clinical Interview for DSM-IV and examined by means of MRI at 3 Tesla. The Mood Disorder Questionnaire (MDQ), Panic Disorder Severity Scale (PDSS) and Albanic Panic and Phobia Questionnaire (APPQ) were administered. Fractional Anisotropy (FA) data were compared using tract-based spatial statistics (TBSS).

Results: TBSS results showed that the FA values of patients in PD + B were significantly higher than PD-B in clusters of left middle frontal lobe WM, right temporal lobe WM, right posterior corona radiata and right superior longitudinal fasciculus (SLF). Conducting correlation analysis in the patients in PD + B shows significant positive correlations between the APPQ scores and the FA values of the right SLF and right inferior frontal WM.

Conclusion: These results suggest that comorbid bipolar disorder could influence fronto-temporal connectivity in PD. Further studies with a larger numbers of patients should be replicated to confirm our findings.

Keywords: panic disorder, comorbid bipolar disorder, white matter connectivity, neuroimaging

Mirror neuron activity and symptom dimensions in drug-naïve mania- a transcranial magnetic stimulation study

R Basavaraju, UM Mehta, J Thirthalli

Psychiatry, National Institute of Mental Health and Neurosciences Bangalore, India

Aims: Reduced mirror neuron activity (MNA) has been associated with social-cognitive impairments in schizophrenia. MNA and its functional correlates have not been investigated in patients with mania. Preliminary evidence suggests that a loss of inhibitory control over the mirror system may result in hyper-imitative or hyper-empathetic states in humans. We examined the association between putative MNA measured using transcranial magnetic stimulation (TMS) in drug-naïve manic patients and its associations with symptom dimensions. We hypothesized that MNA will have direct correlations with symptom dimensions.

Methods: Twelve patients with mania (DSM-IV criteria) were studied. Symptom severity was assessed using Young's Mania Rating Scale (YMRS). TMS was used to measure motor evoked potentials (MEP) from the right first dorsal interosseous (FDI) during action observation (of the right-FDI muscle) relative to rest state (a static image), to give a putative index of MNA. 10 MEP recordings each were obtained with four stimulus-paradigms: (a) 120% of resting motor threshold (120%RMT); (b) motor threshold 1 (MT1); (c) short interval intra-cortical inhibition (SICI) and (d) long interval intra-cortical inhibition (LICI). MEP difference between rest and action-observation conditions formed the measure of putative MNA. Spearman's correlation was used to compare MNA measures with three YMRS symptom dimensions (*irritable mania*- scores on irritability, increased motor activity and aggressive behaviour; *elated mania*- scores on elevated mood, abnormalities of language, sexual interest and insight; and *psychotic mania*- scores on abnormalities in thought content, appearance, sleep and speech).

Results: Significant correlation was observed between MNA calculated using SICI paradigm and total YMRS score ($\rho = 0.770$,

$p = 0.003$), irritable mania ($\rho = 0.695$, $p = 0.012$), elated mania ($\rho = 0.634$, $p = 0.027$) and psychotic mania ($\rho = 0.717$, $p = 0.009$). MNA calculated using the 120% RMT paradigm had a significant correlation with total YMRS score ($\rho = 0.703$, $p = 0.011$) and elated mania ($\rho = 0.602$, $p = 0.038$). Baseline cortical excitability had no significant correlations with YMRS scores, thus ruling out the possibility of generalised neuronal hyperactivity contributing to these symptoms.

Conclusions: Greater MNA was associated with increasing symptom severity of mania across different symptom dimensions. These preliminary findings suggest that a possible mirror neuron disinhibition may contribute to symptoms of mania.

Keywords: mirror neuron activity, disinhibition, mania, transcranial magnetic stimulation

Maternal oxytocin to induce labor increases the risk for offspring bipolar disorder and impaired cognition

D Freedman^a, Y Bao^b, L Shen^c, CA Schaefer^c, AS Brown^b

^aEpidemiology, Columbia University, New York, NY, USA,

^bPsychiatry, Columbia University, New York, NY, USA, ^cDivision of Research, Kaiser Permanente, Oakland, CA, USA

Background: Oxytocin is a commonly used means for inducing labor and its use has increased in recent decades. However, oxytocin is associated with a greater need for neonatal intensive care, lower Apgar scores, increased risk of ADHD, autism, and cognitive impairments. Oxytocin as a risk for bipolar disorder (BP) has not been tested previously.

Methods: A nested case-control design drawn from the Child Health and Development Study (CHDS) birth cohort which enrolled more than 19,000 live births 1959–1966 in Northern California. Potential cases with BP were ascertained by database linkages between CHDS, Kaiser Permanente Medical Care Plan (KPNC), and Alameda County Behavioral Health Care Services, and mailed questionnaires. Consensus diagnoses were made with the SCID for DSM-IV-TR. The total number of BP cases was 94. Controls were selected from the birth cohort and matched on date of birth, sex, and KPNC membership or residence in Alameda County. Labor induction was documented contemporaneous to birth in the CHDS. Cognition in childhood was measured at ages 5 and 9 to 11 in randomly drawn subsets of the entire birth cohort with the Raven Matrices and Peabody Picture Vocabulary Test (PPVT).

Results: Maternal oxytocin to induce labor is associated with a significantly increased risk of developing BP later in life (HR: 2.45, CI: 1.08–5.58, $p = 0.03$). Controlling for gestational age does not affect this result (HR: 2.44, CI: 1.07–5.55, $p = 0.03$). Maternal oxytocin is also associated with worse performance on the Raven Matrices ($N = 7017$) but not the PPVT ($N = 6959$) in childhood. Using GEE models, oxytocin was associated with a 0.16 (CI: -0.27 – -0.04) reduced score on standardized Raven (mean = 0, SD = 1) and a 0.42 lower standardized score on the PPVT (mean = 100, SD = 15). Controlling for maternal education and race did not reduce the significant effect of oxytocin on Raven performance.

Conclusions: Although a common medical procedure, labor induction with oxytocin is associated with an increased risk of BP and with worse performance on cognitive testing in childhood. This study provides additional evidence that oxytocin increases the risk of psychiatric illness and cognitive impairments. Further study of these associations is warranted.

Cortisol secretion patterns in hair: the biomarker of the future in mood disorders?

A Herane Vives^a, VDe Angel^b, A Papadopoulos^a, D Arnone^a, L Risco^b, A Cleare^a

^aPsychological Medicine, Institute of Psychiatry, London, UK,

^bTrastornos del Animo, Clinica Psiquiatrica Universidad de Chile, Santiago, Chile

The role of stress on health and its contribution to the development of mood disorders is highly controversial. Most studies looking at chronic stress and its effects on mood disorders have used either inappropriate scales or biological specimens which do not accurately reflect chronicity. The use of hair is proposed as a novel specimen, where cortisol levels can be obtained and averaged out over relatively long periods of time, therefore representing chronic levels of this hormone. Obtaining these chronic levels will allow better understanding of the role of stress in stress-related conditions and disorders. This review makes an attempt at synthesizing all the published studies on hair cortisol concentration related to stress and some psychiatric disorders; particularly in mood disorders. It describes and summarizes their findings in the aim of providing a clear picture of the current state of this line of research. This review uncovers a potential for certain disorders—like major depressive disorder—to show hypercortisolemia, while others reveal a potential hypocortisolemia (*posttraumatic stress disorder and general anxiety disorder*). Hair cortisol concentration shows promise as a specimen to differentiate between different subtypes of affective disorders, and may help further unravel the biological links between stress and related psychiatric conditions, helping diagnosis, prognosis and treatment. Future directions in this area are described. Importantly, this review proposes a new biomarker: the combination of hair and saliva measures of cortisol as a possible complete and specific pattern for each subtype of affective disorders.

Staging and profiling bipolar disorder: clinical and neurobiological approaches

R Kupka^a, F Kapczinski^b

^aPsychiatry, VU University Medical Center, Amsterdam,

Netherlands, ^bPsychiatry, Federal University do Rio Grande do Sul, Porto Alegre, Brazil

Staging of psychiatric disorders is an evolving area that will add dimensional aspects to the current classification, leading to a better understanding of pathophysiology and treatment response. Several approaches have been suggested for staging bipolar disorders, focusing more on illness progression or on inter-episodic functioning. Bipolar disorder seems to progress in portion with the number of episodes in some bipolar patients. Thus, preventing episodes may be a means to avoid progression from early stage BD into more refractory and severe late-stage BD. Recent evidence suggests that apart from number of episodes, the level of functioning during euthymia may have important clinical use. Next to defining the stage of illness progression, an individual profile of protective versus harmful factors may have prognostic value and help to choose effective interventions and avoid treatment resistance. The aim of this “brain storm” is to help investigators to establish a common language in terms of staging in order to plan future prospective studies.

A genome-wide association study of bipolar disorder using a subphenotype: sleeplessness bipolar mania

H Lee^a, C Cho^a, H Woo^b, T Greenwood^c, D Kripke^c, J Kelsoe^c

^aPsychiatry, Korea University College of Medicine, Seoul, Korea,

^bPhysiology, Ajou University School of Medicine, Suwon, Korea,

^cPsychiatry, University of California San Diego, La Jolla, CA, USA

Even though bipolar disorder (BD) is highly heritable psychiatric disorder, the investigation of specific genetic variations has suggested limited findings. It has been suggested that dividing BD to subgroups according to clinical subphenotypes is a possible approach for further genetic studies in BD. We performed a genome-wide association study (GWAS) of sleeplessness bipolar mania (SBM) versus non-sleeplessness bipolar mania (NSBM) in bipolar I disorder subjects. A total of 2,200 cases, 1,436 controls, and 703,012 SNPs in the merged samples of the Translational Genomics Institute (TGEN) and the Genetic Association Information Network (GAIN) were investigated. We identified 44 associated SNPs with $p < 10^{-4}$ in this case-only analysis, the most significant of which was rs10492908 (OR = 0.1832; $p = 9.27 \times 10^{-7}$; Permutated $P = 1.00 \times 10^{-6}$) which is located within a region of the gene encoding WW domain containing oxidoreductase (*WWOX*) on chromosome 16q23. We identified a total of eight of genomic regions of interest (ROIs) on chromosomes 3, 5, 8, 9, 12 and 17 defined as regions containing at least two SNPs with $p < 10^{-4}$ and adequate support for association (i.e., $p < 10^{-3}$) from surrounding SNPs within 100 kb. ROI5 and ROI7 showed matching genes *ROR2* and *ANKFN1*, respectively. The functional enrichment analysis showed a significant enrichment of cell development-related, cell adhesion-related, signal transduction-related, cell recognition-related, synaptic transmission-related, and cell motility-related pathways. *WWOX* is known as a putative tumor suppressor gene. But, several studies show that *WWOX* is involved in regulation activity of GSK3beta which is important in circadian rhythm and lithium mechanism of action. *ROR1* is known to be related to insomnia, and it modulates neurite growth and synapse formation in complex with *ROR2*. A GWAS of cannabis dependence reported *ANKFN1* as significantly related gene. We have explored about BD by using of a subphenotype, which is SBM, for more homogenous group of subjects with more similar clinical courses. Taken together, we speculate several candidate genes and pathways are related to sleeplessness bipolar mania. In the future, more replication study will confirm the results of present study.

Cross-disorder GWAS of ADHD and bipolar disorder

A Reif^a, Kvan Hulzen^b, CJ Scholz^c, A Arias-Vasquez^b, KP Lesch^d, SV Faraone^e, B Franke^b

^aDepartment of Psychiatry, University of Würzburg, Würzburg, Germany, ^bDonders Institute, Radboud UMC, Nijmegen, Netherlands, ^cIZKF, University of Würzburg, Würzburg, Germany,

^dDepartment of Psychiatry, University of Würzburg, Würzburg, Netherlands, ^eDepartments of Psychiatry and Neuroscience & Physiology, SUNY Upstate Medical University, Syracuse, NY, USA

There is considerable evidence that ADHD and bipolar disorder (BPD) can be co-morbid conditions. Coming from primary bipolar samples, the co-morbidity between BPD and ADHD has been estimated to be between 9 and 18%. Coming from primary ADHD samples, comorbidity rates vary more, although the mean seems to be between 9% and 19% as well. Also, family-based studies argue for a shared genetic liability between both disorders which however has not yet been addressed in depth. We have thus aimed to identify both shared as well discriminating risk genes by analyzing the ADHD and BPD GWAS datasets from the PGC; bipolar cases have been restricted to an age

of onset before the 21st birthday. The main analysis focuses on the PGC BPD and ADHD GWAS datasets on the categorical level. Hypothesis-free analyses were run by meta-analytic treatment of the data. Intriguingly, we identified two novel loci above the threshold of genome-wide significance, as well as several highly interesting suggestive loci. Polygenic analyses of genetic components of the two psychiatric diseases were also performed, training on one and using the other as target set. Finally, the fact that twice as many SNPs at a $p > 0.05$ had an OR in the same direction than in the opposite direction further added evidence to the hypothesis that ADHD and BPD have a shared genetic basis. Further description of the genetic architecture underlying the co-morbidity of ADHD and BPD will aid in identifying mechanisms of disease and hopefully also biomarkers in order to enable better differential diagnosis of these conditions.

Keywords: co-morbidity, ADHD, genetics, GWAS

Socioeconomic decision making in manic and euthymic patients with bipolar disorder: the feedback-related negativity study

RY Ha^a, V Ryu^b, SJ Lee^c, HS Ryu^c, HS Cho^c

^aPsychiatry, Seoul Bukbu Hospital, Seoul, Korea, ^bPsychiatry,

Konyang University, Daejeon, Korea, ^cPsychiatry, Yonsei University, Seoul, Korea

Bipolar disorder is characterized by behavioral changes such as risk-taking and increased goal directed activity. These kinds of behaviors may account for the abnormal reward processing in bipolar patients which result from impaired reward learning. Bipolar patients have been reported to show impaired reward learning in situations that require integration of feedbacks over time. Feedback-related negativity (FRN) is one of electrophysiological index reflecting reward learning after presentation of feedback from 200 ms to 500 ms. We investigated euthymic and manic bipolar patients during Ultimatum Game which is one of reward-related paradigm. We recruited 24 manic, 19 euthymic patients with bipolar disorder and 30 healthy controls. In Ultimatum Game, two players must split a sum of money. The proposer offers a portion to the responder, who decides to either accept or reject the offer. If responder refuses the offer, no income will be made to either of the participants. Our study showed that euthymic and manic patients rejected more than controls for unfair offers. Healthy people showed FRN amplitude was more prominent for unfair offers compared to fair offers. However, both bipolar patients' groups no significant differences in FRN amplitudes. Conclusively, these findings suggest that bipolar I patients may be impaired in socioeconomic processing which is involved in emotion recognition and decision making which result in deficits in reward learning and related electrophysiological changes.

Electrophysiological finding of syntactic anomalies in patients with bipolar disorder and schizophrenia: a P600 study

CW Lee^a, V Ryu^b, RY Ha^c, SJ Lee^a, HS Ryu^a, HS Cho^a

^aPsychiatry, Yonsei University, Seoul, Korea, ^bPsychiatry, Konyang University, Daejeon, Korea ^cPsychiatry, Seoul Bukbu Hospital, Seoul, Korea

Manic patients are known to show the symptoms of abnormal semantic and formal thoughts. The P600 is an event-related potential which is thought to be elicited by syntactical errors in listening and reading condition. We examined the alteration of the P600 wave according to auditory syntactic violation in patients with bipolar disorder and schizophrenia compared with healthy controls. Twenty-five manic patients, twenty-one bipolar euthymic

patients, nineteen schizophrenia and thirty healthy controls were recruited. We recorded the electroencephalogram during the task employing auditory syntactic violation sentence paradigm. We could find the main effect of syntactic violation during task and main effect of groups ($F = 14.41$, $p < 0.001$). The healthy controls showed the increased P600 amplitude like other previous studies. The manic, euthymic and schizophrenic patients showed decreased P600 amplitude to syntactically violated and unviolated stimuli compared to healthy controls. However, there were no significant differences among three groups. This result suggests electrophysiological alteration of syntactic anomalies in bipolar and schizophrenic patients. And manic and euthymic patients with bipolar disorder have difficulties in the syntactic processing, while the differential syntactic processing to violated and unviolated stimuli were maintained. Manic patients are known to show the symptoms of abnormal semantic and formal thoughts. The P600 is an event-related potential which is thought to be elicited by syntactical errors in listening and reading condition. We examined the alteration of the P600 wave according to auditory syntactic violation in patients with bipolar disorder and schizophrenia compared with healthy controls. Twenty-five manic patients, twenty-one bipolar euthymic patients, nineteen schizophrenia and thirty healthy controls were recruited. We recorded the electroencephalogram during the task employing auditory syntactic violation sentence paradigm. We could find the main effect of syntactic violation during task and main effect of groups ($F = 14.41$, $p < 0.001$). The healthy controls showed the increased P600 amplitude like other previous studies. The manic, euthymic and schizophrenic patients showed decreased P600 amplitude to syntactically violated and unviolated stimuli compared to healthy controls. However, there were no significant differences among three groups. This result suggests electrophysiological alteration of syntactic anomalies in bipolar and schizophrenic patients. And manic and euthymic patients with bipolar disorder have difficulties in the syntactic processing, while the differential syntactic processing to violated and unviolated stimuli were maintained.

Effects of antipsychotic drugs on the expression of synapse-associated proteins in the frontal cortex of rats subjected to immobilization stress

CH Lee^a, MK Seo^a, HY Cho^a, JG Lee^b, BJ Lee^b, SW Park^c, YH Kim^b

^aNeuroscience, Paik Institute for Clinical Research, Busan, Korea,

^bPsychiatry, School of Medicine Haeundae Paik Hospital Inje University, Busan, Korea, ^cHealth Science and Technology, Graduate School of Inje University, Busan, Korea

Purpose: Regulation of synaptic plasticity has been implicated in the pathophysiology and treatment of schizophrenia. The present study examined the effects of three antipsychotic drugs, olanzapine, aripiprazole, and haloperidol, on the expression of synapse-associated proteins in the frontal cortex of rats with and without immobilization stress.

Methods: Rats were subjected to immobilization stress 6 h/day for 3 weeks. The effects of two atypical antipsychotic drugs, olanzapine (2 mg/kg) and aripiprazole (1.5 mg/kg), on expression of serine9-phosphorylated GSK-3 β , β -catenin, BDNF, PSD-95, and synaptophysin were determined by Western blotting. A typical antipsychotic drug, haloperidol (1.0 mg/kg), was used for comparison.

Results: Immobilization stress significantly decreased the expression of phosphorylated GSK-3 β , β -catenin, BDNF, PSD-95, and synaptophysin in the frontal cortex (all $p < 0.01$). Chronic administration of olanzapine and aripiprazole significantly attenuated the immobilization stress-induced decrease in the levels of these proteins ($p < 0.01$ or $p < 0.05$), whereas chronic administration of haloperidol had no effect in this regard. Additionally, chronic

administration of olanzapine ($p < 0.05$) and aripiprazole ($p < 0.01$) significantly increased levels of phosphorylated GSK-3 β under normal conditions without stress, and chronic administration of aripiprazole also increased BDNF levels under this condition ($p < 0.01$).

Conclusions: These results indicate that two atypical antipsychotics, olanzapine and aripiprazole, and one typical one, haloperidol, differentially regulate the levels of synapse-associated proteins in the rat frontal cortex. These findings may contribute to our understanding of how olanzapine and aripiprazole improve the cognitive symptoms of patients with schizophrenia by suggesting that their mechanism of action involves up-regulation of synapse-associated proteins.

Keywords: atypical antipsychotic drugs, typical antipsychotic drugs, synaptic plasticity, synapse-associated proteins, Immobilization stress

Effects of mood-stabilizing drugs on dendritic outgrowth and synaptic protein levels in the primary hippocampal neurons

CH Lee^a, MK Seo^b, JG Lee^b, BJ Lee^b, SW Park^a, YH Kim^b

^aNeuroscience, Paik Institute for Clinical Research, Busan, Korea,

^bPsychiatry, School of Medicine Haeundae Paik Hospital Inje University, Busan, Korea

Purpose: Mood stabilizers are used to treat bipolar disorder, a disease marked by recurrent episodes of mania and depression. Growing evidence suggests that lithium (Li) exerts neurotrophic and neuroprotective effects, leading to an increase in neural plasticity. The present study investigated whether other mood-stabilizing drugs produce similar effects in primary hippocampal neurons.

Methods: Effects of the mood-stabilizing drugs Li, valproate (VPA), carbamazepine (CBZ), and lamotrigine (LTG) on hippocampal dendritic outgrowth were examined. Western blotting analysis was used to measure the expression of synaptic proteins, i.e., brain-derived neurotrophic factor (BDNF), postsynaptic density protein-95 (PSD-95), neuroligin 1 (NLG 1), β -neurexin, and synaptophysin (SYP), under toxic conditions induced by B27 deprivation, which causes hippocampal cell death.

Results: Li (0.5–2 mM), VPA (0.5–2 mM), CBZ (10–50 μ M), and LTG (10–50 μ M) at therapeutic plasma levels significantly increased dendritic outgrowth ($p < 0.05$ or $p < 0.01$, respectively). The neurotrophic effect of Li and VPA was blocked by inhibition of phosphatidylinositol 3-kinase (PI3K), extracellular signal-regulated kinase (ERK), and protein kinase A (PKA) signaling ($p < 0.05$ or $p < 0.01$); the effects of CBZ and LTG were not affected by inhibition of these signaling pathways. Li, VPA, and CBZ significantly prevented B27 deprivation-induced decreases in BDNF, PSD-95, NLG 1, β -neurexin, and SYP levels ($p < 0.05$ or $p < 0.01$), whereas LTG had no effect.

Conclusions: Taken together, these results suggest that Li, VPA, CBZ, and LTG exert neurotrophic effects by promoting dendritic outgrowth; however, the mechanism of action differs. Furthermore, certain mood-stabilizing drugs may exert neuroprotective effects by enhancing synaptic protein levels against cytotoxicity in hippocampal cultures.

Keywords: mood-stabilizing drugs, neural plasticity, dendritic outgrowth, synaptic proteins, signaling

Effects of tianeptine on motor signaling in rat hippocampal neurons

MK Seo^a, CH Lee^a, HY Cho^a, SW Park^b, BJ Lee^c, WG Seol^d, JG Lee^c, HY Kim^c

^aNeuroscience, Paik Institute for Clinical Research, Busan, Korea,

^bHealth Science and Technology, Graduate School of Inje

University, Busan, Korea, ^cPsychiatry, School of Medicine Haeundae

Paik Hospital Inje University, Busan, Korea, ^dInAm Neuroscience

Research Center, Wonkwang University Sanbon Hospital, Gunpo, Korea

Objectives: Recent studies have demonstrated that antidepressant effect of NMDA antagonist ketamine activates rapidly the mTOR pathway and increase synaptic proteins the prefrontal cortex. mTOR is a protein kinase involved in the regulation of translation initiation and protein synthesis required for synaptic plasticity. Recent studies suggest that mTOR activation may be related to the antidepressant action. However, the mTOR signaling underlying antidepressant drugs action has not been well elucidated. The aim of the present study was to find out whether alterations in mTOR signaling could be observed following treatment with tianeptine. Additionally, we investigate whether this drug affect the synaptic proteins and neurite outgrowth via mTOR signaling.

Methods: For purposes of western blotting and neurite assay, primary rat hippocampal neuronal cultures were cultured for 4 days and 5 days, respectively, with tianeptine. Control cells were cultured without tianeptine under the B27-deprived condition (for western blotting) or normal condition (for dendrite outgrowth assay). Using Western blotting, we measured changes in the phosphorylation of mTOR, its well-known downstream regulators (4E-BP-1 and p70S6K), and its upstream regulators (Akt and ERK) under toxic conditions induced by B27 deprivation in rat hippocampal neuronal cultures. Dendritic outgrowth of hippocampal neurons was determined by dendrite outgrowth assay. Dendrites were visualized by immunostaining with MAP2 known as a dendritic marker. Additionally, the synaptic proteins, PSD-95 and synaptophysin, were also examined by Western blotting.

Results: In this study, tianeptine significantly elevated the levels of phospho-mTOR, phospho-4E-BP-1, and phospho-p70S6K in a concentration-dependent manner. Moreover, tianeptine elevated the phosphorylation of Akt and ERK. Additionally, increased mTOR phosphorylation induced by tianeptine was significantly blocked by the specific PI3K, MEK, or mTOR inhibitors, respectively. Tianeptine also provoked hippocampal dendritic outgrowth and simultaneously increased levels of the synaptic proteins, PSD-95 and synaptophysin. The effect of tianeptine was blocked by the mTOR inhibitor, rapamycin.

Conclusions: In this study, we observed novel *in vitro* evidence indicating that tianeptine promoted dendritic outgrowth and increased synaptic protein levels through mTOR signaling. mTOR signaling may be a promising target for discovery of new antidepressant drugs.

Keywords: tianeptine, mammalian target of rapamycin, dendrite outgrowth, synaptic proteins, hippocampus

DNA methylation analysis of quetiapine: possible role as a mood stabilizer

H Sugawara^a, M Bundo^b, T Asai^c, F Sunaga^b, J Ueda^d, J Ishigooka^a, K Kasai^e, T Kato^d, K Iwamoto^a

^aPsychiatry, Tokyo Women's Medical University, Tokyo, Japan,

^bMolecular Psychiatry, Graduate School of Medicine University of

Tokyo, Tokyo, Japan, ^cNeuropsychiatry, Graduate School of

Medicine University of Tokyo, Tokyo, Japan, ^dLaboratory for

Molecular Dynamics of Mental Disorders, RIKEN Brain Science Institute, Wako, Japan

Introduction: The onset of mental disorders may relate to epigenetic mechanism based on gene-environmental interaction. We previously reported the hypermethylation of serotonin transporter, *SLC6A4* in patients with bipolar disorder (BD), and the methylation level in the same region was decreased in human neuroblastoma cells treated with mood stabilizers. BD is a severe mental disorder because of high recurrence rate and suicide risk, and treatment for both acute phase and relapse prophylaxis are very important. Quetiapine (QTP), which is one of atypical antipsychotics, has various effects for BD suggesting the possible role as a mood stabilizer.

Methods: We performed genome-wide methylation analysis using human neuroblastoma cells treated with QTP using Infinium HumanMethylation 27 BeadChip. We also examined common methylation changes with other mood stabilizers by QTP treatment. Furthermore, we performed bisulfite sequencing analysis to examine the effect of QTP on the DNA methylation level of the promoter region of *SLC6A4*.

Results: Promoter region of 1173 genes showed altered methylation by QTP, which were generally hypomethylated changes occurred in the CpG islands. These genes were related to cellular process, intracellular part and protein binding. There was no common effect of QTP with other three mood stabilizers (lithium, valproate, and carbamazepine). However, common methylation changes of some genes were found between lithium and QTP treatments, including *ADRA1A* gene. We detected the decreased DNA methylation level of the promoter region of *SLC6A4* by bisulfite-sequencing analysis, which was consistent change with other mood stabilizers.

Conclusion: QTP altered DNA methylation levels at the CpG sites located to the genes with various functions. Although whether these effects are directly related to drug efficacy remain unknown, decreased methylation of the promoter region of *SLC6A4* suggests the mood stabilizer-like role of QTP. Future studies such as gene expression analysis and animal model experiments will be required.

The effect of vitamin D treatment on GLIA derived neurotrophic factor in cortical neurons

S Yilmazer, T Ulutin, E Dursun, D Gezen-Ak

Department of Medical Biology, Istanbul University Cerrahpaşa

Faculty of Medicine, Istanbul, Turkey

Neurotrophins play a role in synaptic plasticity in addition to survival and growth of neurons. The role of glia derived neurotrophic factor (GDNF) has been a matter of debate in bipolar disorders. Recent studies have pointed out that vitamin D can exert protective effects on nervous system by modulating the synthesis of neurotrophins, calcium channels and calcium binding proteins. Vitamin D regulates the expression of neurotrophic factors in several cell types. Our previous study has showed that vitamin D receptor silencing showed similar effects with beta amyloid treatment and up regulated L type voltage sensitive calcium channels alpha 1C (LVSCC A1C) and nerve growth factor (NGF). These results might indicate the potential role of vitamin D–VDR pathway in neurodegeneration. The aim of this study was to investigate the level of GDNF release in 1,25-dihydroxyvitamin D₃ treated primary corti-

cal neurons. Cerebral cortex dissected from brains of Sprague Dawley rat embryos on the embryonic day 16 and cultured. GDNF release was determined by ELISA. Our preliminary findings showed that vitamin D treatment induces GDNF release. Our results indicated that the GDNF expression might be regulated by vitamin D in cortical neurons and vitamin D supplementation might be used as a tool for regulating neurotrophic factors in mood disorders.

Cytogenetic analysis and oxidative damage activity in lymphocytes of schizophrenia patients

B Vellingiri, S Mohanadevi, B Balamuralikrishnan, S Sureshkumar, M Arun, S Kathannan, K Sasikala

Zoology, Bharathiar University, Coimbatore, India

Objectives: Schizophrenia is a neurodevelopmental disorder which causes dopaminergic neuronal loss in the nigro striatal pathway. The aim of our research is to explore the relation between chromosome instability and oxidative stress biomarkers in schizophrenia using a variety of strategies.

Methods: We determined peripheral markers for oxidative damage in schizophrenia by testing for spontaneous and induced chromosomal damage, DNA strand breaks, in peripheral blood and cultured lymphocytes, and measured glutathione S-transferase activity in the plasma of patients and controls. The schizophrenia patient group comprised of 62 individuals and equal numbers of control groups were selected.

Results: Compared to healthy controls, schizophrenia patients show higher frequencies of micronuclei (17.2 ± 4.8 versus 9.0 ± 3.4 , $p < 0.001$) and a significant increase in the levels of SSB. Significant differences were also obtained in the distribution of oxidised purine bases between the two groups. Glutathione S-transferase activity in plasma from schizophrenia patients and controls was also measured and the enzymatic activity in schizophrenia patients was lower than in healthy controls.

Conclusions: Thus, we cannot speculate about the significance of our findings, although in brain, other authors have also reported no significant differences in GST activity between schizophrenia patients and controls. Further work needs to be carried out to increase the sample size in order to confirm our findings and to determine the contribution of each isoenzyme to the total GST activity in both schizophrenia and controls.

Keywords: schizophrenia, comet assay, micronuclei, glutathione S-transferases

Neuroanatomical predictors of psychoeducation response in euthymic bipolar patients: a voxel-based morphometric study

P Favre^a, M Baci^u, A Perrin^b, C Pichat^a, T Bougerol^b, M Polosan^b

^aLPNC CNRS UMR 5105, Univ. Grenoble Alpes F-38040, Grenoble, France, ^bPôle Psychiatrie et Neurologie, CHU de Grenoble, Grenoble, France

Aims: Structural neuroimaging studies concerned with bipolar disorders (BD) have mainly reported grey matter abnormalities in prefrontal and limbic regions. Although psychosocial interventions such as psychoeducation therapy have shown great promise for relapses prevention in BD, little is known about the neural basis of its prophylactic effect. This MRI study aims to assess the neuroanatomical predictors of psychoeducative outcome in euthymic bipolar patients (EBP).

Methods: We used voxel-based morphometry to compare gray-matter volume (GMV) in 14 EBP and 14 matched healthy control (HC) subjects, and implemented all the methodological improvements that have been recently developed in order to limit possible errors associated with image processing. Clinical assessment of

EBP was carried out before and after a three-month psychoeducative program. A regression analysis was performed between the whole brain GMV in EBP measured before the psychoeducation and subsequent relapse status after an 18-month follow-up period. Following this, correlations between the GMV of identified regions and clinical improvement after psychoeducation were undertaken.

Results: The comparison of EBP versus HC before psychoeducation revealed increased GMV in the left insula and right inferior prefrontal gyrus (IFG) and a decrease in right occipital and left temporal GMV in EBP as compared to HC. Moreover, the GMV of the right IFG correlated significantly with the duration of the disease, age of the first episode and the number of past manic episodes. The volume of the left dorsal caudate predicts relapse status during the 18 month follow-up period, and was negatively correlated with improvement in coping strategies subsequent to the psychoeducation program.

Conclusions: This study argues for structural abnormalities in fronto-limbic areas in BD patients. The hypertrophy of the right IFG appears to be strongly linked with the severity and the length of the disease, in accordance with the kindling hypothesis. Furthermore, the psychoeducation outcome could be predicted by subcortical structural abnormalities in BD patients. Indeed, patients with higher volume of the dorsal caudate nucleus are less likely to remain in remission following psychoeducation. This may be explained by cognitive impairments and difficulties in modifying their coping strategies.

Hippocampal volumes are correlated to inflammatory markers in early stage bipolar disorder

M Vianna-Sulzbach^a, PD Goi^a, R Massuda^a, M Vasconcelos-Moreno^a, B Panizzutti^a, G Colpo^a, R Reckziegel^a, M Costanzi^a, BT dos Santos^a, MD Curra^a, SL Polita^a, JA Duarte^a, AL Teixeira^b, F Kapczinski^a, CS Gama^a

^aLaboratório de Psiquiatria Molecular, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil, ^bLaboratory of Immunopharmacology, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

Aims: The staging model proposed by Kapczinski for Bipolar Disorder (BD) indicates that exist a neuroprogressive pattern of modifications in peripheral biomarkers and in specific neuroanatomical structures related to emotional memory consolidation, such as the hippocampus. This model suggests that there are five distinct stages (latent, yet without the disorder; stage I, with complete recover between episodes; stage II, with mild cognitive and functional decline; stage III, with prominent cognitive and functional decline; and stage IV, with complete inability to live autonomously). Inflammatory markers are among the most assessed peripheral biomarkers in psychiatric disorders, and are different among stages. The objective of the present pilot study is to assess the relationship between serum inflammatory markers (IL-2, IL-4, IL-6, IL-10 and IFN-gamma) with hippocampal volumes in different stages of BD and in matched controls.

Methods: Images were acquired by a Philips Achieva 1.5T MRI scanner at the Hospital de Clínicas de Porto Alegre, Brazil. Volumes were determined using Freesurfer v 5.1. In order to control confounding factors, gender, age, years of education and intracranial volume were regressed out from total hippocampal volumes.

Results: There was no statistical difference in inflammatory markers neither in total hippocampal volumes between patients and controls. There was no statistical difference in inflammatory markers neither in total hippocampal volumes between staging I patients and their matched controls. When assessing stage IV patients, there was no correlation between inflammatory markers and total hippocampal volumes. The same result was found among healthy con-

trols. But, in early stages of BD (Stage I patients), there is a negative correlation between total hippocampal volumes and IL-2 ($\rho = -0.642$, $p = 0.013$) and IFN- γ ($\rho = -0.650$, $p = 0.012$).

Conclusions: Available data indicates that other inflammatory markers such as IL-6 and TNF α show that patients with BD are in a proinflammatory state in both early and late stages, but the anti-inflammatory IL-10 cytokine was increased only in the early stages. Our results are in line with those, showing another facet of the same inflammatory state, and that this state is correlated to neuroanatomical modifications in the hippocampus.

Regional gray matter volume abnormalities related to cyclothymia in female subjects with bipolar II disorder

TH Ha^a, JS Kim^a, JY Hei^a, JH Kim^b, JS Chang^a, DY Lee^a, K Ha^a

^aPsychiatry, Seoul National University Bundang Hospital, Seongnam si Gyeonggi-do, Korea, ^bRadiology, Seoul National University Bundang Hospital, Seongnam si Gyeonggi-do, Korea

Objective: Bipolar II disorder with cyclothymia (BD II 1/2) is highly prevalent among clinical subjects with a major depressive episode. This subtype has a worse course and is difficult to treat. The aims of the current study was to investigate regional gray matter abnormalities related to cyclothymia in female patients with bipolar II disorder (BD II).

Methods: Thirty-two female subjects with BD II (including 13 subjects with cyclothymia) and 25 healthy female subjects were included. Clinical evaluation included structured diagnostic interview and TEMPS-A. High resolution brain magnetic resonance images were acquired from the subjects and the relation of regional gray matter volume and cyclothymia was explored using a voxel-wise analysis.

Results: Subjects with BD II only had a smaller total gray matter volume compared to the subjects with BD II 1/2 and the controls. Compared to controls, subjects with BD II only had decreased gray matter volumes in the medial prefrontal, anterior cingulate, and bilateral temporal regions. On the other hand, subjects with BD II 1/2 had no regional gray matter volume reductions. In the whole BD II group, the cyclothymia score on TEMPS-A was significantly correlated with the gray matter volume in the left superior temporal gyrus.

Conclusion: Our results suggest differential neurobiological mechanisms between BD II with and without cyclothymia. The role of superior temporal region in affective temperament and regulation needs further studies.

The effect of cortisol and bdnf on serotonin transporter in bipolar I disorder

WC Hsieh^a, YT Jou^b, JL Lin^c, SJ Wang^d, YH Chou^a

^aPsychiatry, Taipei Veterans General Hospital, Taipei, Taiwan,

^bIndustrial and Systems Engineering, Chung-Yuan Christian University, Taoyuan, Taiwan, ^cPsychiatry, Taoyuan Armed Forces General Hospital, Taoyuan, Taiwan, ^dNuclear Medicine, Taipei Veterans General Hospital and National Yang Ming University, Taipei, Taiwan, ^ePsychiatry Taipei Veterans General Hospital and National Yang Ming University, Taipei, Taiwan

Previous studies have demonstrated that there was an association between the cortisol and serotonin transporter (SERT) availability in both healthy subjects and patients with major depressive disorder (MDD). The aim of this study was to assess if this association could be replicated in bipolar disorder (BD). Furthermore, a second biomarker, brain derived neurotrophic factor (BDNF), was also inserted into the regression model to test the role of BDNF on SERT availability in BD. Twenty-eight BD I euthymic patients and 28 sex- age- matched controls were recruited. ¹²³I-ADAM with sin-

gle photon emission computed tomography (SPECT) was applied for the measurement of the SERT availability. Ten ml venous blood was withdrawn when the subject underwent SPECT measurement. Simple ratio method was used for derivation of the SERT availability. There was a significant decreased in SERT availability in patients compared with controls (2.4 ± 0.6 versus 2.9 ± 0.7 , $p = 0.002$), whereas the cortisol and BDNF was not different between patients and controls. Regression model showed that the SERT availability can be explained by cortisol but not by BDNF and their interaction in controls (whole model: $R^2 = 0.19$, $p = 0.02$, cortisol: $\beta = 0.64$, $p = 0.013$, BDNF: $\beta = 0.22$, $p = 0.418$, Cortisol*BDNF: $\beta = 0.39$, $p = 0.158$). Notably, the finding cannot be found in BD patients. The result implicated that the role of cortisol in regulating SERT availability is different between MDD and BD.

Neuroanatomical correlates of inhibited temperament in offspring of parents with bipolar disorder

EJ Kim^a, A Garrett^b, S Boucher^b, M Howe^b, E Sanders^c, A Reiss^b, M Singh^c, KD Chang^c

^aDepartment of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Palo Alto, CA, USA, ^bCenter for Interdisciplinary Brain Sciences Research, Stanford University School of Medicine, Palo Alto, CA, USA, ^cPediatric Bipolar Disorder Program, Stanford University School of Medicine, Palo Alto, CA, USA

Objective: Offspring of parents with bipolar disorder (OBP) who have ADHD or mood symptoms are known to be at higher risk for developing mood disorders. Studying temperamental characteristics that are known to have a link with psychopathology, such as inhibited temperament, may help identify vulnerability markers for illness in this population. Therefore, we investigated the relationship between temperamental predisposition and specific subcortical brain volumes in OBP with psychiatric diagnosis.

Method: OBP with mood symptoms ($N = 24$, mean age years, range 9–17) but not full bipolar disorder were scanned at 3T MRI. Freesurfer software was used to measure subcortical brain volumes. The main outcome measures were approach-withdrawal subscale scores of the Dimensions of Temperament-Revised (DOTS-R) scale and volumetric measures of a priori brain regions of interest (amygdala and hippocampus).

Result: Multiple regression analysis showed that right hippocampal volumes ($\beta = 0.60$, $p = 0.007$) and left amygdala volumes ($\beta = 0.57$, $p = 0.02$) are positively associated with DOTS-R approach/withdrawal scores in OBP with psychiatric diagnosis. Partial correlation analysis showed a significant positive correlation between right hippocampal ($r = 0.58$, $p = 0.007$) and left amygdala volumes ($r = 0.45$, $r = 0.046$) and DOTS-R approach/withdrawal scores. DOTS-R approach score was not significantly correlated with either the depression ($r = -0.286$) or anxiety scale ($r = -0.268$) scores, and this implies that DOTS-R approach might be independent of mood state and anxiety in our samples.

Conclusions: Our results provide support for a neuroanatomical basis for individual differences in temperament in OBP with psychiatric diagnosis. This line of research is important for early identification and intervention of youth at high risk for the development of the illness by detecting vulnerability factors early before the development of any psychiatric symptoms.

Regional gray matter volume alterations related to predominant polarity in bipolar I disorder

J Kim, TH Ha, JY Her, J Kim, JS Chang, K Ha

Psychiatry, Seoul National University Bundang Hospital, Gyeonggi-do, Korea

Objective: The predominant polarity may represent important clinical characteristics of bipolar I disorder (BD I). Though recent neuroimaging studies revealed that several brain regions including anterior limbic structures and prefrontal cortices had gray matter volume reductions in BD I, it remains elusive how these regional brain abnormalities are related to clinical features of the disorder. The aim of the present study was to investigate regional brain abnormalities and their relations to predominant polarity in BD I.

Methods: Subjects with BD I ($n = 35$) and healthy controls ($n = 35$) underwent high resolution brain magnetic resonance imaging. Images were processed according to the optimized voxel-based morphometry protocol using DARTEL normalization. The preprocessed gray matter maps were compared between the patients and controls. Correlation of regional gray matter volumes with ratio of manic episodes (number of manic episodes/number of all episodes) was explored using regression models. Regional gray matter volumes that showed significant correlations were compared between groups stratified by predominant polarity.

Results: Patients with BP I revealed gray matter reductions in the bilateral prefrontal, insular, temporal, and parietal regions compared to controls (FEW corrected $p < 0.05$ at cluster-level). In the patients group, the ratio of manic episode negatively correlated to the gray matter volumes in the right superior frontal gyrus. The mean gray matter volume of this region in the manic predominant group was significantly lower than those of the depressive predominant group and the control group.

Conclusion: Our findings provide neurobiological evidence for subtyping BD I by predominant polarity. The prefrontal regions may have a role in developing and shaping the courses of the disorder through polar determinant in BD I.

Correlation between neurofunctional and neurocognitive performance of BD I euthymic patients

C Lopez Jaramillo^a, C Vargas^a, M Valencia-Escobar^a, A Vanegas^b, S Rascovsky^b

^aPsychiatry, Universidad de Antioquia, Medellin, Colombia,

^bImagenology, Instituto de alta tecnologia Medica de Antioquia, Medellin, Colombia

Background: There's evidence of cognitive and neuroimaging alterations in BD euthymic patients; however this data may be influenced by methodological differences between studies and confounding factors like clinical characteristics of the patients, and the medications that are given, there're doubts on the correlation on neurocognitive and neurofunctional variables, because of that there's need of a study that controls all those variables.

Objectives: To correlate and clarify the relationship between neuroanatomy, neurofunctional activation and cognitive performance in neurofunctional paradigms and the main clinical variables (age, number of manic and depressive episodes, age of diagnosis, number of hospitalizations, total years of illness) in a sample with adequate confounding factors control.

Methods: Forty seven euthymic BID patients (17 on lithium monotherapy for at least 2 years, 17 on valproic acid monotherapy and 13 without) diagnosed according DSM-IV-TR criteria, a structured questionnaire-abbreviated, DIGS-Hamilton and Young criteria to rule out subsyndromatic symptoms, and 46 healthy control subjects (all right-handed, with no history of other psychiatric/neurologic diagnoses, electroconvulsive therapy, encephalocranial trauma nor substance abuse), were evaluated in a

descriptive-correlation, cross-sectional study that used fMRI working memory, verbal episodic memory with semantic association tests to identify differences in the BOLD activation, response time to the paradigms and neurocognitive outcome as well as correlation between clinical variables, response time and BOLD activation.

Results: Significant differences were found in the cerebral activation patterns between BD I patients and control patients, with more activation of dorsolateral and orbitofrontal prefrontal cortex in the control group ($p = 0.000212$ CI 97%), the relationship between BOLD activation and demographical, clinical and response time variables were not statistically significant.

Conclusion: Our study showed important differences in the activation of dorsolateral and orbitofrontal prefrontal cortex being more prominent in control group reflecting a better coordination of thoughts and actions, a better performance of executive functions as well as a better capacity on making decisions and complex thoughts. No other statically significant findings were noted.

The effects of lithium on brain function: preliminary neural network changes

G Curran, P Das, K Fritz, GS Malhi

CADE Clinic, Department of Psychiatry, Sydney Medical School, Northern ARCHI Facility, Kolling Institute, Sydney Medical School-Northern, University of Sydney, Sydney, Australia

Background: Lithium is a widely used and well established mood stabilizer in the treatment of bipolar disorder. In addition, it has a number of unique effects including neuroprotection and the mitigation of suicidal ideation. It can also cause neurocognitive side effects which reduce treatment adherence.

Aim: This exploratory study set out to determine neural network differences in brain function in patients with bipolar disorder due to the effects of lithium treatment.

Methods and materials: Twenty four bipolar patients in total with 11 on lithium underwent clinical neuropsychological and functional MRI investigation. Patients were recruited from the community and diagnosed using structured clinical assessments. They underwent a series of clinical and neuropsychological assessments adapted from the CADE Clinic battery. Patients also underwent structural and functional MRI involving a variety of task related and resting state paradigms.

Results and conclusions: Preliminary analysis of data suggests no significant neuropsychological difference between the groups attributable to the effects of lithium. However there are potential differences identifiable using functional MRI.

Conclusion: Subtle functional differences in brain function attributable to lithium use may be identifiable using fMRI and shed light on the mechanisms of lithium with respect to its unique properties in the treatment of bipolar disorder.

Bipolar and borderline patients display differential patterns of functional connectivity among resting state networks

P Das^a, V Calhoun^b, GS Malhi^a

^aCADE Clinic, Department of Psychiatry Sydney, Medical School Northern ARCHI Facility, Kolling Institute Sydney Medical School-Northern, University of Sydney, Sydney, Australia, ^bDepartment of ECE, University of New Mexico & Mind Research Network, Albuquerque, NM, USA

Background: Clinically, Bipolar (BD) and Borderline Personality (BPD) disorder have overlapping presentations commonly referred to as emotion dysregulation, however their course and treatment differ which suggests that the underlying neurobiological mechanisms behind this may be different in these disorders. Understanding the basis of emotion dysregulation will facilitate accurate

diagnosis and ensure the administration of appropriate treatment strategies.

Aim: To determine whether impairments between networks involved in mentalizing, affect regulation, and self-referential processing (as they can lead to emotion dysregulation) can differentiate neural underpinning of emotion dysregulation in BD and BPD.

Methods and materials: A cross sectional comparison of three groups of subjects involving in total 43 aged matched female participants was conducted. 16 had bipolar disorder, 13 had borderline personality disorder and 14 were healthy controls. Resting state functional MRI data was analyzed using a data-driven analytical technique. Functional network connectivity was determined and correlated with measures of emotional dysregulation.

Results and conclusions: In both BD and BPD the network underpinning mentalizing and the determination of social salience displayed impaired functional network connectivity. But the pattern of connectivity and the networks with which it displayed impaired functional connectivity differed between groups. Moreover, the strength of connectivity between these networks correlated with constructs of emotion regulation suggesting that the neurobiological mechanism underpinning emotion dysregulation in these disorders are different and this may have implications for treatment.

Altered auditory steady-state magnetic fields in bipolar disorders: a source localization study

Y Oda^a, N Hironaga^b, S Hirano^a, R Tsuchimoto^a, T Maekawa^a, T Onitsuka^a, S Tobimatsu^b, S Kanba^a

^aPsychiatry, Kyushu University, Fukuoka, Japan, ^bNeurophysiology, Kyushu University, Fukuoka, Japan

Auditory steady-state response (ASSR) is considered to reflect automatic sounds gating function. In bipolar disorder (BD), we reported the reduced gamma band power and phase locking factors (PLF) in the magnetic fields of ASSR (PloS ONE 2012). However, the neural mechanism of altered ASSR in BD has not been fully elucidated. Therefore, we investigated the ASSR using magnetoencephalography with focusing on auditory cortical activities. ASSR was recorded by presenting 20 Hz, 30 Hz, 40 Hz and 80 Hz binaural click trains (500 ms duration). The inter-train interval was 500 ms and sound intensity was 80 dB SPL. Three BDs and three normal controls (NCs) having own MRI image were selected for this study. Minimum norm estimates was applied to evaluate the cortical activations via ASSR. A region of interest (ROI) was marked on superior-temporal area for both left and right hemispheres. Induced power and PLF in ROI were analyzed using wavelet analysis to make a comparison between BD and NC. The PLF results especially at 40 Hz condition showed the clear difference between BD and NC. The strong power and increased PLFs in time-frequency domain were robustly observed in all NCs while the attenuation of power and PLFs was remarkable in BDs. Although the number of subjects was small, our pilot study indicated the promising results of altered ASSR of BD at the source level. This yields the improvement of neurobiological understanding of BD for the role of each superior-temporal area and interaction between them.

Keywords: ASSR, bipolar disorders, magnetoencephalography, superior-temporal area, a source localization

Normal metabolic levels in prefrontal cortex in euthymic bipolar I patients with and without suicide attempts

M Rocha^a, F Nery-Fernandes^a, AP Jackowski^b, LC Quarantini^a, CA Araújo-Neto^c, JL Guimarães^a, IR Oliveira^a, A Miranda-Scippa^a

^aProgram of Mood and Anxiety Disorders (CETHA), Federal University of Bahia, Salvador Bahia, Brazil, ^bDepartment of Psychiatry, Federal University of São Paulo, São Paulo, Brazil, ^cImaging Diagnosis, Federal University of Bahia, Salvador Bahia, Brazil

Background: Evidence suggests that prefrontal cortex has been implicated in the pathophysiology of Bipolar Disorder (BD), but few neurochemical studies have evaluated this region in bipolar patients and there is no information from BD suicide attempters using Proton Magnetic Resonance Spectroscopy (HMRS).

Objective: This study evaluated the function of medial orbital frontal cortex in euthymic BD type I suicide and non-suicide attempters compared to healthy subjects by HMRS.

Methods: Thirty six euthymic bipolar I patients, 19 without and 17 with history of suicide attempt, and 16 healthy subjects were interviewed using the Structured Clinical Interview with the DSM-IV axis I (SCID-I), the Hamilton Depression Rating Scale (HDRS), the Young Mania Rating Scale (YMRS) and underwent HMRS.

Results: Distribution of gender and age were similar between bipolar patients as a group and healthy controls. The clinical and sociodemographics characteristics did not differ between patients with and without suicide attempts. There were no differences on spectral curve between BD suicide and non-suicide attempters, and also we did not find any evidence of metabolic abnormality in prefrontal regions of BD patients as a group, compared to healthy subjects. In our study, 30 patients (83.3%) (attempters and non-attempters) were receiving lithium, and 21 (58.3%) were also receiving at least one psychiatric drug in addition to lithium, including mood stabilizers, antipsychotics, or antidepressants.

Conclusions: The findings from the present study are in agreement with some reports, which did not find differences in brain metabolites levels in prefrontal cortex of euthymic bipolar I patients compared to healthy controls. We speculated that combined chronic use of psychotropic drugs with neuroprotective or neurotrophic effects leading to a euthymic state for longer periods of time may normalize neuronal function, at least measured by HMRS, even in suicide attempters. In our study, the brain metabolites measured by HMRS were normal in medial orbital frontal lobe of medicated BD type I euthymic patients, suicide attempters or not, what can represent a phase-dependent metabolic profile or a positive neurotrophic effects of the pharmacological treatment. However, additional studies are needed on larger patient samples in order to clarify these issues.

Reduced activation of the temporal cortex in patients with euthymic bipolar disorder during a verbal fluency task: a multi-channel near-infrared spectroscopy study

N Tsujii^a, W Mikawa^a, H Akashi^a, E Tsujimoto^b, E Kirime^a, T Adachi^a, M Takaya^a, H Ono^b, M Yanagi^a, O Shirakawa^a

^aNeuropsychiatry, Kinki University Faculty of Medicine, Osaka-sayama, Japan, ^bPsychological Science Graduate School of Humanities, Kwansei Gakuin University, Hyogo, Japan

Background: Bipolar disorder (BD) is a chronic and highly debilitating mood disorder. Recent neuroimaging studies using multi-channel near-infrared spectroscopy (NIRS) have provided compelling evidence about the dysfunction of the prefrontal and temporal cortices in bipolar disorder. However, whether this pattern of dysfunction persists during euthymia remains unclear. The aim of this

study is to clarify the existence of brain dysfunction in euthymic BD, using NIRS.

Methods: Twenty-eight patients with bipolar depression (BPD), 20 patients with euthymic bipolar disorder (BPE), and 24 healthy control (HC) subjects participated in the study. Regional hemodynamic changes during a verbal fluency task (VFT) were monitored using a multi-channel NIRS apparatus (ETG-4000 Optical Topography System; Hitachi Medical Co., Tokyo, Japan).

Results: There were no significant differences among the groups in age, sex, years of education, handedness, or task performance. After a false discovery rate (FDR) correction using 52 channels, an ANOVA indicated significant differences among the groups (FDR-corrected $p = 0.000-0.0108$). Post hoc analyses showed that the oxy-Hb activation by the VFT in patients with BPD and BPE was significantly smaller than that in the HC group in the bilateral temporal regions (BPD in 16 channels, $p = 0.000-0.008$; BPE in 14 channels, $p = 0.000-0.02$). However, there were no differences in the oxy-Hb changes induced by the VFT between patients with BPD and BPE.

Discussion: Individuals with bipolar disorder, even during euthymia, have a persistent hypofunction of the temporal cortical regions. These findings may represent underlying trait abnormalities in bipolar disorder associated with cognitive impairment.

Reduction of left temporal cortex activation in suicide attempters with bipolar disorder after a verbal fluency task: a multi-channel near-infrared spectroscopy study

N Tsujii^a, W Mikawa^a, E Tsujimoto^b, E Kirime^a, H Akashi^a, M Takaya^a, M Yanagi^a, T Adachi^a, H Ono^b, O Shirakawa^a

^aNeuropsychiatry, Kinki University Faculty of Medicine, Osaka-sayama, Japan, ^bPsychological Science Graduate School of Humanities, Kwansei Gakuin University, Hyogo, Japan

Background: Bipolar disorder (BD) is a mental disorder most strongly associated with attempted and completed suicides. Recent neuroimaging studies using multi-channel near-infrared spectroscopy (NIRS) have provided compelling evidence about the dysfunctions of the prefrontal and temporal cortices in BD. However, whether the difference in this pattern of dysfunction exists between suicide attempters and non-attempters with BD remains unclear. The aim of this study is to identify brain dysfunction associated with suicidality in BD, using NIRS.

Methods: Forty patients with bipolar depression participated in this study. They were divided into two groups: suicide attempters ($n = 15$) with a history of at least one suicide attempt (defined as a self-destructive act with some degree of intent to die) and non-attempters ($n = 25$) having no such history. Regional hemodynamic changes during a verbal fluency task (VFT) were monitored using a NIRS apparatus (ETG-4000 Optical Topography System; Hitachi Medical Co., Tokyo, Japan).

Results: There were no significant differences between suicide attempters and non-attempters in age, sex, years of education, handedness, depressive symptom severity, or task performance. In both groups, the oxy-Hb of the bilateral temporal regions increased gradually at the beginning of the VFT and continued to increase during the task. After the task, the oxy-Hb of the left temporal regions decreased immediately and gradually in suicide attempters and non-attempters, respectively. After a false discovery rate (FDR) correction using 31 channels, no differences in oxy-Hb activation during the VFT were observed between suicide attempters and non-attempters. However, oxy-Hb activation after the VFT in suicide attempters decreased significantly quicker than that in non-attempters in the left temporal regions in 5 channels (FDR-corrected $p = 0.000-0.007$).

Discussion: Our results suggest the reduced left temporal cortex activation after a VFT is related to suicidality in BD. NIRS may therefore be a useful tool for identifying brain dysfunctions associated with suicidal behavior in BD.

MRI investigation of a 6-week trial of lithium in medication-free patients with bipolar depression

MV Zanetti^a, MCG Otaduy^b, RTde Sousa^c, MG Soeiro-de-Souza^d, KT Chaim^b, WF Gattaz^e, GF Busatto^a, CC Leite^b, R Machado-Vieira^c

^aLaboratory of Psychiatric Neuroimaging (LIM-21), Department & Institute of Psychiatry University of Sao Paulo, Sao Paulo, Brazil,

^bLaboratory of Magnetic Resonance in Neuroradiology (LIM-44), Department of Radiology University of Sao Paulo, Sao Paulo, Brazil,

^cLaboratory of Neuroscience (LIM-27), Department & Institute of Psychiatry University of Sao Paulo, Sao Paulo, Brazil,

^dMood Disorders Unit (GRUDA), Department & Institute of Psychiatry University of Sao Paulo, Sao Paulo, Brazil

Aims: To evaluate fronto-limbic morphometric abnormalities in acute bipolar depression before and after lithium monotherapy, and to assess neuroanatomical patterns specific to bipolar disorder (BD) type II (BD-II). **Methods:** Twenty-three medication-free patients with bipolar depression (82.6% treatment-naïve; 17 subjects with BD-II) and 31 age-matched healthy controls were studied with 3.0T high resolution (1 mm³) structural MRI. BD patients were examined at baseline and after a 6-week trial of lithium monotherapy. Clinical assessments, including plasma lithium levels, were performed at baseline and at the end of weeks 1, 2, 4 and 6. Measures of cortical thickness (CT) of frontal, temporal and limbic regions as well as of the volumes of hippocampi and amygdalae were obtained by Freesurfer image analysis suite. Between group-comparisons and longitudinal analyses of images before and after lithium treatment were conducted for both the whole group of BD ($n = 23$) and the BD-II subgroup ($n = 17$) with the SPSS package.

Results: At baseline, the 23 acutely depressed BD patients exhibited decreased CT in the left rostral anterior cingulate cortex (R-ACC) and increased volume in the right amygdala relative to controls. BD-II patients ($n = 17$) showed an additional finding of increased CT in the right insula. After 6 weeks of lithium monotherapy, CT increases were observed in the left superior temporal gyrus (STG) and right isthmus of cingulate cortex (ICC) of BD patients ($n = 23$). Interestingly, BD patients who failed to achieve remission at week 6 ($n = 9$, 39.1%) showed a significant CT increase in the right R-ACC, whereas this structure remained stable in remitters ($n = 14$, 60.9%) during follow-up.

Conclusions: Acute bipolar depression is associated with reduced CT in the left R-ACC and increased volume in the right amygdala, whereas increased CT in the right insula might be a specific marker of BD-II. Short-term treatment with lithium produces CT increases in the STG and ICC that seem to be independent of its clinical efficacy. BD patients who failed to achieve remission exhibited a different pattern of morphometric change in the right R-ACC relative to remitters.

Dense cranial electroacupuncture stimulation, a novel brain stimulation therapy for mood disorders: rationale and clinical trials

Z Zhang

School of Chinese Medicine, The University of Hong Kong, Hong Kong, China

Dense cranial electroacupuncture stimulation (DCEAS) is a novel brain stimulation mode in which electrical stimulation is delivered on dense forehead acupoints innervated by the trigeminal sensory pathway. Neuroanatomical evidence suggests that, compared to the spinal-supraspinal pathways, the trigeminal sensory pathway

has much intimate connections with the brainstem reticular formation, in particular the dorsal raphe nuclei and the locus coeruleus, both of which are the major resources of serotonergic (5-HT) and noradrenergic neuronal bodies, respectively, and play a pivotal role in processing perception, emotion, and sleep. This has led to the hypothesis that direct stimulation on forehead acupoints in the trigeminal territory could more efficiently produce therapeutic response in neuropsychiatric disorders. We have completed 4 clinical trials of DCEAS as adjunctive treatment in patients with major depression, postpartum depression and post-stroke depression. These clinical trials demonstrated that DCEAS is considerably beneficial in alleviating the severity of depression symptoms, accelerating onset of antidepressant action, enhancing clinical response and reducing antidepressant doses taken. This talk will report the results of these trials and discuss the rationale of DCEAS. [The studies were supported by HMRP (06070831), GRF/RGC (786611) and HA funds].

References: Zhang et al., Dense cranial electroacupuncture stimulation for major depressive disorder—a single-blind, randomized, controlled study. *PLoS ONE* 2012; 7: e29651. Qu et al., A 6-week randomized controlled trial with 4-week follow-up of acupuncture combined with paroxetine in patients with major depressive disorder. *J Psychiatric Res* 2013; 47: 726–732. Chung et al., Randomized non-invasive sham-controlled pilot trial of electroacupuncture for postpartum depression. *J Affective Disorders* 2012; 142: 115–21.

Efficacy of cariprazine in patients with acute manic or mixed episodes associated with bipolar I disorder: results from 2 phase III, placebo-controlled trials

J Calabrese^a, K Lu^b, I Laszlovszky^c, M Debelle^c, W Earley^b, S Durgam^b

^aPsychiatry, University Hospitals Case Medical Center, Cleveland, OH, USA, ^bForest Research Institute, Jersey City, NJ, USA, ^cGedeon Richter Plc, Budapest, Hungary

Aims: Cariprazine is an orally active and potent dopamine D₃ and D₂ receptor partial agonist with preferential binding to D₃ receptors. Cariprazine previously demonstrated efficacy and tolerability in a Phase II, randomized, double-blind, placebo-controlled trial in patients with bipolar mania. Here we report efficacy results from 2 Phase III, randomized, double-blind, placebo-controlled, flexible-dose, 3-week trials of cariprazine 3–12 mg/d (NCT01058096) and cariprazine 3–6 mg/d or 6–12 mg/d (NCT01058668) in adults with acute manic or mixed episodes associated with bipolar I disorder.

Methods: Primary and secondary efficacy parameters in both studies were change from baseline to Week 3 on the Young Mania Rating Scale (YMRS) and Clinical Global Impressions-Severity (CGI-S), respectively, and were analyzed using a mixed-effects model for repeated measures. Additional efficacy parameters included YMRS response (≥50% improvement in YMRS total score) and remission (YMRS total score ≤12) rates at Week 3, Clinical Global Impressions-Improvement (CGI-I) score at Week 3, and mean change from baseline to Week 3 in PANSS and MADRS total scores.

Results: Randomized patient populations: 312 (NCT01058096; 154 placebo, 158 cariprazine 3–12 mg/d) and 497 (NCT01058668; 161 placebo, 167 cariprazine 3–6 mg/d, 169 cariprazine 6–12 mg/d). Improvement from baseline to Week 3 on YMRS was significantly greater for each cariprazine group versus placebo ($p < 0.001$): least square mean difference (LSMD) was -4.3 (3–12 mg/d), -6.1 (3–6 mg/d) and -5.9 (6–12 mg/d). For all cariprazine groups compared with placebo, significantly more patients met YMRS response and remission criteria. Cariprazine also was significantly superior to placebo on CGI-S (3–12 mg/d, $p = 0.003$; 3–6 mg/d, $p < 0.001$; 6–12 mg/d, $p < 0.001$), CGI-I (all doses, $p < 0.001$), and PANSS total scores (3–12 mg/d, $p = 0.004$; 3–6 mg/d, $p < 0.001$; 6–12 mg/d,

$p < 0.001$). Mean change from baseline in MADRS total score significantly favored cariprazine over placebo in the 3–6 mg/d ($p = 0.002$) and 6–12 mg/d ($p = 0.023$) dose groups; between group differences were not significant in the 3–12 mg/d group.

Conclusions: Cariprazine demonstrated efficacy on primary, secondary, and most additional efficacy parameters in both studies. These results support the efficacy of cariprazine in the treatment of acute manic or mixed episodes associated with bipolar I disorder.

Safety and tolerability of cariprazine in patients with acute manic or mixed episodes associated with bipolar I disorder: results from two phase-III, placebo-controlled trials

T Ketter^a, K Lu^b, M Debelle^c, I Laszlovszky^c, S Durgam^b, W Earley^b

^aPsychiatry, Stanford University School of Medicine, Stanford, CA, USA, ^bForest Research Institute, Jersey City, NJ, USA, ^cGedeon Richter Plc, Budapest, Hungary

Aims: Cariprazine is an orally active and potent dopamine D₃ and D₂ receptor partial agonist with preferential binding to D₃ receptors. Two Phase III, randomized, double-blind, placebo-controlled trials were conducted to evaluate the efficacy, safety, and tolerability of cariprazine in patients with acute manic or mixed episodes associated with bipolar disorder. Here, we summarize the safety and tolerability results from these 2 Phase III cariprazine studies.

Methods: Patients received flexibly dosed cariprazine 3–12 mg/d (NCT01058096) or 3–6 mg/d or 6–12 mg/d (NCT01058668) for 3 weeks of double-blind treatment. Safety assessments included treatment-emergent adverse events (TEAEs), clinical laboratory evaluations, vital signs, electrocardiograms, extrapyramidal symptom scales, and the Columbia-Suicide Severity Rating Scale.

Results: A total of 312 patients in NCT01058096 (154 placebo, 158 cariprazine 3–12 mg/d) and 497 patients in NCT01058668 (161 placebo, 167 cariprazine 3–6 mg/d, 169 cariprazine 6–12 mg/d) were randomized and received study medication. Common cariprazine-related TEAEs (≥5% and twice rate of placebo) that occurred in both studies were akathisia (3–12 mg/d, 3–6 mg/d, and 6–12 mg/d) and tremor (3–12 mg/d and 6–12 mg/d). Sedation was

Conclusions: Cariprazine was generally well tolerated in the treatment of bipolar mania. Similar to other atypical antipsychotics, the incidence of some EPS-related TEAEs was higher with cariprazine than placebo. Cariprazine was not associated with other adverse effects commonly associated with antipsychotic treatment such as metabolic issues, weight gain, or prolactin elevation.

Olanzapine induced prolonged thrombocytopenia

N Kathirvel, J Xiao, C Ankur, S Naik

General Psychiatry, Institute of Mental Health/Woodbridge Hospital, Singapore, Singapore

Aims: To present a rare case of olanzapine induced prolonged thrombocytopenia.

Methods: We are presenting a case report of a patient who developed a rare side effect of prolonged thrombocytopenia secondary to olanzapine treatment and the literature review of the topic.

Results: A 60-year-old gentleman presented to the psychiatric hospital with relapse of schizophrenia and was commenced on risperidone 2 mg on which subsequently was increased to 4 mg on. A week later risperidone was discontinued as the patient developed leukopenia and thrombocytopenia. His blood count returned to his baseline level in a week after risperidone was discontinued. The patient was started on olanzapine 5 mg on and 12 days later his platelet count started decreasing and the platelet count fluctuated between $70\text{--}108 \times 10^9/\text{L}$. Hence his olanzapine was discontinued. His haemoglobin and WBC (white cell count) were within normal

limits. The patient was referred to one of the general hospitals for a haematology opinion and investigations including peripheral blood film, factor VIII, Von Willibrand factor antigen and lupus anticoagulant antibodies were within normal limits. However his APTT and PT were slightly prolonged. Haematology opinion was that the thrombocytopenia was olanzapine induced. The patient was monitored closely without antipsychotics and the patient's platelet count gradually returned to the baseline level after a period of 6–8 weeks.

Conclusion: Although we have highlighted a case of schizophrenia here, Olanzapine is a commonly used antipsychotic in the treatment of bipolar disorder. Cases of olanzapine induced thrombocytopenia have been reported in the literature. In these cases, the patients had comorbid medical conditions such as idiopathic thrombocytopenia (ITP) and folate deficiency. In one of the cases the patient developed thrombocytopenia in combination with benzotropine mesylate.¹ In our case, the patient had no history of idiopathic thrombocytopenia or folate deficiency, the thrombocytopenia appeared to be directly caused by olanzapine and unusually prolonged.² This raises the importance of doing baseline full blood count prior to commencing atypical antipsychotics and the need for monitoring the patient for side effects.

Keywords: olanzapine, prolonged thrombocytopenia

Clinical satisfaction and preference between oral and long-acting injectable medication: views from psychiatrists

J Lee

General Psychiatry, Taoyuan Psychiatric Center Ministry of Health and Welfare, Taoyuan County, Taiwan

Background: There are many aspects to consider when clinical physicians treat bipolar patients, including controlling disrupted behaviors, efficacy, tolerability, symptoms, and adherence. Relapse prevention and social functioning are also important to note. Although we have more and more approved drugs to treat bipolar patients, clinicians are still not satisfied with the existing treatment. Disparity toward the strategies and choices of pharmacotherapy also persists. Through this study, we want to know psychiatrists' opinions of clinical satisfaction and preference between oral and long-acting injectable medication for bipolar disorder treatment.

Method: The study group consisted of expert opinions from 90 psychiatric specialists in Taiwan. We used a self-rating, visual analogue questionnaire to investigate their clinical opinions, including the diagnostic proportion of all patients they treated, the proportion of bipolar disorder, bipolar patient's demographic distribution and diagnostic subtypes, disease course, history of hospitalization, drug adherence, and history of receiving long-acting injectable drugs. Psychiatrists' choices of oral medication, effectiveness of controlling bipolar manic symptoms, tolerability of medication, subjective perception of patient's and family's satisfaction, and functional improvement were recorded. We also surveyed the experience of short-term and long-term prescription of long-acting injectable antipsychotics (LAIA), both typical and atypical. Questionnaires are fulfilled anonymously.

Results: According to the expert opinions we collected, 56% of their bipolar patients had illness course more than 5 years, and 28% had bipolar course more than 10 years in their life. 79% patients are diagnosed as bipolar I disorder. About 76% had at least one episode in most recent 1 year, and 51% hospitalized. As for the expert opinion of oral medication, mood stabilizer and atypical antipsychotics were most commonly used, but generally lower scores than LAIA within subjective perception toward mood controlling, tolerability, enhancing insight and adherence, relapse prevention, and improving functioning. There are 70% patients received atypical LAIA (risperidone long-acting depot). Better satisfaction and confidence by long-term prescription than short-term were also detected.

Conclusion: By the expert opinions from Taiwanese psychiatric specialist, their bipolar patients tend to be chronic and easily relapsed. The satisfaction and preference of LAIA are better than oral medication for bipolar patients, especially atypical LAIA.

Effect of lurasidone monotherapy or adjunctive therapy on anxiety symptoms in patients with bipolar I depression

J Cucchiaro, A Pikalov, J Hsu, H Kroger, A Loebel

Clinical Development, Sunovion Pharmaceuticals Inc., Fort Lee, NJ, USA

Aims: To evaluate the efficacy of lurasidone as monotherapy or adjunctive with lithium (Li) or valproate (VPA) in treating anxiety in patients with Bipolar I Depression (BPD).

Methods: Patients meeting DSM-IV-TR criteria for BPD were randomized, in two double-blind trials (combined $n = 845$), to 6 weeks of once-daily treatment with lurasidone (20–120 mg/d) adjunctive with Li or VPA; or monotherapy treatment with lurasidone (fixed-flexible doses of 20–60 mg/d or 80–120 mg/d, combined in the current analysis). In both studies, the primary outcome was change in depressive symptoms, assessed by the MADRS. Anxiety symptom severity was assessed using the Hamilton Anxiety Scale (HAM-A).

Results: In the adjunctive study, treatment with lurasidone adjunctive with Li or VPA significantly reduced HAM-A total score compared with placebo (−8.0 versus −6.0; $p = 0.003$; LOCF); significant improvement versus placebo was also observed for the HAM-A psychic ($p = 0.009$) and somatic ($p = 0.008$) factors. In the adjunctive study, 32% of patients met criteria for moderate-to-severe anxiety (HAMA ≥ 18) at baseline. Treatment with lurasidone was associated with higher endpoint anxiety responder rates ($\geq 50\%$ reduction in HAM-A) compared with placebo in both the total sample (60.5% versus 40.9%; $p < 0.001$) and in the moderate-to-severe anxiety subgroup (68.8% versus 45.1%; $p = 0.009$; LOCF). In the monotherapy study, treatment with lurasidone significantly reduced HAM-A total score compared with placebo (−6.6 versus −4.6; $p < 0.001$; LOCF); significant improvement versus placebo was also observed for the HAM-A psychic factor ($p \leq 0.001$), but not the somatic factor ($p = 0.108$). In the monotherapy study, 34% of patients met criteria for moderate-to-severe anxiety (HAMA ≥ 18) at baseline. Treatment with lurasidone was associated with higher endpoint anxiety responder rates compared with placebo in both the total sample (52.9% versus 31.1%; $p < 0.001$) and in the moderate-to-severe anxiety subgroup (51.0% versus 37.3%; $p = 0.131$; LOCF). A comparison of the moderate-to-severe and low anxiety subgroups found that the incidence of adverse events, and discontinuation due to adverse events was not influenced by the severity of baseline anxiety.

Conclusions: In this analysis, treatment of BPD with lurasidone, either as monotherapy or adjunctive therapy with lithium or valproate, significantly improved both psychic and somatic symptoms of anxiety. Sponsored by Sunovion Pharmaceuticals, Inc.

Short- and longer-term treatment with lurasidone in patients with bipolar I depression: effect on metabolic syndrome

S McElroy^a, A Pikalov^b, J Cucchiaro^b, J Hsu^b, H Kroger^b, D Phillips^b, A Loebel^b

^aPsychiatry, Lindner Center of HOPE Mason and University of Cincinnati College of Medicine, Cincinnati, OH, USA, ^bClinical Development, Sunovion Pharmaceuticals Inc. Fort Lee, NJ, USA

Aims: To evaluate the effect of short- and longer-term treatment with lurasidone on the prevalence of metabolic syndrome in bipolar I depression.

Methods: The metabolic effects of lurasidone, in doses of 20–120 mg/d, were evaluated using data from three short-term studies and one longer-term study. In the three short-term studies, patients with bipolar I depression were randomized to 6 weeks of once-daily, double-blind, placebo-controlled treatment with lurasidone, either as monotherapy (one study, $N = 499$), or adjunctive therapy with lithium (Li) or valproate (VPA; two studies, combined $N = 694$). Patients completing the three 6-week studies continued to receive 6 months of additional treatment with lurasidone 20–120 mg/d in an open-label extension study ($N = 494$). NCEP criteria (JAMA 2001;285:2486–2497) for metabolic syndrome were used. Change at 6 months (for completers) was calculated from double-blind baseline of the 6-week acute study.

Results: At baseline, the prevalence of metabolic syndrome was similar in the adjunctive studies (lurasidone, 14.8%; placebo, 13.5%) and in the monotherapy study (lurasidone, 14.3%; placebo, 15.5%). After 6 weeks of adjunctive therapy, the prevalence of metabolic syndrome in the lurasidone versus placebo groups was 17.0% versus 12.4% (LOCF); after 6 weeks of monotherapy, the prevalence was 15.8% versus 17.7% (LOCF). For patients who completed 6 months of extension phase treatment (30 weeks of total exposure), the prevalence of metabolic syndrome was 23.8% (adjunctive therapy) and 17.9% (monotherapy). For the subgroup with metabolic syndrome at baseline in the adjunctive therapy studies ($n = 31$), the following median changes were observed: weight (0.0 kg), cholesterol (-6.0 mg/dL), triglycerides ($+11.0$ mg/dL), and glucose ($+2.0$ mg/dL). For the subgroup with metabolic syndrome at baseline in the monotherapy study ($n = 30$), the following median changes were observed: weight (-0.3 kg), cholesterol (-4.0 mg/dL), triglycerides (-22.0 mg/dL), and glucose (-2.0 mg/dL).

Conclusions: In patients with acute bipolar I depression, up to 7 months of treatment with lurasidone, either as monotherapy, or as adjunctive therapy with lithium or valproate, was associated with only minimal metabolic changes. In at-risk patients who met metabolic syndrome criteria at study entry, treatment with lurasidone was not associated with worsening of metabolic parameters. Sponsored by Sunovion Pharmaceuticals Inc.

Efficacy and safety of treatment with lurasidone adjunctive with lithium or valproate in bipolar I depression: results of two 6-week studies

J Calabrese^a, T Suppes^b, K Sarma^c, R Silva^c, H Kroger^c, J Cucchiari^c, A Pikalov^d, A Loebe^d

^aPsychiatry, University Hospitals Case Medical Center Case Western Reserve University/Sunovion Pharmaceuticals Inc., Cleveland, OH, USA, ^bPsychiatry, Stanford School of Medicine Stanford and VA Palo Alto Health Care System, Palo Alto, NJ, USA, ^cClinical Development, Sunovion Pharmaceuticals Inc, Fort Lee, NJ, USA, ^dClinical Development, Sunovion Pharmaceuticals Inc, Fort Lee, NJ, USA

Aims: To evaluate the efficacy and safety of lurasidone adjunctive with lithium (Li) or valproate (VPA) in bipolar I depression.

Method: Data were pooled from two adjunctive therapy studies with similar designs: patients meeting DSM-IV-TR criteria for bipolar I depression were randomized to 6 weeks of once-daily, double-blind treatment with lurasidone. 20–120 mg/day ($N = 355$) or placebo ($N = 327$), adjunctive with either Li or VPA. Changes from baseline in MADRS (primary outcome) and Clinical Global Impression Bipolar Severity of Illness (CGI-BP-S; key secondary assessment) were analyzed using MMRM. Secondary efficacy outcomes included the Quick Inventory of Depressive Symptomology–Self Report (QIDS-SR₁₆) and the Hamilton Anxiety Rating Scale (HAM-A).

Results: For the pooled analysis sample, treatment with lurasidone (versus placebo) was associated with significant improvement in the

mean MADRS score (-14.4 versus -11.9 ; $p = 0.003$; effect size: 0.25) at week 6. Treatment with lurasidone (versus placebo) was also associated with significant improvement in CGI-BP-S scores (-1.7 versus -1.3 ; $p = 0.001$), QIDS-SR₁₆ scores (-7.4 versus -5.7 ; $p \leq 0.001$), and the HAM-A score (-7.0 versus -5.0 ; $p \leq 0.001$ [LOCF]) at week 6. Responder rates ($\geq 50\%$ reduction in MADRS at week 6) were significantly higher with lurasidone versus placebo (48% versus 37%; $p = 0.002$; LOCF-endpoint). In the pooled safety population, minimal LOCF-endpoint changes were observed for adjunctive lurasidone versus placebo in mean weight ($+0.1$ versus $+0.2$ kg), median total cholesterol (-4.0 versus -1.0 mg/dL), LDL (-3.0 versus -1.0 mg/dL), triglycerides ($+4.0$ versus -2.0 mg/dL), and glucose (0.0 versus 0.0 mg/dL). Discontinuation rates due to treatment-emergent adverse events were similar (5.8% versus 4.8%); adverse events ($\geq 5\%$ incidence and greater than placebo) were nausea (13.9% versus 10.2%), Parkinsonism (12.8% versus 8.1%), somnolence (11.4% versus 5.1%), and akathisia (10.8% versus 4.8%). The incidence of protocol-defined treatment-emergent mania was similar (lurasidone = 0.8% versus placebo = 1.5%).

Conclusions: Results of data pooled from two similarly designed studies demonstrated that lurasidone adjunctive therapy with lithium or valproate was effective in treatment of patients with bipolar I depression. Significant improvement was observed in depressive symptoms, with a low rate of discontinuation due to adverse events and minimal effect on weight or metabolic parameters. Sponsored by Sunovion Pharmaceuticals Inc.

Mood-stabilizing medication after hospitalization for bipolar disorder in Sweden: a register-based cohort study

J Reutfors^a, L Scheen^a, L Brandt^a, R Bodén^a, A Tanskanen^b, M Andersen^a, J Tiihonen^b

^aDepartment of Medicine Solna, Karolinska Institutet, Stockholm, Sweden, ^bDepartment of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden

Aim: To investigate the utilization patterns of mood stabilizers (MS) in the first month after hospitalization for bipolar disorder (BD).

Methods: Patients with a diagnosis of BD (ICD-10 codes F30.0–F31.9) in Sweden between July 1, 2006 and December 31, 2011 were identified in the National Patient Register, from which data on previous psychiatric hospitalizations was also extracted. Drug dispensing data was obtained from the Prescribed Drug Register. A run-in period of one year prior to diagnosis was used to exclude prevalent users of MS (i.e., lithium, antipsychotics, and anticonvulsants with an indication for the treatment of BD). The patients were followed for 30 days post discharge regarding MS dispensing. The patients were censored at death.

Results: There were 6,030 unique hospitalizations of patients with BD who were not prevalent users of MS. The median age of these patients was 47 years (range 10–104 years), 3 581 (59%) were women, and 2 828 (47%) had a previous diagnosis of BD. The proportion of patients with no dispensing of a MS within the first month after hospitalization was 43%, whereas 35% were dispensed one, 19% were dispensed two, and 3.5% were dispensed three or more different MS. Overall, the proportion of patients who were dispensed lithium was 18.8%, antipsychotics 38.4%, and anticonvulsants 21.8%. The proportion of patients who were dispensed lithium only was 8.1%, an antipsychotic only 19.1%, and an anticonvulsant only 9.8%. A concomitant dispensing of lithium and an antipsychotic or an anticonvulsant was found in 7.3% and 0.9% of the patients, respectively. A concomitant dispensing of an anticonvulsant and an antipsychotic was found in 8.5%.

Conclusions: Our results suggest that among patients with BD with no recent use of a MS, just above half of the patients are dispensed

a MS in the first month after hospitalization. Among patients with BD who do use a MS, the majority are dispensed antipsychotics, although this is not usually considered a first-line treatment in the maintenance phase.

Topiramate as an adjuvant treatment for obsessive compulsive symptoms in patients with bipolar disorder, a randomized double blind placebo controlled clinical trial

A Sahraian, M Bigdeli, A Ghanizadeh, V Rezaee

Research Center for Psychiatry and Behavioral Sciences, Shiraz University of Medical Sciences, Shiraz, Iran

Background: There is no well-controlled evidenced based literature regarding treating obsessive compulsive symptoms in patients with bipolar disorder. Current trial examines the effect of topiramate for treating obsessive compulsive symptoms in patients with bipolar disorder.

Methods: Four month double-blind placebo-controlled randomized clinical trial investigates the efficacy of topiramate as an adjuvant medication for treating patients with bipolar disorder, manic phase, type-I and obsessive compulsive disorder symptoms.

Results: 9 (52.9%) out of 17 patients in the topiramate group and 2 (12.5%) out of 16 patients in the placebo group showed more than 34% decline in YBOC score ($\chi^2 = 6.0$, $df = 1$, $p < 0.01$).

Conclusions: Topiramate more than placebo, as an adjuvant medication, improves patients with bipolar disorder and obsessive compulsive symptoms. No serious adverse effect was detected.

Efficacy of lithium in the long-term treatment of bipolar disorders: a new meta-analysis

E Severus^a, M Taylor^b, C Sauer^a, A Pfennig^a, M Bauer^a, J Geddes^c

^aDepartment of Psychiatry and Psychotherapy, University Hospital

Dresden, Dresden, Germany, ^bDepartment of Psychosis Studies,

Institute of Psychiatry King's College London, London, UK,

^cDepartment of Psychiatry, University of Oxford, Oxford, UK

Lithium is one of the best established treatment options in the long-term treatment of bipolar disorders. In a previous meta-analysis (Geddes et al., 2004) lithium was significantly superior to placebo in preventing all affective episodes and manic episodes. However the efficacy regarding the prevention of depressive episodes was equivocal. Since then the evidence base has grown further, particularly through the use of lithium as an active comparator in approval-seeking trials of new treatment options and in "real world" effectiveness studies. Therefore we decided to conduct a new meta-analysis including these new trials. In this new meta-analysis, we will also present data on how lithiums performs regarding tolerability and study completion compared to placebo and/or the other active compound, respectively.

Keywords: meta-analysis, bipolar disorders; maintenance treatment; lithium

A prospective 4 years naturalistic follow up of 300 bipolar I & bipolar II patients

C Simhandl^a, B König^b, B Amann^c

^aOrdination, BIPOLAR Zentrum Wiener Neustadt, Wiener

Neustadt, Austria, ^bPsychiatrie, LKH Neunkirchen, Neunkirchen,

Austria, ^cPsychiatrie, FIDMAG Research Foundation CIBERSAM, Barcelona, Spain

Objective: Naturalistic long-term data of bipolar disorder are rare. The information of highly selected and well funded research populations based on randomized controlled trials might bring us a lot of information, but the usefulness for practical treatment in every day life must be challenged.

Methods: We followed up 300 patients out of 515 bipolar patients who were admitted the first time to a new installed regional psychiatric department for a catchment area of 200,000 inhabitants between 2000 and 2004. Patients were treated by their physician and followed up for 4 years until 2008. The information was gathered by trained physicians from the department when patients were seen at the hospital or by telephone or in semi-structured web based interview at least once a year. Patients were assessed with respect to time to relapse, type of relapse and used medication.

Results: 204 (68%) of 300 patients relapsed within 4 years, with a mean of 208 days (SD = 356.2) until the next affective episode. Relapses correlated statistically significant with the index episode. We found no differences in the demographic variables and in the relapse rates between bipolar I and bipolar II patients. Using a Kaplan survival analysis, only lithium, not in combination with other prophylactic medication, delayed statistically significant the time to the next affective relapse. Other mood stabilizer medications like valproic acid, carbamazepine, lamotrigine, olanzapine and risperidone showed over the observational period no statistical significant results. Survival was also statistically significant reduced when medication was replaced by the psychiatrist or stopped by the patient.

Conclusion: Bipolar patients have in a naturalistic setting a high risk of relapses. Lithium seems to have an advantage compared to other medication in preventing or delaying affective episodes. Patients in our sample tend to relapse with the same episode they suffered when they entered into the observation period. Replacement and changes of medication by the patient or the physician seem high risk factors for an earlier relapse.

Predictors of adherence to psychopharmacological and psychosocial treatment in bipolar I or II disorders—an 18-month prospective study

P Arvilommi^a, O Mantere^b, S Leppämäki^c, HV Valtonen^a, E Isometsä^d

^aDepartment of Social Services and Health Care Psychiatry, City of

Helsinki, Helsinki, Finland, ^bDepartment of Psychiatry, Helsinki

University Central Hospital, Helsinki, Finland, ^cPsychiatry, Finnish

Institute of Occupational Health, Helsinki, Finland, ^dDepartment of

Psychiatry, University of Helsinki, Helsinki, Finland

Aims: Poor treatment adherence among patients with bipolar disorder (BD) is a common clinical problem. However, whether adherence is mostly determined by patient characteristics or attitudes, type of treatment or treatment side-effects remains poorly known.

Methods: The Jorvi Bipolar Study (JoBS) is a naturalistic prospective 18 month study representing psychiatric in- and outpatients with DSM-IV BD I and II in three Finnish cities. During the 18 month follow-up we investigated the continuity of, attitudes towards and adherence to various types of psychopharmacological and psychosocial treatments among 168 psychiatric in- and outpatients with BD I or II.

Results: One-quarter of the patients using mood stabilizers or atypical antipsychotics discontinued medication during at least one treatment phase of the follow-up autonomously, mostly during depression. When pharmacotherapy continued, adherence was compromised in one-third. Rates of non-adherence to mood stabilizers or antipsychotics did not differ, but the predictors did. One-quarter of the patients receiving psychosocial treatments were non-adherent to them.

Conclusions: More than one-half of BD patients either discontinued pharmacotherapy or use it irregularly. Autonomous discontinuation takes place mostly in depression. Although rates of non-adherence do not necessarily differ between mood-stabilizing

medications, the predictors for nonadherence do. Moreover, adherence to one medication does not guarantee adherence to another, nor does adherence at one time-point ensure later adherence. Attitudes towards treatments affect adherence to medications as well as to psychosocial treatments and should be repeatedly monitored. Non-adherence to psychosocial treatment should be given more attention.

Keywords: bipolar disorder, treatment, adherence, prospective study

Guidelines concordance for acute bipolar depression in mainland China

Z Wang^a, W Hong^b, M Xing^b, Z Wu^b, J Chen^b, Y Fang^b

^aDepartment of Psychiatry, Hongkou District Mental Health Center of Shanghai, Shanghai, China, ^bDivision of Mood Disorders, Shanghai Mental Health Center Shanghai Jiao Tong University School of Medicine, Shanghai, China

Background and objectives: With recent attention to evidence-based medicine in psychiatry, a number of treatment guidelines had emerged. This study was designed to investigate the situation of prescribing psychotropic agents and guideline concordance for acute bipolar depression in China nationwide.

Methods: A total of 1078 patients diagnosed with bipolar depression were screened consecutively in 25 sites (14 psychiatric hospitals and 11 psychiatric units of general hospitals) in China nationwide. The demographic and clinical characteristics were recorded using a standardized data collection procedure.

Results: Of the 1078 patients who were enrolled, 452 (41.9%) patients had been prescribed with one psychotropic agent, in which the most common prescribing pattern was monotherapy of antidepressant ($n = 341$, 31.6%). The next most common prescribing pattern was the combination treatment of two psychotropic agents ($n = 330$, 30.6%). One hundred and sixty-three (15.1%) patients were prescribed with the combination treatment of three psychotropic agents. Meanwhile, 133 (12.3%) patients were not prescribed with any psychotropic agent. The non-depressive first-onset, current co-morbidity with mental disorders, older age at study entry, and earlier first-onset, were significantly associated with combination treatment of two or more psychotropic agents. Therefore, 537 (49.5%) patients were prescribed concordant with pharmacological treatment guideline. The psychiatric units of general hospitals, hypomanic/manic episode at first onset, current co-morbidity with mental disorders, older age at study entry, earlier first-onset, and more frequent episodes in past year, were significantly associated with guideline concordance. Among all surveyed patients, 729 (67.6%) patients had been prescribed with antidepressant monotherapy or combination treatment of antidepressant plus other psychotropic agent(s). The depressive episode at first onset and no current co-morbidity with physical disorders were significantly associated with antidepressants taken.

Conclusions: The concordance with treatment guidelines for acute bipolar depression is not common under naturalistic conditions.

Keywords: bipolar; depression; guidelines; treatment; antidepressant

Guidelines concordance for acute manic and mixed episodes in mainland China

Z Wang^a, W Hong^b, M Xing^b, Z Wu^b, J Chen^b, Y Fang^b

^aDepartment of Psychiatry, Hongkou District Mental Health Center of Shanghai, Shanghai, China, ^bDivision of Mood Disorders, Shanghai Mental Health Center Shanghai Jiao Tong University School of Medicine, Shanghai, China

Background and objectives: With recent attention to evidence-based medicine in psychiatry, a number of treatment guidelines had

emerged. This study was designed to investigate the situation of prescribing psychotropic agents and guideline concordance for acute manic and mixed episodes in China nationwide.

Methods: A total of 2828 patients diagnosed with bipolar disorder (hypo-manic/manic episode or mixed state) were screened consecutively in 25 sites (14 psychiatric hospitals and 11 psychiatric units of general hospitals) in China nationwide. The demographic and clinical characteristics were recorded using a standardized data collection procedure.

Results: Of the 2828 patients who were enrolled, 2162 (76.4%) were prescribed with guideline concordant pharmacological treatment, in which the most common prescribing pattern was lithium or valproate plus an antipsychotic ($n = 1508$, 53.3%). Two hundred and fourteen patients (7.6%) had not been prescribed with any psychotropic agent, 617 (21.8%) patients had been prescribed with one psychotropic agent (mood stabilizers $n = 275$, antipsychotics $n = 245$, others $n = 97$), and 344 (12.2%) patients had been prescribed with combination treatment of three and more psychotropic agents (mood stabilizers plus antipsychotics $n = 134$, others $n = 210$). The common factors influencing guideline concordance and prescribing pattern were age at study entry and first onset, mood state at study entry, hospital category, and current co-morbidity with mental disorders. Meanwhile, 343 (12.1%) patients were prescribed with antidepressants. The relative risk factors to prescribing antidepressants were hospital category, mood state at study entry and at first onset, and current co-morbidity with mental disorders.

Conclusions: The concordance with treatment guidelines for acute manic and mixed episodes is very common under naturalistic conditions.

Keywords: bipolar; mania; guidelines; treatment; mood stabilizer

Effectiveness of long-acting injectable antipsychotics in patients with bipolar I disorder

YC Yen^a, CY Huang^b

^aDepartment of Psychiatry, E-Da Hospital and I-Shou University, Kaohsiung, Taiwan, ^bDepartment of Psychiatry, E-Da Hospital, Kaohsiung, Taiwan

Objective: Risperidone long-acting injection (RLAI) as a monotherapy or as adjunctive therapy to mood stabilizer for the maintenance treatment of bipolar I disorder has been approved in Taiwan since 2010. This study aimed to explore the effectiveness of RLAI in bipolar I disorder patients.

Methods: We collected medical records of patients with bipolar I disorder according to the ICD code from a university hospital in southern Taiwan from June 2010 to September 2013. Patients who had continuously received RLAI treatment for at least 3 months were recruited as the LAI group. Patients without any RLAI treatment through the course were recruited as the non-LAI (N-LAI) group. Patient's characteristics, admission to acute care unit in one year, duration of hospital stay in acute care unit, and emergency service use in 1 year were followed up after treatment.

Results: Totally there were 369 bipolar I disorder patients were recruited in this study. The mean age of the study population was 39.5 years with a standard deviation of 12.1. Thirty-five percent of them were male. There was no significant difference between age, sex, and medical conditions. One year before the study began, 75% of patients in the LAI group had ever been admitted to the psychiatric acute care unit. On the other hand, only 23% of patients in the N-LAI group had ever been admitted to the acute care unit one year before the study. The incidence of re-admission for bipolar I disorder during the one-year follow-up were 20.8% for the LAI group, which was significantly fewer than the re-admission of 26.4% for the N-LAI group ($p = 0.002$). Hospital stay for the LAI group, 17 days (SD 7.4), was significantly shorter than that of the N-LAI group, 29 days

Sixteenth Annual Conference on Bipolar Disorders

(SD 19.8) ($p = 0.022$). The emergency room visit rate of the LAI and the N-LAI groups were 19.4% and 16.7%, respectively without significant difference ($p = 0.363$).

Conclusion: RLAI is associated with significant reduction in psychiatric service utilization including less re-admission to acute care unit and shorter hospital stay even though RLAI is prescribed for more clinically severe bipolar I disorder patients.

Keywords: bipolar disorder, antipsychotics, rehospitalization

Psychopharmacological treatment of bipolar disorder in pregnancy: recommendations and clinical monitoring systems

M Snellen, M Assoc. Prof. Galbally

^a*Perinatal Psychiatry, Mercy Hospital for Women, Heidelberg, Australia*

The antenatal management of women with bipolar disorder presents a major challenge for both obstetric and mental health ser-

vices due to the inherent risks associated with both the condition and its treatment: each of which can be considered to be teratogenic in their own right. The possibility of pregnancy in all women of reproductive age should be considered when making treatment decisions from the outset, especially given that unplanned pregnancy is particularly common in this patient group. For all women with bipolar disorder it is essential that specific considerations be attended to, and monitoring systems established and followed perinatally in order to improve overall outcome for both mother and baby. The presentation will explore: the process of obtaining informed consent to prescribe during pregnancy, prescribing guidelines, inherent risks to both mother and foetus of both treatment and non-treatment, and recommend guidelines established at the Mercy Hospital for Women (Australia) for monitoring in the perinatal setting.

Keywords: pregnancy, bipolar disorder, psychopharmacology, monitoring, guidelines

Poster Session II

Smoking during pregnancy and the risk of bipolar disorder

R Chudal^a, M Gissler^{a,b,c}, A Suominen^a, AS Brown^{b,d,e}, A Sourander^{a,d,f,g}

^aDepartment of Child Psychiatry, University of Turku, Turku, Finland, ^bNordic School of Public Health, Gothenburg, Sweden, ^cNational Institute for Health and Welfare, Helsinki, Finland, ^dDepartment of Psychiatry, Columbia University College of Physicians and Surgeons, New York State Psychiatric Institute, New York, NY, USA, ^eDepartment of Epidemiology, Columbia University, Mailman School of Public Health, New York, NY, USA, ^fDepartment of Child Psychiatry, Turku University Hospital, Turku, Finland, ^gRegional Centre for Child and Youth Mental Health and Child Welfare, University of Tromsø, Tromsø, Norway

Background: Prenatal smoking exposure affects fetal growth and development and is associated with increased risk of various neurodevelopmental disorders and increased psychiatric morbidity. Only one previously published study has specifically examined the association between maternal smoking during pregnancy and the risk of bipolar disorder (BPD).

Methods: This is a nested case control study derived from all singleton live births in Finland between January 1st 1987 and December 31st 1998. We identified 724 children diagnosed and/or treated for BPD by December 31, 2008 and 1419 matched controls based on information obtained from four nationwide registers. Conditional logistic regression models were used to examine the association between maternal smoking during pregnancy and BPD adjusting for potential confounding due to maternal age and educational level, and parental psychiatric history.

Results: Among the study children, 18.5% were exposed to maternal smoking during pregnancy. In the unadjusted analysis, smoking during pregnancy in the total sample was associated with a 1.41-fold (95% CI 1.12–1.79) increased risk of BPD. In the final model adjusting for all potential confounders, smoking during pregnancy was associated with a statistically non-significant 1.14-fold (95% CI 0.88–1.49) increased risk.

Conclusion: In this first nationwide population based epidemiological study, we demonstrated an increased risk of BPD among offspring of mothers who smoked during pregnancy, although the risk is most likely due to confounding by other co-existing risk factors.

Keywords: prenatal, smoking during pregnancy, bipolar disorder

Standardization of bipolar depression rating scale (BDRS) in Korean children and adolescents with bipolar disorder: preliminary analysis

DY Lee^a, EK Won^b, JW Choi^b, HJ Min^c, KS Ha^a, JS Chang^d, Y Kim^d

^aGeneral Psychiatry, Seoul National Hospital, Seoul, Korea, ^bChild Psychiatry, Seoul National Hospital, Seoul, Korea, ^cAdolescent Psychiatry, Seoul National Hospital, Seoul, Korea, ^dNeuropsychiatry, National University Bundang Hospital, Seongnam, Korea

Objectives: We explored the psychometric properties of the Korean version of the Bipolar depression rating scale (BDRS) in Korean children and adolescents with Bipolar disorder.

Methods: The Bipolar depression rating scale (BDRS) was administered along with the Hamilton Depression Rating Scale (HAM-D), Montgomery-Asberg Depression Rating Scale (MADRS) and Young Mania Rating Scale (YMRS) to participants aged

9–18 years (32 males and 17 females) with diagnosis of Bipolar disorder based on Kiddie-SADS-Present and Lifetime (K-SADS-PL).

Results: Of the 49 participants, 27 participants were in depressive state, 14 euthymic and eight manic states. There were no differences in sex and age between the mood states. The total scores of BDRS in depression state (mean = 27.2 ± 9.7) were significantly different from that of euthymic (6.9 ± 4.7 , $p < 0.01$) and manic (10.0 ± 3.8 , $p < 0.01$) state. In patients who were experiencing depressive symptoms, the BDRS exhibited good internal consistency (Cronbach's alpha = 0.82), and demonstrated significant correlations with the HAM-D ($r = 0.74$, $p < 0.01$), MADRS ($r = 0.80$, $p < 0.01$), while no correlation with YMRS ($r = -0.29$, $p = 0.15$). For item to scale correlations, all items of BDRS were significantly correlated with BDRS total scores ($r = 0.38$ – 0.68), except for items 16 (Irritability), 18 (increased motor drive) and 19 (increased speech). The item with highest mean scores and endorsement were item 1 (depressive mood) and item 11 (worthlessness).

Conclusions: Our preliminary analysis suggests that BDRS may be a valid and reliable tool for the assessment of bipolar depression in Korean child and adolescents with bipolar disorder.

Keywords: bipolar disorder, depression, children, adolescents, rating scale

Opportunities and challenges in establishing the Emory longitudinal cohort of offspring of mothers with bipolar disorder (ELCOM-BD)

DI Simeonova, T Nguyen, HC Hsu, S Juul, J Mast, T Goldsmith, E Craighead, K Ressler

Psychiatry and Behavioral Sciences, Emory University, Atlanta, GA, USA

Aims: There is growing evidence that approximately 50% of high-risk offspring of parents with bipolar disorder (OBD) develop moderate to severe forms of psychopathology during childhood and adolescence, including bipolar spectrum disorders. Despite exposure to multiple risk factors, however, the remaining 50% of OBD follow normative and resilient developmental trajectories and do not experience psychopathology. Currently, very limited knowledge exists on resilience in this population and mechanisms contributing to adaptive development remain unknown. The present study, designed to establish the Emory Longitudinal Cohort of Offspring of Mothers with Bipolar Disorder (ELCOM-BD), aims to address this gap in the field.

Methods: A repeated-measures design was used to assess mothers and infants during a pregnancy screening visit and at 5 days, 3, 6, 12, 18, and 24 months postpartum. The clinician-rated measures include: SCID-II, SCID-II Mood Module, Hamilton Rating Scale for Depression, Hamilton Rating Scale for Anxiety, and Mania Rating Scale. The maternal measures include: Postpartum Social Support Questionnaire, Social Support Questionnaire, Social Adjustment Scale, Dyadic Adjustment Scale, Parenting Sense of Competence Scale, Beck Depression Inventory I, and State-Trait Anxiety Inventory. The infant measures include: Brazelton Neonatal Behavioral Assessment Scale, Infant Behavior Questionnaire-Revised, Ages and Stages Questionnaire: Social-Emotional, and Infant-Toddler Social and Emotional Assessment. In addition, mother-infant interactions focused on emotion regulation/face-to-face still-face paradigm, free play, and feeding were recorded and pre- and post-interaction saliva was collected to assay for oxytocin.

Results: 14 women with BD (mean age = 32.5; SD = 3.9; range = 25–39; BD I = 8; BD II = 6) were enrolled into the study during pregnancy. The recruitment and data collection are ongoing.

ing. To date, 10 infants were born into the study (male = 6; female = 4) and the following study visits were completed: screening visit (n = 14), 5 days postpartum (n = 10), 3 months postpartum (n = 8), 6 months postpartum (n = 6), 12 months postpartum (n = 4).

Conclusions: This longitudinal investigation is the first study to enroll mothers with BD during pregnancy and to follow a cohort of OBD during the earliest stages of development. The emerging data will facilitate: (1) answers to research questions focused on the trajectory of social-emotional development, mother-infant interaction, and resilience and risk factors in infants and toddlers of mothers with BD and (2) development of novel primary prevention and early intervention approaches.

Keywords: high-risk, resilience, infants, early intervention, prevention

Adolescence and impulsivity evolution and treatment of one adolescent with comorbidity between bulimia nervosa, bipolar disorder, and adhd

JA Vargas Castro^a, A Canudas^b, T Grau^c, G Faus^d, M Sánchez Povedano^e

^aChild & Adolescent Psychiatry, Institute de Trastorns Alimentaris ITA & Conducta, Barcelona, Spain, ^bChild & Adolescent Psychology, Institute de Trastorns Alimentaris ITA & Conducta, Barcelona, Spain, ^cResearch Department ITA, Institute de Trastorns Alimentaris ITA & Conducta, Barcelona, Spain, ^dPsychiatry, Institute de Trastorns Alimentaris ITA & Conducta, Barcelona, Spain, ^ePsychology, Institute de Trastorns Alimentaris ITA & Conducta, Barcelona, Spain

Introduction: Eating disorders, has a prevalence of 3.5% to 5.5% within the Spanish adolescent population are increasing day by day in our treatment centers. Multiple diseases are based on the pattern of impulsivity, which must be studied in their overall comorbidity, because the general approach to their different etiologies could create the need for a Unique Therapeutic Plan (UTP), in some cases.

Background: There is a high comorbidity between the impulsivity seen in Eating Disorders (ED) such as Bulimia Nervosa, Obesity, Binge (ED), Pica, with Externalizing disorders (ExtD), and Bipolar disorder (BD), because of their low tolerance to frustration, irritability, outbursts, and low awareness of limits. And many times there is also the presence of disorders related to substance use.

Objective: Demonstrate by reviewing a case, the diagnostic comorbidity between Bulimia Nervosa, Bipolar disorder and one type of Attention Deficit Disorder with Hyperactivity, associated with a pattern of substance abuse with the same effective psychoterapeutic and psychopharmacological treatment and demostrating the posible same neurobiological root.

Methodology: A seventeen-year-old adolescent, with a five year history of hyporexia, vomiting and bingeing, with hyperactivity, inattention, and impulsivity (BMI = 17) in the context of greater family dysfunction. There was also cannabis abuse. The patient had received treatment with antidepressives and mood stabilizers. By age fourteen, she was diagnosticated with Bulimia Nervosa in comorbidity with Attention Deficit Disorder with Hyperactivity in the Eating Disorders Institute (ITA). We needed to change the psychopharmacological treatment, because the sintomatology with irritability, distractibility restlessness, anger outburst, hyperactivity, grandiosity and dysphoria. In the test of Young Mania Rating Scale and HCL-32, the results were compatible with BD. The new pharmacological treatment was with the Methylphenidate (already begun with the diagnosis of ADHD) and Aripiprazol, associated with psychotherapeutic management and family therapy. Now the

prognosis is excellent (CHIP-AE), and there is absence of substance use over 3 months.

Conclusions: The eating disorders, with impulse control deficits, have a high etiopathogenic relationship with Bipolar disorder, and externalizing disorders-ADHD, and the same psychotherapeutic and psychopharmacological treatment, could be effective in treating of these classes of disorders.

Bipolar disorder vs disruptive mood dysregulation disorder: MRI studies

CP Zeni^a, S Tramontina^a, M Anes^b, T Peruzzolo^c, G Motta^c, J Brun^d, FP Kapczinski^c, LA Rohde^e

^aPsychiatry, Hospital de clinicas de porto alegre, Porto Alegre, Brazil, ^bPhysics, Hospital de clinicas de porto alegre, Porto Alegre, Brazil, ^cPsychiatry, Hospital de clinicas de porto alegre, Porto Alegre, Brazil, ^dPsychology, PUC-RS, Porto Alegre, Brazil

Aims: A frequent controversy in the diagnosis of BD in children and adolescents is the presence of continuous mood symptoms. However, symptoms of chronic irritability, temper outbursts, and extremely low tolerance to frustration, have been categorized as Disruptive Mood Dysregulation Disorder in DSM-5. Currently there are no biomarkers that could help in the differentiation between these mental health conditions. Thus, many of our young patients may be exposed to ineffective and potentially harmful therapeutic agents. Neuroimaging studies allow in vivo investigation of physiopathological mechanisms of the brain. They can assess brain regions and processes involved in emotional regulation, and the integration between emotion and cognition. Our objectives are to evaluate the brains of children and adolescents with BD and DMDD. Specifically, we will compare total brain, amygdala, hippocampus, globus pallidus, and striatum volumes between BD and DMDD; white matter in limbic-thalamic-cortical, and limbic-striatal-pallidal-thalamic circuits; and functional connectivity between dorsolateral prefrontal cortex and temporal superior gyrus bilaterally.

Methods: Children and Adolescents will be recruited from clinical settings. Parental written consent and child and adolescent assent will be obtained. Patients undergo: (a) evaluation with K-SADS-PL, and a supplemental module of DMDD; (b) clinical evaluation of BD, DMDD, and comorbid conditions using KSADS results in the interviews. Inclusion criteria are: (a) boys and girls 6–17 years-old; (b) DSM-IV diagnoses of BD; (c) DSM-five diagnosis of DMDD. Structural, Diffusion Tensor Imaging (DTI), and Resting State Functional Connectivity (RSFC) MRI images are acquired in a 1.5 T Philips Achieva full-body scanner at the Hospital de Clínicas de Porto Alegre. Analyses will be performed using ANCOVA. The subject group (BD or DMDD) will be the independent variable, and volume measures, DTI and RSCN as dependent variables.

Results: By this time, data have been collected from 30 subjects with BD and six subjects with DMDD. Since preliminary analyses would not provide significant data, we will present results at the meeting.

Conclusions: The results have the potential to help understand differences between these conditions, strengthening neurobiological and physiopathological knowledge in this field.

Predictors of transition into bipolar disorder after the first lifetime depressive episode

JD Bukh, LV Kessing

Research Unit for Affective Disorders, Psychiatric Center Copenhagen, Copenhagen, Denmark

Background: The prevalence of change from unipolar to bipolar disorder is estimated to 1% each year and as much as 40–50 % over lifetime. There has been increasing interest in defining clinical

differences between unipolar and bipolar depressions and detecting subtypes of depression, which are associated with increased risk of later development of bipolar disorder. However, most previous studies have assessed these characteristics retrospectively. Therefore, it is not possible to distinguish clearly between predictors of transition into bipolar disorder, present already from onset of the disorder, and secondary consequences of different courses of illness.

Aim: To assess the effect of clinical, demographic and genetic variables on the risk of development of bipolar disorder after the first lifetime episode of depression.

Method: A total number of 301 patients aged 18–70 years with recent onset of the first lifetime depressive episode were systematically recruited using the Danish Psychiatric Central Research Register in 2005–2007. Clinical characteristics of the first episode depression, psychiatric co-morbidity including personality disorders, treatment history and outcome, the level of neuroticism, family history of psychiatric disorders, and the experience of stressful life events during a 6 month period preceding onset of depression were assessed by structured interviews, and polymorphisms in the genes encoding the serotonin transporter, brain derived neurotrophic factor, tryptophan hydroxylase, and the serotonin receptors 1A, 2A, and 2C were genotyped. In 2011–2013, 264 of the study participants (93% percent of the living individuals) have been reassessed in a follow-up study aiming to examine the course of the illness and the demographic, clinical and genetic variables associated with transition into bipolar disorder as well as development of recurrent and chronic depressions.

Results: Data on the risk of recurrence and transition into bipolar disorder during the first 5 years following the first lifetime episode of depression are currently being analysed and will be presented.

Conclusion: This is the first study of predictors of various courses of illness among patients followed prospectively from onset of the first lifetime episode of depression. The design and new unpublished results will be presented.

Lifetime experiences of hypomanic symptoms are associated with delayed and irregular sleep-wake cycle and seasonality in non-clinical adult samples

M Bae^a, K Lee^a, JS Kim^b, Y Cho^a, S Ryu^a, JH Baek^a, K Ha^b, KS Hong^a

^aDepartment of Psychiatry, Samsung Medical Center, Seoul, Korea,

^bDepartment of Neuropsychiatry, Seoul National University Bundang Hospital, Kyunggi-Do, Korea

Background: Disturbances of the sleep-wake cycle and seasonality have been reported in patients with bipolar disorder (BD). Considering that BD seems to be a spectrum condition in terms of clinical and biological characteristics, circadian and seasonal rhythm related to BD could be detected in non-clinical individuals with subthreshold bipolarity. The aim of this study was to screen past hypomanic symptoms in non-clinical samples and investigate their association with deviated sleep-wake cycle and seasonality.

Methods: Lifetime history of hypomanic symptoms was assessed with the Hypomania Checklist-32 (HCL-32). Circadian preference, variability of the sleep-wake time and seasonal changes in mood and behavior were evaluated on a lifetime-basis in non-clinical adult samples ($n = 313$), using the Composite Scale of Morningness (CSM), the Sleep Timing Questionnaire (STQ), and the Seasonal Pattern Assessment Questionnaire (SPAQ).

Results: Two subdomains of hypomanic symptoms were identified through factor analysis of HCL-32, i.e., “active/elated” factor and “irritable/risk-taking” factor. The HCL-32 total score ($p < 0.001$) and the “active/elated” factor score ($p = 0.028$) were weakly correlated only with seasonality, whereas the “irritable/risk-taking” factor score was associated not only with seasonality ($p < 0.001$), but

also with evening preference ($p < 0.001$) and irregularity of sleep-wake times ($p = 0.001\text{--}0.011$).

Limitations: Retrospective measurement relying on self-report.

Conclusions: This study revealed that circadian and seasonal characteristics related to BD are also associated with past history of hypomanic symptoms in non-clinical samples, especially “irritable/risk-taking” symptoms, suggesting the existence of subclinical presentation of BD and their biological traits.

Keywords: hypomanic symptom, HCL-32, sleep-wake cycle, circadian preference, seasonality

Clinical correlates of resilience in euthymic patients with bipolar disorder

B Cha^a, JW Choi^b, IY Ahn^b, JH Jang^b, SY Lee^b, CS Park^a, BJ Kim^a, CS Lee^a, SJ Lee^a

^aPsychiatry, Gyeongsang National University College of Medicine, Jinju, Korea, ^bPsychiatry, Gyeongsang National University Hospital, Jinju, Korea

Objective: Resilience is ability to cope with adversity. It has been reported that resilience is associated with demographic and clinical characteristics and treatment outcomes in patients with anxiety disorder, especially posttraumatic stress disorder, and depressive disorder. However, there are a few studies about resilience in patients with bipolar disorder (BD). The present study aimed to investigate relationship between resilience and clinical characteristics including impulsivity in euthymic patients with BD.

Methods: A total of 59 outpatients with BD type I, II and NOS who were in remission state were recruited and completed Connor-Davidson Resilience Scale (CD-RISC), Barratt Impulsiveness Scale-11(BIS-11). The control group consisted of 59 healthy individuals matched with the patients group in term of age and sex, without any history of psychiatric treatment. Psychiatrists administered the Clinical Global Impression (CGI) for BD and then interviewed the subjects to assess clinical variables. A multiple linear regression model was used to find predictive factors of resilience.

Results: BD patients group presented significantly higher all BIS-11 subscale score and lower CD-RISC score than control. The CGI, number of depressive episode and BIS-11 score showed negative correlation with the CD-RISC score. In multiple linear regression model, the BIS total score and number of depressive episode were strongly predictive factors for low resilience.

Conclusion: Our results suggest that low resilience is important clinical characteristic in euthymic patients with BD. Also, this study shows inverted relationship between impulsivity as a trait characteristic of BD and resilience. Further studies are warranted to investigate whether low resilience is associated with poor treatment outcome in patients with BD.

Effects of bipolarity on drinking behavior according to age and gender

J Lee

Psychiatry, Pusan National University Hospital, Busan, Korea

Introduction: Many studies suggest that bipolar disorders are related to alcohol use disorder. We aimed to investigate whether bipolarity is associated with drinking behavior according to age and gender.

Methods: We recruited 291 participants who do not take psychiatric treatment currently in community. Bipolarity was measured by Bipolar Spectrum Diagnostic Scale (BSDS). Drinking behavior was evaluated by Alcohol Use Disorder Identification Test (AUDIT). We analyzed the effects of bipolarity on drinking behavior according to age and gender using univariate linear regression.

Results: Total scores of BSDS were associated with AUDIT scores. ($B = 0.180$, $\beta = 0.120$, $t = 2.060$, $p = 0.040$) Especially, there was significant association between BSDS and AUDIT in middle-aged

adult group. ($B = 0.374$, $\beta = 0.223$, $t = 2.764$, $p = 0.006$) Drinking behaviors in middle-aged man were related to mania subscale of BSDS ($B = 1.568$, $\beta = 0.371$, $t = 3.366$, $p = 0.001$), but those in middle-aged woman were related to mania subscale of BSDS, as well as depression subscale of BSDS. (mania subscale, $B = 0.534$, $\beta = 0.241$, $t = 2.119$, $p = 0.037$; depression subscale, $B = 0.496$, $\beta = 0.290$, $t = 2.589$, $p = 0.001$).

Conclusion: These results suggest that bipolarity may be associated with drinking behaviors, especially in middle-aged group. Furthermore, bipolarity may have differential influences on drinking behaviors according to age and gender. Consideration on bipolarity can be important to establish strategies for decreasing drinking in middle-age.

Keywords: social drinking, problematic drinking, mood fluctuation, bipolarity

Personality traits depending on mood state in patients with bipolar disorder

S Park, SJ Lee, U Yoon, Y Joo

Psychiatry, Asan Medical Center, Seoul, Korea

This study aimed to investigate whether the personality traits are dependent on current mood state which is euthymia or mania or depression, and how the mood state was expressed as personality trait in the patients with bipolar affective disorder (BD). Also, we investigated clinical characteristics depending on polarity in patients with BD.

Methods: A total of 102 BD patients were divided into three groups which were euthymic state ($n = 48$), manic episode ($n = 21$) and depressive episode ($n = 33$) based on mood state and completed the Temperament and Character Inventory (TCI) and the HEXACO Personality Inventory-Revised (HEXACO-PI-R) to evaluate the temperament and the personality.

Results: Depressive state was associated with increased Harm Avoidance (HA) and decreased Self-Directedness (SD), and manic state was associated with increased Persistence (P) and Cooperativeness (C). Between a presence of psychotic features and personality dimensions were not related. The scores of extraversion and openness in HEXACO-PI-R were increased in manic state. We compared personality traits between stable and unstable group during euthymic state, and stable euthymic state showed lower Extraversion in HEXACO-PI-R.

Conclusions: There are clear state effects of mood on self-reported personality. Personality disturbances in HA, SD, P, C, extraversion and openness may be enduring characteristics of patients with BD depending on current mood states. Extraversion reflected the sub-syndromal symptoms in euthymic state. Also, dominant polarity was associated the first-episode polarity and future course of illness.

Informing intervention strategies for bipolar disorder using dynamic treatment regimes

F Wu^a, E Laber^a, I Lipkovich^b, E Severus^c

^aStatistics, North Carolina State University, Raleigh, NC, USA,

^bStatistics, Quantiles, Morrisville, NC, USA, ^cPsychiatry, University of Munich, Munich, Germany

There is substantial uncertainty regarding the efficacy of antidepressants in the acute treatment of bipolar depression. The available evidence from randomized controlled trials is limited and controversial. Furthermore, traditional randomized controlled trials are not designed to tell who (of the target population) will benefit from the intervention - and who might do better without. In addition, as bipolar disorders are chronic mood disorders, with a series of interventions being the rule rather than the exception (in case of bipolar depression, to reach remission), they do not closely

mimic clinical reality as the effects of previous treatments on the efficacy and tolerability of subsequent treatment are not well captured. Therefore other methodological approaches are urgently needed which allow to practice personalized, evidence-based medicine in patients with bipolar depression. Dynamic treatment regimes operationalize clinical decision making as a sequence of decision rules, one per stage of clinical intervention, that map up-to-date patient information to a recommended treatment. Dynamic treatment regimes therefore personalize treatment according to the evolving health status of each patient. An optimal treatment regime maximizes the expectation of a desired cumulative clinical outcome when applied to a patient population of interest. Thus, estimated optimal dynamic treatment regimes can inform clinical decision making and generate evidence-based hypotheses about time-varying treatment response heterogeneity. Using data from the acute depression randomized care (RAD) pathway of the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) study (Sachs et al., 2007, NEJM), we estimate an optimal dynamic treatment regime via Q-learning, an extension of regression to multi-stage decision problems. The estimated optimal dynamic treatment regime performs statistically significantly better than any estimable non-tailored treatment strategy. The estimated optimal dynamic treatment regime presents strong evidence that patients in RAD pathway of STEP-BD with a (hypo) manic episode prior to onset of the current depressive episode should not be given an antidepressant in addition to a mood stabilizer.

Semantic priming and hypomanic personality: an electrophysiological study

S Terrien^a, G Lakimova^b, C Besche-Richard^c

^aLaboratoire Cognition Santé Socialisation – C2S EA 6291,

Université de Reims Champagne-Ardenne, Reims, France,

^bLaboratoire d'Anthropologie et de Psychologie Cognitive et Sociale – LAPCOS EA 7277, Université de Nice Sophia-Antipolis, Nice,

France, ^cLaboratoire Cognition Santé Socialisation - C2S EA 6291, Université de Reims Champagne-Ardenne & Institut universitaire de France, Reims, France

Background: There are few studies on semantic memory in bipolar disorders while thought and language disorders are common in this disease (Bora et al., 2010; Ivleva et al., 2012). Only two studies have been published on the semantic priming effects in bipolar disorder: one behavioral (Andreou et al., 2013.) and one in event related potential (Ryu et al., 2012). Results concerning the event-related potential study showed that bipolar patients have a significant reduction of the N400 effect associated with an increase in the amplitude of the N400 for related words compared to healthy participants. No study has yet explored the processes involved in different types of semantic priming forward and backward associative priming. In forward associative priming, there is an association from the prime to the target (Draine & Greenwald, 1998). In contrast, backward associative priming consists of a post lexical process, it occurs as a result of a strong associative link from the target to the prime (Koivisto, 1998). Actually, there are no results about the neurophysiologic processes mediating the processing of forward and backward semantic priming as a cognitive marker of vulnerability of bipolar disorder.

Objectives: The goal of this study is to explore the forward and the backward semantic priming processes in relation with the level of hypomanic personality in a general population.

Methods: Healthy participants will be evaluated on hypomanic personality (HPS). The ERPs will be recorded during a semantic priming task which will allow participants to make a lexical decision on 208 word pairs with five experimental conditions: forward related pairs, forward unrelated pairs, backward pairs, backward unrelated pairs and pseudo-words.

Results: We expect to observe that high hypomanic participants, contrary to the low, will exhibit particularities on the modulation of amplitude of N400.

Conclusions: The major discussion points will concern the components of ERP associated with semantic integrative processes and their disturbances as cognitive markers of a vulnerability to bipolar disorders.

Keywords: hypomanic traits, semantic priming, forward and backward associations, N400

Emotional meaning in context in relation to hypomanic traits: an ERP study

C Besche-Richard^a, S Terrien^b, G Iakimova^c, P Mazzola-Pomietto^d, V Baltazar^e, A Kaladjian^f

^aLaboratoire Cognition Santé Socialisation C2S EA 6291, Université de Reims Champagne-Ardenne & Institut universitaire de France, Reims, France, ^bLaboratoire Cognition Santé Socialisation C2S EA 6291, Université de Reims Champagne-Ardenne, Reims, France, ^cLaboratoire d'Anthropologie et de Psychologie Cognitive et Sociale LAPCOS EA 7277, Université de Nice Sophia Antipolis, Nice, France, ^dCNRS UMR 6193, Institut des Neurosciences de la Timone, Marseille, France, ^eLaboratoire Cognition Santé Socialisation C2S 6291, Université de Reims Champagne-Ardenne, Reims, France, ^fLaboratoire Cognition Santé Socialisation C2S 6291, CHU de Reims & Université de Reims Champagne-Ardenne, Reims, France

Background: Bipolar patients are impaired in their ability to process social situations that implicate emotional processing in reference to facial emotional recognition (Martino et al., 2011), affective and cognitive theory of mind (Bora et al., 2005). The ability to integrate contextual information is an important mechanism to the comprehension of emotional and social information (Baez et al., 2013). Studies using the method of Event-Related Potentials (ERPs) showed that schizophrenic patients exhibit impaired ability to integrate contextual information (Baez et al., 2013) as demonstrated by abnormalities of the N400 component. No study have yet explored this mechanism in bipolar disorder but some authors consider that cognitive disorders in bipolar patients are qualitatively similar from those identified in schizophrenic patients (Jabben et al., 2010). In the aim to study cognitive markers of vulnerability of bipolar disorders, we propose to explore the neurocognitive processes mediating the processing of emotional information during the integration of semantic and contextual social information as in general population according to their hypomanic scores.

Objectives: The goal of this ongoing study is to explore the semantic-emotional integrative processes in relation with the level of hypomanic personality and the self-report abilities of theory of mind in general population.

Methods: Healthy participants will be evaluated on hypomanic personality (HPS). The ERPs will be recorded during a linguistic task which will allow participants to saliently read 66 sentences-pairs which will describe short social situations. The first sentence implicitly conveys the emotional state of a person, either positive or negative. In the second sentence (congruent or incongruent with the emotional context of the first), the last word is neutral, positively or negatively valenced.

Results: We expect to observe that low hypomanic participants will exhibit both N400 and Late Positivity (LP) modulation by emotional valenced words contrary to high hypomanic participants.

Conclusions: The major discussion points will concern the components of ERP associated with semantic-emotional integrative processes and their disturbances as cognitive markers of a vulnerability to bipolar disorder.

Keywords: hypomanic traits; emotional valence; sentence context; integrative processes; N400

Implicit motor learning in bipolar disorder and schizophrenia

A Chrobak^a, K Siuda^a, G Siwek^a, M Siwek^b, M Pilecki^c, D Dudek^b

^aStudents Scientific Association of Adult Psychiatry, Jagiellonian University, Cracow, Poland, ^bDepartment of Affective Disorders, Jagiellonian University, Cracow, Poland, ^cDepartment of Psychiatry, Jagiellonian University, Cracow, Poland

Aims: There is only scarce data concerning implicit motor learning in bipolar disorder (BD), while there is growing number of evidence about such deficits in schizophrenia (SZ). The aim of our study was to evaluate this cognitive function with a use of Serial Reaction Time Task (SRTT) paradigm in BD patients in comparison with SZ patients' results and to seek for possible unilateral dysfunctions during this task.

Methods: 18 patients with SZ, 11 patients with BD and 20 healthy control subjects were examined. During the SRTT task numbers ranging from 1 to 4, one at the time, were displayed on the computer monitor. Subject's task was to push an adequate button, each with a different finger of the hand, on the response pad containing four buttons numbered 1–4. Task consisted of five blocks, in the first and fifth block numbers were displayed randomly, whereas blocks 2–4 consisted of a 10 items long sequence. Each subject performed two versions of SRTT, each for one hand.

Results: In blocks with random numbers BD group was significantly slower than SZ (block 1: $p = 0.001$, block 5: $p < 0.001$) and control group (block 1 and 5: $p < 0.001$), which did not differ from each other. In the sequence blocks control group performed significantly faster than BD. Additionally, in the control group the rebound of reaction time in the fifth block compared to the fourth block was noted (mean of reaction time (RT) in block 5–reaction time in block 4 = 0.01), suggesting that this group have learned the sequence. No such effect appeared in the BP (mean of RT in block 5–RT in block 4 = -0.08 , $p < 0.001$) or the SZ group (mean of RT in block 5–RT in block 4 = -0.03 , $p = 0.028$).

Conclusions: To our knowledge this is the first study comparing implicit motor learning in BP and SZ, examining both left and right hand separately. Our results show that in both groups of patients implicit motor learning is impaired. Those results may be caused by possible disruption in higher motor control structures.

Keywords: bipolar disorder, schizophrenia, serial reaction time task, implicit motor learning

Care-oriented moral reasoning among patients with bipolar disorder

N Czyżowska^a, R Epa^a, M Siwek^a, D Dudek^a, JK Gierowski^b

^aChair of Psychiatry, Jagiellonian University Medical College, Institute of Affective Disorders, Krakow, Poland, ^bChair of Psychiatry, Jagiellonian University Medical College, Institute of Medical Psychology, Krakow, Poland

Background: Since several decades researchers have tried to understand the process of moral development and its relationship with other constructs such as empathy or theory of mind (ToM). There are data implying abnormalities of empathy among persons diagnosed with bipolar disorders. There is also evidence that bipolar disorder patients show deficits in ToM as well as cognitive deficits. What is more, impairment on personal moral dilemma has been noticed among this group of patients. However, little is known about moral reasoning in bipolar disorder. We sought to investigate moral reasoning in bipolar disorder patients, comparing them to healthy individuals and between phases.

Methods: Moral reasoning was evaluated by The Ethic of Care Interview (ECI) in 52 bipolar disorder patients (20 patients in manic phase, 16 patients in depressed phase and 16 euthymic patients) and 52 healthy volunteers. To rate the severity of symptoms among bipolar patients the following scales also have been

used: Hamilton Depression Rating Scale, Montgomery–Asberg Rating Scale and Young Mania Rating Scale.

Results: Compared with healthy controls, individuals with bipolar disorder reached lower stages of moral development ($p < 0.001$). There were also significant differences in stages of moral reasoning between manic and depressed ($p = 0.035$) and manic and euthymic patients ($p = 0.027$) but there were no differences among the euthymic subjects and those in depressed phase. There was a significant negative correlation between the severity of manic symptoms and the stages of moral development ($p = 0.01$).

Conclusion: These findings suggest that patients with bipolar disorder (especially manic patients) seem to have some difficulties in moral reasoning what can influence their functioning in social and interpersonal sphere.

Keywords: moral development, ethic of care, mental disorders

Effects of cognitive remediation on cognitive dysfunction in partially or fully remitted patients with bipolar disorder: a randomised controlled trial

KM Demant, M Vinberg, LV Kessing, KW Miskowiak

Copenhagen Affective Disorder Clinic, Rigshospitalet Copenhagen University Hospital, Copenhagen, Denmark

Aims: Despite medical treatment a large proportion of patients with bipolar disorder experience persistent and debilitating cognitive dysfunction. In particular, trait-related cognitive deficits are present in 30–60% of bipolar patients, reducing their occupational and social functioning and quality of life. The cognitive deficits are broad and have been demonstrated in verbal memory, sustained attention, executive function and social cognition. Cognitive remediation is a new psychological treatment which aims to improve cognitive function, compensational skills, coping skills and, consequently, psychosocial function. There is substantial evidence for beneficial effects of cognitive remediation in patients with schizophrenia, but only few trials have investigated the efficacy in patients with bipolar disorder. The aim of the present trial is to investigate if cognitive remediation has beneficial effects on cognitive function in patients with bipolar disorder in complete or partial remission who experience persistent cognitive difficulties.

Methods: 40 patients are randomised (1:1) to receive either add-on cognitive remediation in a group setting or standard treatment in an evaluator-blind between-groups design. The cognitive remediation programme consists of 12 weekly group sessions of 2×45 min and a booster session at week 15. Sessions mainly target memory, attention and executive functions. A computer program with cognitive training exercises is also employed at the end of each session and as homework in-between sessions. Primary outcome is enhancement of verbal memory from baseline to post-treatment (week 12). Secondary outcomes are improved sustained attention and executive and psychosocial function. Tertiary outcomes are improved self-reported cognitive and psychosocial function, increased plasma Brain Derived Neurotrophic Factor (BDNF) and reduced stress response. Assessments of study outcomes are made at baseline, post treatment (week 12) and at follow-up (week 26).

Results: Results will be presented at the conference.

Conclusion: If the results show beneficial effects of cognitive remediation versus standard treatment this would highlight cognitive remediation to target cognitive dysfunction in patients with bipolar disorder. This may have important implications for the future management of bipolar disorder and costs for society.

Neurocognitive performance in first episode bipolar I disorder compared to first episode schizophrenia and healthy controls

C Demmo, IM Melle, LK Kvitland, OAA Andreassen, TVL Vik Lagerberg, TU Ueland

Psychosis Research Unit, Oslo University Hospital, Oslo, Norway

Background: There is a higher prevalence of neurocognitive impairment in patients with bipolar disorders compared to the general population. While it is well documented that patients with first episode schizophrenia spectrum disorders have significant cognitive dysfunction, less is known about the early phases of bipolar disorders. Hence, the aim of the current study is to investigate neurocognitive functioning in first episode bipolar I disorder, compared to patients with first episode schizophrenia and healthy controls.

Methods: A total of 288 participants, 96 with a broad DSM-IV schizophrenia spectrum disorder, 96 with bipolar I disorder and 96 healthy controls (mean age: 30.7 years, gender: 43.8% males), were recruited to the Thematically Organized Psychosis (TOP) Study. Diagnoses were obtained with the Structured Clinical Interview for DSM-IV Axis I disorders (SCID-I) and neurocognitive functioning was assessed with a comprehensive test battery. The groups were matched on sex, age and education before comparing neurocognitive functioning using multivariate analysis of variance (MANOVA) with Bonferroni corrections between the three groups.

Results: The first episode bipolar I group performed in between the first episode schizophrenia group and healthy controls on all measures. Compared to healthy controls they showed impaired psychomotor speed, impairment on most measures of executive functioning, and a trend level for measures of working memory and long term memory. Compared to the first episode schizophrenia group, they performed better on measures of fluency, processing speed and psychomotor speed, while no differences were found on a measure of interference control, set shifting or measures of learning and memory. Consistent with previous literature, the first episode schizophrenia group performed significantly worse than the healthy controls on all neurocognitive measures except for one simple measure of attention and one measure of working memory.

Conclusion: The first episode bipolar I group showed a variable pattern of neurocognitive performance falling between patients with first episode schizophrenia and healthy controls on all measures. This suggests that neurocognitive dysfunctions are present early in the disease development, and are not only secondary to disease progression or treatment.

Treatment nonadherence is not associated with cognitive impairment in euthymic bipolar disorder

R Ekinci^a, E Ozalp^b, E Karakurt^b, E Karslioglu^b, A Caykoylu^c

^aPsychiatry, Gazi Mustafa Kemal State Hospital, Ankara, Turkey,

^bPsychiatry, Ankara Oncology Research and Training Hospital, Ankara, Turkey, ^cPsychiatry, Yildirim Beyazit University Faculty of Medicine, Ankara, Turkey

Introduction: Treatment nonadherence is a major problem in bipolar disorder and little is known about the relationship between treatment adherence and cognitive dysfunction. This study aimed to investigate whether treatment nonadherence is associated with cognitive impairment in euthymic bipolar patients and whether other factors may be associated with both adherence and cognitive functioning.

Method: 78 patients who met DSM-IV diagnostic criteria for euthymic bipolar disorder for at least 3 months completed the neuropsychological battery. 56 euthymic patients [49 patients (87.5%) had bipolar type I] completed the study. Any patients who experienced any bipolar episode, or who had a score of HAMD ≥ 8 and

of YMRS ≥ 6 were excluded from the study. In this study, euthymic bipolar patients who presented to the Ankara Oncology Training and Research Hospital between May 2012 and January 2013, were enrolled. 26 patients were adherent to treatment, and 30 patients were not adherent to treatment. All of the patients were evaluated by HAM-D, YMRS, UKU, SCID-I, WCST, Stroop, RAVLT and CPT. Adherence to treatment was assessed at baseline, and at the 3rd and 6th month during follow-up. The groups were compared according to their scores on the neuropsychological battery and their clinical characteristics.

Results: We found that, in euthymic bipolar patients treatment adherence was 44.6%. Treatment nonadherence was associated with socioeconomic status, age of onset of the illness, and drug side effects. The groups did not significantly differ from each other in terms of neurocognitive dysfunction. The treatment nonadherent group was lower in socioeconomic status, and had an earlier onset of illness. The medical comorbidity rate was high in the treatment adherent group. There was no relationship between mood stabilizer class and treatment adherence.

Discussion: There was no association between treatment nonadherence and cognitive impairment. Drug side effects, socioeconomic status and younger age at onset of illness may influence treatment adherence. Treatment side effects may be an important predictor of treatment nonadherence.

Keywords: treatment adherence, bipolar disorder, cognitive impairment

The relations between the bipolar affective disorder and the development of justice-oriented moral reasoning

R Epa^a, N Czyzowska^a, M Siwek^a, JK Gierowski^b, D Dudek^a

^aChair of Psychiatry, Jagiellonian University Medical College, Institute of Affective Disorders, Kraków, Poland, ^bChair of Psychiatry Jagiellonian University Medical College, Institute of Medical Psychology, Kraków, Poland

Background: There is a lot of data suggesting that the moral functioning of persons diagnosed with the bipolar affective disorder is altered. This includes e.g. changes in experiencing moral emotions (like empathy, shame and guilt) or an increased tendency to behave inadequately according to common norms. Yet still little is known about how is moral reasoning developing in persons with the bipolar disorder. The presented research was designed to look into the matter of moral reasoning in bipolar patients by means of comparing them with healthy persons. An attempt was also made to establish whether there is a dependency between the profile of moral reasoning and the phase of the disorder.

Methods: 86 persons took part in the research: 43 diagnosed with the bipolar affective disorder (13 in manic phase, 13 in depressed phase and 17 euthymic patients) and 43 healthy volunteers. To divide the group with the disorder into three subgroups (persons with mania, depression and euthymia), three scales of mood were used: Hamilton Depression Rating Scale, Montgomery–Asberg Depression Rating Scale and Young Mania Rating Scale. Moral reasoning among all of the participants was evaluated by the Defining Issues Test (DIT).

Results: The statistical analysis proved the existence of a relation between the bipolar disorder and the profile of moral reasoning: the bipolar patients chose less often than healthy persons answers indicating post-conventional thinking ($p = 0.000$) and more often answers belonging to the anti-institutional thinking indicator ($p = 0.000$). A dependency was also revealed between the phase of the disorder and moral reasoning with regard to chosen indicators of those variables: patients with mania chose less often than the euthymic patients answers characteristic for the final stadium of moral reasoning ($p = 0.048$).

Conclusions: The results expose the fact that the mental state of a person is not without effect on their moral reasoning process: the sole presence of the bipolar affective disorder may modify the profile of this type of reasoning. The gathered data seems to underline additionally the specific nature of the manic phase, which remains related to the post-conventional thinking of the person with the disorder.

Keywords: bipolar affective disorder, cognitive-developmental theory, moral emotions, moral reasoning

Implicit processing of negative emotion impairs saccadic control in euthymic bipolar disorder

N Guyader^a, A Chauvin^b, L Beynel^b, S Harquel^b, B Fredembach^c, T Bougerol^d, C Marendaz^b, M Polosan^e

^aImages and Signal, Univ. Grenoble Alpes GIPSA-lab. UMR 5216 CNRS, Grenoble, France, ^bPsychology, Univ. Grenoble Alpes LPNC. UMR 5105 CNRS, Grenoble, France, ^cPsychiatry and Neurology, University Hospital of Grenoble, Grenoble, France, ^dPsychiatry and Neurology, Univ. Grenoble Alpes University Hospital of Grenoble LPNC. UMR 5105 CNRS, Grenoble, France, ^ePsychiatry and Neurology, Univ. Grenoble Alpes University Hospital of Grenoble GIN INSERM U836, Grenoble, France

Introduction: Bipolar disorder (BD) patients have abnormal emotional face processing. In euthymic phase, BD patients have greater activity during sad face inhibition (go no-go task) compared to happy face in frontal regions. This suggests that abnormal neural activity during inhibition processes is dependent on emotional content in BD (Hummer et al., 2013). The present study investigates whether an implicit emotional face processing influences inhibition response during a saccadic task.

Method: 21 euthymic BD patients performed a task mixing antisaccades (AS), prosaccades (PS) and no saccade (NS) (Malsert et al., 2012). On each trial, a central face, either happy or sad, appeared, surrounded by a colored frame that indicated the type of saccade to perform: red (AS), green (PS) or blue (NS). Then, a cue appeared on the right or left. Patients were not asked to process the face but to focus on the color and to look as quickly as possible to the cue (PS) or to the mirror position (AS). Saccadic reaction time (SRT) and inhibition error rate were reported.

Results: ANOVAs were run on SRT and error rate with the Saccade Type (AS, PS for SRT; AS, PS, NS for error rate) and the Emotion Type (happy, sad) as within-subject factors. Saccade Type had a main effect on SRT and error rate. As expected, AS had longer SRT ($F(1, 20) = 48, 45$; $p < 0.001$) and more inhibition errors ($F(2,20) = 35, 41$; $p < 0.001$) than PS. More interestingly, a simple effect of the Emotion was observed with longer AS SRT for sadness compared to happiness ($F(1,20) = 6.32$; $p < 0.05$) and no effect on PS. Moreover, with sad faces, BD patients made more inhibition errors on AS ($F(2,20) = 7.41$; $p < 0.02$) and PS ($F(2,20) = 4, 55$; $p < 0.05$).

Conclusion: Implicit processing of sadness versus happiness faces interferes with the ability of euthymic BD patients to manage saccadic control: sad faces are followed by more inhibition errors during AS and longer SRT for AS and PS. In accordance with Hummer et al. (2013), this result suggests an impaired inhibitory process of sad emotion in BD, whatever the degree of awareness of emotional stimuli (explicit, implicit and subliminal (Kim et al., 2011)).

Keywords: emotion, control, prosaccade, antisaccade, bipolar

Comparison of neurocognitive deficits in patients with schizophrenia, bipolar I disorder and their unaffected first-degree relatives

DH Kim, JW Kim, TH Koo, SH Won

Department of Psychiatry, Kyungpook National University Hospital, Daegu, Korea

Objectives: This study aimed to identify the differences and the profiles of cognitive deficits in euthymic bipolar patients, remitted schizophrenia patients and unaffected first-degree relatives of both patients group.

Methods: 31 remitted schizophrenia patients, 29 euthymic bipolar I patients, unaffected first-degree relatives of both probands (schizophrenia 26, bipolar I disorder 25) and 31 Health control group without psychiatric history were included in the study. Every group was matched on age, sex, years of education. Cognitive assessments were done using Digit Span Test, Continuous Performance Test, Rey Auditory & Visual Learning test, Complex Figure Test, Verbal Fluency Test, Wisconsin Card Sorting Test, Finger Tapping Test. The effect of subsyndromal symptomatology was controlled.

Results: Schizophrenia patients group showed a large, generalized cognitive deficits (language intelligence, working memory, verbal memory, visual memory, verbal fluency, cognitive flexibility) and the worst results among other groups. Some domains of cognitive function in bipolar I patients were also impaired (attention, working memory, verbal memory) and, to a lesser degree by schizophrenia patients. Both family groups showed significant worse than healthy controls in working memory. Schizophrenia relatives group also showed verbal fluency dysfunction. There were no differences between the two family groups.

Conclusion: Schizophrenia patients showed the most severe cognitive dysfunctions when compared to other groups. Bipolar I patients also showed some cognitive impairments but less severe than schizophrenia patients. Our study suggests that the deficit in working memory could be the common potential endophenotype marker of genetic vulnerability to Bipolar I disorder and Schizophrenia, and working memory and verbal fluency are also candidates for endophenotype marker of schizophrenia.

Keywords: bipolar disorder, drug utilization, lithium, antipsychotics, anticonvulsants

Mental rotation and working memory in euthymic patients with bipolar I disorder

JY Kim^a, SJ Lee^b, HS Ryu^b, V Ryu^c, SH Lee^d, HS Cho^e

^aDepartment of Psychiatry, Yonsei University College of Medicine, Seoul, Korea, ^bInstitute of Behavioral Science In Medicine, Yonsei University College of Medicine, Seoul, Korea, ^cInstitute of Behavioral Science in Medicine, Department of Psychiatry, Yonsei University College of Medicine, Konyang University College of Medicine, Seoul/Daejeon, Korea, ^dDepartment of Psychiatry, Bundang Medical Center CHA University, Seongnam, Korea, ^eDepartment of Psychiatry, Institute of Behavioral Science in Medicine, Yonsei University College of Medicine, Yonsei University College of Medicine, Seoul, Korea

Objectives: Some reports show that patients with bipolar disorder have trait-like impairment in working memory (WM) which may be affected by attentional deficit. Components of maintenance and manipulation of internal representation can occur in WM. Recently, impaired maintenance and spared manipulation of representation in WM was found in schizophrenia. We investigated characteristics of working memory performance in euthymic patients with bipolar I disorder.

Methods: Twenty euthymic patients and 23 normal subjects were recruited. To measure maintenance process and manipulation process of working memory, spatial delayed response task (DRT) and two mental rotation tasks were used.

Results: There was no difference in accuracy rate on spatial DRT for maintenance process between bipolar disorder group and normal control group. When accuracy rate and reaction time on mental rotation tasks for manipulation process were compared, no statistically significant difference was found but a trend toward lower accuracy rate in euthymic patients than healthy controls.

Conclusion: These preliminary results suggest that both maintenance and manipulation of representations in WM might be spared in bipolar disorder. The process of WM in bipolar disorder might be different from schizophrenia.

Keywords: working memory, mental rotation, manipulation, maintenance, bipolar disorder

Perceptual-organizational characteristics of the rorschach task in patients with bipolar mania with or without psychotic features: comparison to schizophrenia patients

SH Kim^a, E Lee^b, SJ Lee^c, HS Ryu^c, RY Ha^a, HS Cho^b

^aDepartment of Psychiatry, Yonsei University College of Medicine, Seoul, Korea, ^bDepartment of Psychiatry, Yonsei University College of Medicine, Institute of Behavioral Science in Medicine Yonsei, Seoul, Korea, ^cDepartment of Psychiatry, Institute of Behavioral Science in Medicine Yonsei, Seoul, Korea

Objectives: Recent reports have consistently demonstrated Rorschach-related perceptual-organizational deficits in patients with schizophrenia, but little is known about manic patients with bipolar disorder. We investigated the perceptual-organization characteristics of the Rorschach task in patients with bipolar mania with or without psychotic features in comparison to schizophrenia.

Methods: The Rorschach task and Korean-Wechsler Adult Intelligence Scale (K-WAIS) were performed to measure perceptual-organization capacities with 46 inpatients with bipolar mania (psychotic: 27, nonpsychotic: 19) and 25 inpatients with schizophrenia.

Results: When compared among the three groups, patients with schizophrenia produced significantly more uncommon detail (Dd) responses than patients with bipolar mania with or without psychotic features ($F = 5.051$, $p < 0.01$). But most of variables were not significantly different in performance of the Rorschach task (ideation, cognitive mediation, information processing) and visuospatial organization cognitive tests (K-WAIS: picture completion, picture arrangement, and block design). In patients with bipolar mania, the significant correlation of the some Rorschach variables (Conventional Form: X+%, Active Human Movement: Ma, Processing Efficiency: Zf, Synthesized Developmental quality: DQ) with visuospatial organization tests performance was found.

Conclusion: We didn't find the perceptual-organizational characteristic differences between bipolar mania and schizophrenia, regardless of presence of psychotic features. These results suggest that even if nonpsychotic bipolar mania has similar perceptual-organization characteristics like psychotic bipolar mania and schizophrenia, but further investigation will be needed.

Keywords: perceptual-organization, bipolar mania, rorschach, schizophrenia

Autobiographical memory and its association with neuropsychological function in bipolar disorder

WJ Kim^a, RY Ha^a, JY Sun^a, V Ryu^b, SJ Lee^c, K Ha^d, SJ Kim^a, HS Cho^a

^aPsychiatry, Yonsei University College of Medicine, Seoul, Korea,

^bPsychiatry, Konyang University College of Medicine, Daejeon,

Korea, ^cInstitute of Behavioral Science in Medicine, Yonsei University College of Medicine, Seoul, Korea

^dPsychiatry, Seoul National University Bundang Hospital, Gyeonggi-do, Korea

Aims: The aim of this study was to investigate the overgeneralization of autobiographical memory (AM) in bipolar disorder (BD) and assess its association with multiple cognitive domains.

Methods: Twenty-eight clinically stable bipolar I patients and an equal number of age- and gender-matched healthy controls (HC) were included. All participants were examined using the autobiographical memory test (AMT) and the neuropsychological battery including the general intelligence, attention, verbal memory, verbal fluency, visual memory, and executive functions domain. Demographic, clinical, and test variables were compared between BD and HC groups. Correlation analyses of AMT scores with cognitive functions were performed within each group, controlling for demographic and clinical variables.

Results: Total and negative scores of AMT were significantly lower in BD patients compared to HC individuals. AMT scores were significantly correlated with WAIS similarities, WCST perseverative errors, and WCST categories completed in BD, whereas AMT scores were correlated with verbal memory and verbal fluency in HC.

Conclusions: Our findings suggest that overgeneral AM is a characteristic of BD and is related to executive function. Future studies should investigate the benefit of additional treatment focusing on overgeneral AM in BD.

Keywords: autobiographical memory, neuropsychological test, bipolar disorder

Bipolar disorder and leadership

S Kyaga, P Lichtenstein, M Boman, M Landén

Department for Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden

Objective: It has been suggested that several historical leaders were afflicted with bipolar disorder, and that their families spawned several prominent leaders. This study aims to investigate if persons with bipolar disorder and their siblings have leadership traits and are overrepresented in executive professions.

Method: We performed a nested case-control study based on longitudinal Swedish total population registries. Patients were identified through the National Patient Register providing discharge diagnoses for all inpatient treatment episodes in Sweden 1973–2009, and partial coverage of outpatient treatment episodes in 2001–2009. Data from a semi-structured interview of *officer suitability* ($n = 1,126,519$) and *IQ* ($n = 1,875,261$) was derived from the Swedish Military Service Conscription Register. National censuses and a longitudinal database on labor market studies provided information on professions in the complete Swedish population. Bipolar patients ($n = 68,915$) and their healthy siblings were compared to matched controls.

Results: Patients with bipolar disorder without comorbidity (*pure* bipolar disorder; $n = 22,980$) were overrepresented in both the highest and lowest strata of officer suitability ratings (OR_{highest} 1.46, 95% CI 1.02–2.08; OR_{lowest} 1.56, 95% CI 1.02–2.36). Similar but less pronounced estimates were found in their healthy siblings. Patients with pure bipolar disorder were underrepresented in executive professions, whereas their siblings were overrepresented in these professions (OR 1.08, 95% CI 1.02–1.15). This overrepresent-

ation was particularly pronounced in the subgroup of political professions (OR 1.85, 95% CI 1.25–2.75).

Conclusions: The results of this study support that bipolar disorder and associated traits are linked to superior leadership qualities.

Relations of executive cognitive functions with rorschach variables in patients with bipolar mania

CW Lee^a, SJ Lee^b, HS Ryu^b, RY Ha^b, JI Kang^a, KS Ha^c, HS Cho^a

^aDepartment of Psychiatry, Yonsei University College of Medicine,

Seoul, Korea, ^bInstitute of Behavioral Science in Medicine, Yonsei

University College of Medicine, Seoul, Korea, ^cDepartment of

Psychiatry, College of Medicine Seoul National University, Seoul, Korea

The Rorschach is the commonly used personality and symptom assessment in clinical practices including schizophrenia or bipolar disorder. We investigated the association between the executive functions probably required to respond to the Rorschach task and mania-related Rorschach variables in patients with bipolar mania. The Rorschach task as well as some subtests of Korean–Wechsler Adult Intelligence Scale (K-WAIS), Trail making test (TMT), Stroop test, and Controlled Oral Word Association Test (COWAT) were performed in 58 inpatients with bipolar mania. There were significant correlations between organizational activities (Zf) and TMT-A and between thought disorder (Wsum6, Sum6) and TMT-B. Semantic fluency of COWAT and “block design” of K-WAIS showed a significant correlation with affective cluster variables (FC, Afr) probably related to emotional regulation. However, Stroop test and the “reasoning” subtest of K-WAIS did not show any significant correlation with the Rorschach variables. Despite some limitations, these findings suggest that cognitive flexibility, verbal fluency and visuo-perceptual organization among executive functions may be differentially associated with cognitive processing or affective regulation-related Rorschach variables in bipolar mania. So this re-sult may support the potential use of the Rorschach in the study of emotion-cognition characteristics in bipolar disorder.

Keywords: bipolar mania, executive function, rorschach

Mental imagery and its relations with clinical characteristics in euthymic patients with bipolar I disorder

DH Oh^a, JH Seok^a, KH Huh^a, SJ Lee^b, HS Ryu^b, HS Cho^c

^aDepartment of Psychiatry, Yonsei University College of Medicine,

Seoul, Korea, ^bInstitute of Behavioral Science in Medicine, Yonsei

University College of Medicine, Seoul, Korea, ^cDepartment of

Psychiatry, Institute of Behavioral Science in Medicine, Yonsei University College of Medicine, Seoul, Korea

Objects: Mental imagery is the experience of accessing perceptual information from memory or cues. Recent studies found out that vivid mental imagery appeared to be present in acute depressive and manic phase of bipolar disorder. Elevated imagery may contribute to the emotional instability by acting as an emotional amplifier. We assessed general imagery use and vividness of mental imagery in euthymic patients with bipolar disorder compared to healthy controls and investigated the relationship with clinical characteristics including psychotic features.

Method: Forty four euthymic bipolar patients and 50 healthy controls were asked to complete Spontaneous Use of Imagery Scale (SUIS) and Visual Vividness of Imagery Questionnaire (VVIQ) to evaluate general imagery and vividness of mental imagery. Participants also completed emotion regulation questionnaire, difficulties in emotion regulation scale, and rumination response scale.

Results: We found no statically-significant differences in SUIS and VVIQ score between euthymic bipolar patients and healthy con-

trols. Patients with no history of psychotic features tended to have lower scores of VVIQ and SUIIS than healthy controls. No correlations between mental imagery scores and emotional regulation characteristics were found.

Conclusion: Our preliminary results show no difference in degree of imagery use and vividness of mental imagery between euthymic bipolar patients and comparison group. But history of psychosis might be related to characteristics of mental imagery, and further analysis and study will be needed to explain its clinical meaning.

Keywords: mental imagery bipolar disorder, psychosis

Working memory capacity and emotional regulation in euthymic patients with bipolar I disorder

HS Cho^a, DH Oh^b, TY Kim^b, SJ Kim^c, RY Ha^b, SJ Lee^d, HS Ryu^d

^aDepartment of Psychiatry, Institute of Behavioral Science in Medicine, Yonsei University College of Medicine, Seoul, Korea,

^bDepartment of Psychiatry, Yonsei University College of Medicine, Seoul, Korea, ^cDepartment of Psychiatry, College of Medicine Konyang University, Daejeon, Korea, ^dInstitute of Behavioral Science in Medicine, Yonsei University College of Medicine, Seoul, Korea

Objects: Working memory is the system that actively holds multiple pieces of transitory information in the mind, where they can be manipulated. It has been suggested that people who had higher working memory capacity suppressed expression of negative emotion and positive emotion better than people lower in working memory capacity. In this study we assessed working memory capacity in euthymic bipolar patients and divided patients into higher versus lower capacity group. We hypothesized that patients with lower working memory capacity had poorer self-regulation of emotional expression and worse clinical features.

Method: Forty three euthymic bipolar I patients and 49 healthy persons were enrolled. All participants conducted operation span task (OSPAN task) for an assessment of their working memory capacity. In task, subjects were asked to perform a simple mathematical verification and then read a word, with a recall test following some number of those read pairs. To evaluate a self-regulation of emotional experience, participants were required to complete Emotion Regulation Questionnaire (ERQ) and Difficulties in Emotion Regulation Scale (DERS).

Results: Euthymic bipolar patients had significantly lower score of OSPAN task than healthy controls. When dividing patients into higher versus lower score group by OSPAN task score and comparing two groups, we found no significant differences in total score of ERQ and DERS between two groups except some sub-items.

Conclusion: These preliminary results suggest that, despite lower working memory capacity, its capacity may not influence emotional self-regulation in bipolar patients.

Implicit self-esteem in bipolar manic and euthymic patients

JY Park^a, V Ryu^b, RY Ha^c, SJ Lee^d, WJ Choi^e, K Ha^f, HS Cho^a

^aDepartment of Psychiatry, Yonsei University College of Medicine, Seoul, Korea, ^bDepartment of Psychiatry, Konyang University College of Medicine, Daejeon, Korea, ^cDepartment of Psychiatry, Seoul Bukbu Hospital, Daejeon, Korea, ^dInstitute of Behavioral Science in Medicine, Yonsei University College of Medicine, Seoul, Korea, ^eDepartment of Psychiatry, National Health Insurance Service Ilsan Hospital, Goyang, Korea, ^fDepartment of Psychiatry, Seoul National University Bundang Hospital, Seongnam, Korea

Despite the fact that self-esteem is considered to be an important psychological element in bipolar disorder, not much is known

about implicit and explicit self-esteem in manic patients. The present study investigated, using the Implicit Association Test (IAT), differences in implicit and explicit self-esteem among bipolar manic patients, bipolar euthymic patients, and healthy controls.

Methods: Total 19 manic patients, 27 euthymic patients, and 27 healthy controls participated. Participants filled out a self-esteem scale to evaluate explicit self-esteem and carried out the self-esteem IAT to evaluate implicit self-esteem.

Results: No differences were found in explicit self-esteem among groups. Implicit self-esteem, however, showed significant differences among groups. Manic patients showed higher IAT scores compared to euthymic patients and a tendency towards higher IAT scores compared to healthy controls.

Conclusions: Current findings indicate that, on the latent level, a manic state is not merely the opposite of a depressed state. Moreover, a discontinuity of implicit self-esteem may exist between manic and euthymic states. These unexpected findings may be due to characteristics of the study subjects or the methods employed to evaluate implicit self-esteem. Nonetheless, they add significant insights on the psychological status of manic patients.

Theory of mind performance using a story comprehension task in bipolar mania compared to schizophrenia and healthy controls

S Russell, TVan Rheenen

Brain and Psychological Sciences Research Centre, Swinburne University, Melbourne, Australia

Introduction: Theory of mind (ToM) refers to the ability to understand the mental state of self and others. It describes an important aspect of human nature that facilitates appropriate social interactions and permits the experience of empathy; the recognition, and to some extent, sharing of feelings that are being experienced by another person. ToM deficits are well documented in schizophrenia. Yet, there is limited research into this topic in bipolar disorder (BD), with no previous study examining ToM in a BD group within a psychotic manic phase.

Methods: Twenty eight psychotic manic BD patients were compared with 30 schizophrenia (SCZ) patients and 29 healthy controls (HC). Participants performed a ToM story comprehension task that compared ToM stories and non-ToM stories (which we re-labelled non-ToM “semantic” stories). Performance was examined by answering comprehension questions.

Results: Both patient groups were equally impaired on their scores for ToM stories (scores BD = 10/24, SCZ = 9/24, HC = 14/24, $p < 0.001$). Interestingly, both patient groups showed reduced performance on non-ToM semantic stories (scores BD = 12/24, SCZ = 9/24, HC = 15/24, $p < 0.001$); SCZ showed a larger deficit. Reduced ToM performance was correlated with delusion severity in the BD group only.

Conclusions: ToM performance was impaired in BD patients experiencing psychotic symptoms. This result is consistent with previous work which has suggested ToM deficits in euthymic and depressed BD patients. Patient performance was also impaired on the control condition (i.e., non-ToM semantic stories) supporting an additional deficit in semantic processing. This result has important implications for studies utilizing the story comprehension task, with tasks that do not have a control “semantic” element recommended. In addition, future research will need to establish whether these findings generalize to other measures of ToM.

Semantic processing deficits in bipolar mania: a potential explanation for flight of ideas

S Russell

Brain and Psychological Sciences Research Centre, Swinburne University, Melbourne, Australia

Background: Patients with mania typically show flight of ideas and loosening of associations. This study examined whether such mania symptoms may be partially explained by semantic processing deficits. Semantic processing referring to our general knowledge and understanding of word meanings and word associations.

Method: 28 patients with bipolar mania (BM), 32 patients with schizophrenia (SZ) and 32 age and education matched healthy controls (HC) performed nine semantic processing tasks that examined word meaning definition, category fluency, homophone meaning generation, semantic priming, synonym recognition, recognition of word associations, word categorisation and story knowledge.

Results: In comparison to HC participants, BM patients had difficulty performing tasks that required accurate usage or identification of associations, for example synonym recognition and recognition of word associations. They additionally demonstrated hyperpriming on a semantic priming task, under controlled, but not automatic processing conditions. Other semantic skills, for example, language production and generation were intact. SZ patients demonstrated deficits on all the semantic tasks.

Limitations: The three groups were not matched for IQ or gender, thus these variables were used as covariates in the analyses.

Conclusions: Patients with BM demonstrate specific problems with semantic associations and do not have a global semantic processing deficit. When engaged in semantic processing patients with mania showed intrusion errors for associated information. We speculate that these findings are the result of controlled or strategic accelerated activation of all items in a semantic network for any particular preposition, which causes difficulties with online associative processing, frequent intrusions, and flight of ideas, clinically. In contrast, thought disorder in SZ is related to a global semantic memory deficit. Thus, this study demonstrates for the first time that thought disorder in BM and SZ is driven by different semantic processing mechanisms.

Neurocognitive impairments in euthymic patients with bipolar disorder

S Shimano^a, T Miura^a, T Onitsuka^a, Y Kaneda^b, I Sora^c, S Kanba^a

^aPsychiatry, Kyushu University, Fukuoka, Japan, ^bPsychiatry, Iwaki Clinic, Anan, Japan, ^cPsychiatry, Kobe University Graduate School of Medicine, Kobe, Japan

Objective: Recently, there are evidences of stable cognitive deficits in bipolar disorder patients as well as schizophrenia patients. However, in euthymic patients, the neurocognitive impairments have received less attention. In the present study, we investigated the neurocognitive functioning in euthymic patients with bipolar disorder in comparison with healthy subjects using the MATRICS Consensus Cognitive Battery (MCCB).

Methods: 12 (8 males, 4 females) patients with bipolar disorder and 31 healthy subjects (17 males, 24 females) participated in this study. All the patients were in euthymic state confirmed by Hamilton Depression Rating Scale (≤ 7) and Young Mania Rating Scale (≤ 8). The Mann–Whitney U test was used to assess the group differences in MCCB subtest.

Results: The score of bipolar patients showed significantly reduction in the test of Trail Making Test-Part A score ($p = 0.03 < p = 0.003$, uncorrected>>), Brief Assessment of Cognition in Schizophrenia-Symbol Coding ($p = 0.03 < p = 0.003$, uncorrected>>) and Continuous Performance Task ($p = 0.01 < p = 0.001$, uncorrected>>) compared to healthy subjects.

Conclusion: We detected some poorer performance on MCCB subtest in patients with bipolar disorder even in euthymic phases. However, the sample size in this study is modest. So, we are reporting this with larger samples on the day.

Multimodal emotion integration in bipolar disorder: an investigation of involuntary cross-modal influences between facial and prosodic channels

T Van Rheenen, SL Russell

Brain and Psychological Sciences Research Centre, Swinburne University, Melbourne, Australia

Objectives: The ability to integrate information from different sensory channels is a vital process that serves to compensate for conflicts in cross-modal sensation and facilitate perceptual decoding in times of unimodal ambiguity. As much of human perception occurs in social contexts that are largely characterized by the non-verbal expression of emotion, the study of cross-modal influences between facial and prosodic sensory sources of emotional information is important. Despite its relevance to psychosocial functioning however, multimodal integration of emotional information across facial and prosodic modes has not been comprehensively addressed in bipolar disorder (BD). In light of this paucity of research we investigated multimodal processing in a BD cohort using a focused attention paradigm.

Methods: 50 BD patients and 52 healthy controls completed a task designed to assess the cross-modal influence of emotional prosody on facial emotion recognition across congruent and incongruent facial and prosodic conditions, where attention was directed to the facial channel.

Results: There were no differences in multi-modal integration between groups at the level of accuracy, but differences were evident at the level of response time; emotional prosody biased facial recognition latencies in the control group only, where a fourfold increase in response times was evident between congruent and incongruent conditions relative to patients.

Conclusions: The results of this study indicate that the automatic process of integrating multimodal information from facial and prosodic sensory channels is delayed in BD. Given that interpersonal communication occurs in real time, these results have implications for social functioning in the disorder. Further research is needed to determine whether these results hold in other BD cohorts, or using alternative multimodal tasks.

Impulsivity and risk taking behaviour linking bipolar disorder and epilepsy

R Verma^a, KS Anand^b, KES Unni^c

^aDepartment of Psychiatry, Lady Hardinge Medical College and Associated Hospitals, Delhi, India, ^bDepartment of Neurology, Post Graduate Institute of Medical Education and Research, Dr. Ram Manohar Lohia Hospital, Delhi, India, ^cDepartment of Neurology, Lady Hardinge Medical College and Associated Hospitals, Delhi, India

Introduction: Risk taking behaviour has been frequently associated with impulsivity in bipolar disorder patients. These may be representative of behavioural manifestations of same underlying neurobiological process. Epilepsy shares many similarities with bipolar disorders and has been postulated to have a common underlying pathophysiology.

Aims and objectives: The current study evaluates and compares the parameters of impulsivity and risk taking behaviour among euthymic subjects with bipolar disorder, subjects with epilepsy and healthy control subjects. The study also aims to identify the predictors of association between impulsivity, violence and risk taking

behaviour among the bipolar remitted patients and epileptic patients.

Methodology: This cross-sectional study done at two tertiary care centres of North India included a consecutive sample of consenting subjects fulfilling the inclusion and exclusion criteria in three groups comprising of bipolar disorder ($n = 32$), epilepsy ($n = 30$) and healthy controls ($n = 32$) respectively. Subjects were assessed for socio-demographic-clinical information, impulsivity and risk taking behaviour on a semi-structured performa, Barratt Impulsivity Scale (BIS-11) and Balloon Analogue Risk Task (BART) respectively. Analysis was done utilizing SPSS ver 17.0.

Results: Bipolar group subjects had a higher mean score of adjusted average pump count (AAVP) than epilepsy group and healthy control subjects ($p = 0.01$ and $p = 0.02$ respectively). Epilepsy group subjects had lower scores than controls for AAVP but only for the last 10 balloons ($p < 0.01$). While bipolar group had comparable total scores of BIS-11 to epilepsy and control groups, epilepsy group had higher scores than healthy controls ($p = 0.04$). History of violence was positively correlated to history of harm to others ($r = 0.71$; $p < 0.01$), history of psychotic symptoms ($r = 0.41$; $p < 0.05$) and cognitive complexity subscale of BIS-11 ($r = 0.38$; $p < 0.05$). A positive correlation between history of self harm and impulsivity (self control and generalized) was observed.

Conclusion: There is a similar presence of trait impulsivity in bipolar disorder and epilepsy patients more than the healthy population. Behavioural impulsivity is found more in epilepsy than bipolar disorder while risk taking behaviour is more in latter than former. Further studies of impulsivity should be conducted across mood states in bipolar disorder comparing with epilepsy employing neuro-imaging data in collaboration with neuropsychological tests.

Evidence for cognitive subgroups in bipolar disorder and the influence of subclinical depression

J Volkert, J Kopf, J Kazmaier, F Glaser, S Kittel-Schneider, A Reif

Psychiatry, University of Würzburg, Würzburg, Germany

Introduction: Recent research in bipolar disorder points at the relevance and persistence of cognitive deficits in bipolar patients (BPD) even beyond acute episodes of depression or mania. Impairments were found in about 60% of BPD (Bora et al., 2010) and affect attention, processing speed, (long-term/working) memory and executive functioning (Mann-Wrobel et al. 2011). Up to now, the mechanisms, why some BPD do not reach their former level of cognitive performance and psychosocial functioning, while others are remitted completely, is not understood.

Method: In this study we aimed to identify a "deficit versus nondeficit subgroup" within BPD. For this purpose, we investigated the association between demographic and disease specific variables and the cognitive performance of BPD. The test performance of 50 acutely depressed inpatients and 70 remitted (euthymic) outpatients (Bipolar-Type I and II) was compared to 70 healthy controls (HC). Participants performed a neuropsychological test battery, which included the domains Alertness, Divided Attention, Flexibility, Working Memory, Stroop-Test, Tower of London, Word fluency and Long/ Short Term Verbal Learning Task.

Results: As expected acutely ill BPD showed a characteristic psychomotor slowing compared to remitted BPD and HCs. Our sample of euthymic BPD performed significantly worse than HCs in three of eight cognitive domains, namely Planning, Cognitive Flexibility and Divided Attention. In line with previous findings, more than a half of the euthymic BPD did not have any neuropsychological deficits. We found no significant correlations between test performance and clinical variables. But interestingly, we revealed significant associations between subthreshold depressive symptom-

atology (measured by depression rating scales) and psychomotor slowing, impaired long term and working memory.

Conclusion: In sum, these results suggest the presence of cognitive subgroups in bipolar disorder. However, we found no evidence of underlying etiologies: Clinical characteristics seem to have no influence on the development of cognitive deficits. However, our results indicate that cognitive deficits found in euthymic BPD could result from a subdepressive syndrome and not per se by disease characteristics.

May a severe course of illness contribute to cognitive impairment in bipolar disorder?

M Vrabie^a, V Marinescu^a, A Talasman^a, I Micluti^a

^a7 Ward, Clinical Hospital of Psychiatry "Al. Obregia", Bucharest, Romania, ^bSecond Psychiatric Clinic, Emergency County Hospital Cluj-Napoca, Cluj-Napoca, Romania

Background: Patients with bipolar disorder often suffer from debilitating cognitive deficits which are more likely to be present in patients who have a more severe course of illness.

Objective: The objective of this study is identifying and assessing the relationship between cognitive impairment and severe course of illness in bipolar disorder.

Method: We examined 75 bipolar (depressive, manic/hipomanic, euthymic) patients (according to DSMIVTR). The cognitive battery included standardized test of IQ, executive functioning, working memory, attention, visual and verbal memory. Demographic data (gender, age, years of education, socioeconomic status and current employment) were systematically obtained. Data about psychiatric history, past and current treatment, psychosis history, illness duration, age of onset and family history were collected. We analyzed statistically these data and assessed the relationships between cognitive deficits and severe course of illness in bipolar patients.

Results: Cognitive deficits are more frequent in bipolar patients with more severe course of illness, as indicated by: longer durations of mood disturbance (negatively correlated with executive function, psychomotor speed, attention, concentration and verbal memory-associated with a higher number of past manic episodes too), younger age at onset, history of multiple and frequent episodes (with manic episodes impacting neuropsychological impairment most extensively; attention and executive function deteriorated by the recurrence of episodes) and higher number of hospitalization (negatively correlated with visual and verbal memory, verbal fluency, spatial memory, psychomotor speed and executive function). Other risk factors are: pharmacological treatments, individual response, familial risk factors (positive family history for mood disorders negatively influences cognition), rapid cycling and seasonality, too. There's as well a specific relationship between executive functioning and admission for mania and between cognitive performance on several tasks and admission for depressive episodes. Females performed better on tests for verbal memory. Besides depressive and manic symptoms, anxiety and psychosis history negatively influence cognition too.

Conclusion: A severe course of illness may contribute to cognitive impairment in bipolar disorder but there's a growing need for further clarification regarding the magnitude, clinical relevance and confounding variables of cognitive deficits in bipolar individuals.

Keywords: neurocognitive, bipolar, manic

Valuable intervention against the excess mortality of psychiatric patients

J Aagaard^a, F Nissen^a, A Wernlund^a, L Foldager^b, L Merinder^b

^aDepartement Q Anxiety and Depression, Aarhus University Hospital, Risskov, Denmark, ^bDepartement M, Aarhus University Hospital, Risskov, Denmark

Introduction: Psychiatric patients and especially SMI have an excess mortality compared with the population, and have an increasing standardized mortality rate (SMR). Studies have identified possible areas of intervention such as: Unhealthy lifestyles, metabolic syndrome, and insufficient treatment of somatic disorders.

Methods: Historical prospective record linkage. Five 3 year cohorts of patients age 20–80 with at least one contact to the PER, AUH, Risskov during 1995 (n = 1,100) to 2007 (n = 2,525) were followed-up.

Results: Average age of death was about 50 years. The cohorts' diagnostic composition was changed from 1995 to 2007 with a significant decrease in the proportion of Schizophrenia and Bipolar disease and a significant increase in the proportion of Anxiety and Personality Disorders as well as Forensic arrangements. The proportion of patients with Substance use was unchanged. The overall SMR was about five. Patients with Substance use (as primary or secondary diagnosis) had about 2.5 times higher SMR than patients without. Among Schizophrenic patients with Substance use SMR was dramatically increased. Substance use was the dominant predictor of premature death with an increasing importance throughout the period.

Perspectives: The mortality of psychiatric patients with Substance use is dramatically high. In order to increase the life-expectancy of psychiatric patients a special focus on patients with Substance use is obligate. An improvement of systematic identification of Substance use and specialized treatment among psychiatric patients visiting Psychiatric Emergency Room (PER) is needed.

Keywords: substance use disorder, mortality, epidemiological study

Prevalence of substance use disorder in Thai patients with bipolar disorders

S Arunpongpaial, S Maneeganondh, N Jarassaeang, V Pimpanit, K Boontooch

Psychiatry, Khon Kaen University, Khon Kaen, Thailand

Background: People with bipolar disorder (BD) are 11 times more likely to abuse alcohol or substances than the general population; such that 30% to 60% of those with BD struggle with alcoholism and/or substance abuse. The prevalence of comorbid substance use disorder in BD in Thailand has not been documented.

Objectives: To determine the prevalence of substance use disorder (SUD) in Thai patients with BDs.

Method: A cross-sectional descriptive study was conducted. Patients with BDs were recruited from the Outpatient Psychiatric Clinic at Srinagarind Hospital between September 1, 2012 and March 31, 2013. The subjects signed informed consent before joining the study. Each was interviewed using the Thai version of the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST-Thai) by well-trained psychiatric nurses in a special private room. Then subjects were examined by a senior psychiatrist to diagnose substance use disorder based on the DSM-IV. Descriptive statistics were used to analyze the data.

Results: The 50 BD patients were: mostly (84%) between 26 and 60 years of age; mostly females (60%); married (52%); undergraduates (60%) and 16% were unemployed. Lifetime prevalence of substance use was 80%; of which alcohol was the most common substance (70%). The point prevalence rate of substance abuse and dependence was 22% and 6%, respectively. The prevalence of tobacco abuse was higher than alcohol abuse (12% versus 8%);

tobacco dependence was 4% while there was no alcohol dependence. We did not encounter cocaine, hallucinogen, or inhalant usage. Only 4% of cases had ever injected substances.

Conclusion: The prevalence of SUD in Thai patients with BD was 28%. Alcohol was the most commonly used substance but only 8% abused it. Tobacco was the second most commonly used substance but with a higher rate of use disorder (16%). These results indicate ASSIST-Thai could serve as a useful screening test for substance use among patients with BD at outpatient clinics.

Keywords: prevalence, bipolar, substance use disorders, ASSIST

Effects of childhood trauma on clinical presentation and prognosis of bipolar disorders

S Cakir, R Tasdelen, I Ozyildirim

Psychiatry, Istanbul University, Istanbul Faculty of Medicine, Istanbul, Turkey

The evidence about neurobiological and genetic correlates of bipolar disorders (BPD) has been growing. However clinical presentation, prognosis and treatment response are still heterogeneous among the patients with BPD. Little is known for additive effects of other mediating factors like childhood trauma, comorbid psychiatric problems and their interactions. We aimed to evaluate clinical presentation, prognosis, treatment response, childhood trauma, comorbidity and the interactions of these variables in patients with BPD. 140 consecutive patients with BPD type I who have been followed up with the structured interviews and life charts in the same Mood Disorders clinic for at least 2 years. Patients were screened with Childhood Trauma Questionnaire (CTQ) and SCID-I for comorbid psychiatric diagnosis. The treatment responses were evaluated with the mirror design methods of life charts. Other clinical features were collected with the structured interviews of patients and their caregivers. In preliminary results of this study we found highly correlation of childhood trauma, comorbid anxiety disorders and poor treatment response. The other details will be presented at the congress.

A cross sectional study to estimate cardiovascular and metabolic risk factors in patients with bipolar disorder

S Damegunta, G Prasad Rao

Psychiatry, Asha Hospital, Hyderabad, India

Aims: There is increasing recognition of cardiovascular mortality and co-morbidity in bipolar disorder in the recent times. Framingham 10-risk of coronary heart disease (CHD) has been a widely studied estimate of cardiovascular risk in the general population and its reliability and validity has been accepted. A few studies have estimated the relative risk of developing CHD in bipolar disorders, in India, the cardiovascular risk assessment in bipolar disorder population has not been studied. In this study, a cross sectional data from a prospective study is being presented.

Methods: A total of 50 patients with bipolar disorder aged between 20 and 60 years fulfilling the inclusion and exclusion criteria were enrolled into this study. Demographic variables and clinical evaluations which included smoking history, medical and pharmacologic treatment history, physical examination, anthropometric measurements and clinical labs for metabolic profiles were assessed. Using the Framingham 10-year risk questionnaire, we calculated the risk for each patient, and then compared with that of normal healthy control group.

Results: The risk of developing a future cardiovascular event was 3.26% in bipolar disorder and 2.02% in controls. We identified that a higher age at onset of illness, waist hip circumference, total cholesterol and unemployment showed a strong positive correlation with future cardiovascular (CVD) risk, whereas administration of valproate, lithium for management of Bipolar disorder,

higher socio economic status and higher educational status, non smokers was associated negatively with the future CVD risk.

Conclusions: It appears that there is a significant association between Bipolar disorder and metabolic factors, CVD, socio demographic variables, and underscores the predictive ability of Framingham risk score in detecting CVD.

Keywords: bipolar disorder, framingham 10 year cardiovascular risk, metabolic risk factors.

MDQ score as a predictor of 6 month outcomes among patients with depression managed under collaborative care

R DeJesus^a, M Williams^b, K Angstman^c

^aInternal Medicine, Mayo Clinic, Rochester, NY, USA, ^bPsychiatry and Psychology, Mayo Clinic, Rochester, NY, USA, ^cFamily Medicine, Mayo Clinic, Rochester, NY, USA

The collaborative care model (CCM) has consistently been proven to be effective in achieving and sustaining treatment remission in patients with unipolar major depression (1). We implemented the model in our institution in March 2008. Eligible patients were adults 18 years and older with PHQ-9 score = ≥ 10 and with no diagnosis of bipolar disorder. Bipolar disorder has been associated with treatment resistant depression, even with CCM (2, 3). Upon enrollment, GAD-7, MDQ and AUDIT were also administered. This study aimed to identify 6 month predictors for persistent depressive symptoms defined as PHQ-9 score of 10 or greater and drop-outs. From March 2008 until August 2013, 3591 patients had been enrolled in CCM. Majority are female Caucasian with a mean PHQ-9 score of 15. Six month PHQ-9 scores were available for 3058 patients. Remission rate was greater than 55% (37% with intention to treat analysis) with a dropout rate of 28%. Twenty two percent of patients had persistent depressive symptoms. Presence of severe anxiety based on initial GAD-7 score and abnormal MDQ (positive response to question #1) were associated with a higher odd of dropping out of CCM although the latter was not a significant predictor (p value: 0.06). The odds of remission was however significantly decreased among those with abnormal MDQ (p value: 0.04) whereas the likelihood of persistent depressive symptoms was significantly increased among this group of patient (odds ratio: 1.9, CI of 1.39–2.67, p value: <0.001).

Conclusion: Abnormal baseline MDQ score is associated with negative 6 month treatment outcomes among patients with depression managed under CCM manifested by lower remission rate, presence of persistent depressive symptoms and increased dropout rate. Further evaluation may be warranted to help identify undiagnosed bipolar depression.

Keywords: collaborative, depression, MDQ, remission, predictor

Anxiety disorders comorbidity in bipolar patients in Turkey

N Dilbaz, A Darcin Enez

Neuropsychiatry Hospital Psychiatry Clinic, Üsküdar Üniversitesi, Istanbul, Turkey

Anxiety comorbidity appears to be highly prevalent and is associated with a negative impact on the patient and on the course of the illness. The presence of anxiety in bipolar patients is also associated with increased rates of suicide and substance abuse, and decreased quality of life. To assess the frequency and clinical features of comorbid anxiety disorders in adult patients with a diagnosis of Bipolar disorder (BP) 174 patients whose diagnoses were assessed by the Structured Clinical Interview for DSM-IV-TR-Patient Version were included into the study. In a population with bipolar patients 41.4 % had at least 1 lifetime anxiety disorder. 19% Panic disorder (PD) 12% without agoraphobia and 7% PD with agoraphobia, 8.6% social anxiety disorder, 5.2% obsessive-compulsive

disorder, 6.9% post-traumatic stress disorder and 25.8% Generalized Anxiety Disorder. The most common anxiety disorder was generalized anxiety disorder followed by panic disorder. Comorbidity with anxiety disorders was correlated with severity of bipolar illness as assessed by the number of hospitalizations, psychotic characteristics, misuse of alcohol and drugs, and suicide attempts (violent and nonviolent). Lifetime attempted suicide rate is 5.2%. Smoking and alcohol abuse is also high.

Bipolar affective disorder in suicide attempters admitted in tertiary care hospital sociodemographic profile and relationship characteristics a study from Kashmir, India

A Gania, A Khan, M Margoob

Department of Psychiatry, SKIMS Medical College, Srinagar, India

Bipolar affective disorder which one of the commonest psychiatric disorders with life time prevalence between 1% and 5% has high risk of suicide in particular. Around 10% of BPAD patients die by suicide and as many as 40% attempt suicide. Statistics from civil war zones/conflict zones has suggested increase in suicide rates in bipolar patients due to continued exposure to environmental stressors.

Aim: The present Study was aimed at studying the prevalence of bipolar affective disorder in suicide attempters. Assessment of Sociodemographic characteristics and risk factors in particular reference to present turmoil was done.

Material and methods: The Study was conducted on 300 suicide attempters admitted in the multispecialty Tertiary care hospital of the valley over the period of 2 years between 2010 and 2012. The patients were diagnosed by M.I.N.I plus.

Results: Total of 58% (n = 174) had psychiatric comorbidity and out of them 32.18% (n = 56) had BPAD as comorbid diagnosis. Majority of patients belonged to 18–38 year age group, lower and middle class, unmarried and Divorced, unemployed and significantly more than 17% attributed their suicidal attempt directly to persistent environmental stress due to turmoil.

Conclusions: Significant number of suicide attempters had bipolar affective disorder as diagnosis at the time of their suicide attempt. Keeping in view significant number had attributed their suicidal attempts to be precipitated by present turmoil, proper evaluation and management of patients with BPAD in civil war zone is needed to prevent suicidal attempts.

Nicotine dependence and bipolar disorders

L Gutiérrez-Rojas^a, JM Martínez-Ortega^a, GI Goldstein^b

^aPsychiatry, Facultad de Medicina Universidad de Granada, Granada, Spain, ^bPsychiatry, University of Toronto, Toronto, Canada

Bipolar disorder (BD) and nicotine dependence (ND) often co-occur. However, the mechanisms underlying this association remain unclear. We aimed to examine, for the first time in a national and representative sample, the magnitude and direction of the temporal relationship between BD and ND; and to compare, among individuals with lifetime ND and BD, the sociodemographic and clinical characteristics of individuals whose onset of ND preceded the onset of BD (ND-prior) with those whose onset of ND followed the onset of BD (BD-prior). The sample included individuals with lifetime BD type I or ND (n = 7958) from the National Epidemiologic Survey on Alcohol and Related Conditions (NES-ARC, n = 43093). Survival analyses and logistic regression models were computed to study the temporal association between ND and BD, and to compare ND-prior (n = 135) and BD-prior (n = 386) individuals. We found that ND predicted the onset of BD and BD also predicted the onset of ND. Furthermore, the risk of developing one disorder following the other one was greatest early in the

course of illness. Most individuals with lifetime ND and BD were BD-prior (72.6%). BD-prior individuals had an earlier onset of BD and a higher number of manic episodes. By contrast, ND-prior individuals had an earlier onset of both daily smoking and ND, and an increased prevalence of alcohol use disorder. In conclusion, ND and BD predict the development of each other. The phenomenology and course of ND and BD varied significantly depending on which disorder had earlier onset.

Keywords: nicotine dependence, bipolar disorder, age of onset, smoking and epidemiology

Comparison of clinical characteristics between panic disorder with and without comorbid bipolar disorder

K Kim, MK Kim, B Kim, SH Lee

Psychiatry, CHA Bundang Medical Center, Gyeonggi-do, Korea

Background and objectives: Subjects with panic disorder (PD) might have an elevated risk of bipolar disorder (BPD). This issue is critical not only for etiological studies but also for clinical practices. While the detection of comorbid BPD is critically important in the treatment of PD, it might often fail because it is difficult to accurately diagnose in clinical settings such as outpatient clinics or primary care facilities, especially for mild cases. However, studies of the clinical and psychological variables that might be related to the comorbidity of BPD in PD could help in its detection. This study aimed to investigate differences of demographic and clinical variables between PD patients with (PD + B) and without bipolar disorder (PD-B).

Methods: We examined data from 67 patients diagnosed with panic disorder and 73 healthy control subjects. We divided the patients with PD into bipolar group (19 patients) and non-bipolar group (48 patients) to compare demographic (age, gender, marriage, monthly income, religion, education, coping strategies) and clinical characteristics (Beck Anxiety Inventory (BAI), Beck Depression Inventory (BDI), Panic disorder severity (PDSS), Anxiety Sensitivity Index (ASI), Albany Panic and Phobia Questionnaire (APPQ), State-Trait Anxiety Inventory (STAI)). SPSS version 19.0 were used for statistical analysis.

Results: There were differences between PD + B group and PD – D group with respect to age, gender, marriage, coping strategies (Emotion, Distance, Acceptance, Reappraisal) and clinical characteristics (BAI, BDI, PDSS, ASI, APPQ, STAI). Compared to the PD – D, PD + B group is younger and has a higher rate of single women. According to clinical symptom severity such as BAI, BDI, PDSS, ASI, APPQ, STAI scores, PD + B group is higher than PD – D group.

Conclusions: Differences of clinical characteristics were associated with comorbid BPD in PD patients in this study. The current study suggests that PD + B patients is younger, have a higher single rate and female rate than PD – B patients. Moreover, PD + B group has more severe symptoms comparing with PD – B group.

Influence of bipolarity on problematic drinking in depressive patients

E Moon^a, JM Park^b, BD Lee^b, YM Lee^a, HJ Jeong^a, JJ Lee^a, Y Choi^a, YI Chung^b

^aDepartment of Psychiatry, Pusan National University Hospital, Busan, Korea, ^bDepartment of Psychiatry, Pusan National University College of Medicine, Busan, Korea

Introduction: Several studies have been supported that patients with bipolar disorders have high comorbidity of alcohol use disorder. However, there is lack of evidence that bipolarity in depressive disorders is associated with problematic drinking. We aimed to investigate whether bipolarity is associated with problematic drinking in depressive patients.

Methods: Seventy three patients with depressive disorders were included in this study. Bipolarity was measured by Mood Disorder Questionnaire (MDQ). Problematic drinking behavior was evaluated by Alcohol Use Disorder Identification Test (AUDIT). We compared the AUDIT score between the depressive disorder with bipolarity and without bipolarity using independent t-test and analysis of covariance (ANCOVA) to adjust the influence of age.

Results: Patients with depressive disorders who screened positive on MDQ showed higher AUDIT scores than those with negative MDQ scores.(independent t-test $t = -2.767$, $p = 0.007$) After controlling age, difference of AUDIT score was still significant between two groups.(ANCOVA $F = 7.380$, $p = 0.008$)

Conclusion: These results suggest that bipolarity may be associated with problematic drinking in depressive patients. Consideration of bipolarity may be necessary in the treatment of alcohol problem in depressive patients. Large-scale study would be needed to confirm these results.

Evolution to bipolar disorder from unipolar first depressive episode in a cohort of patients with substance use disorder comorbidity. A three year follow up prospective study

A Nieto

Salud Pública y Epidemiología, Universidad Autónoma de San Luis Potosí, San Luis Potosí, Mexico

In most cross-sectional studies, comorbid substance use disorder (SUD) was found to exist in 40 to 60% of patients with bipolar disorder. The phenomenological and treatment course of bipolar illness is significantly affected by comorbid SUD. Most of the samples included patients who primarily asked for psychiatric services. The main objective of this study was evaluate the clinical course of a group of patients with no diagnosis of any previous affective disorder, who primarily ask for SUD problems.

Methods: 161 (26% female) patients without any previous diagnosis look for attention in a community centre for SUD related problems. A MINI-Plus two interview was realized. All patient received standard treatment for SUD and psychiatric conditions. Patients was followed according to standard follow up procedure of the centre. After 3 year a new MINI-plus two interview was realized. Change of diagnosis status was reported here using DSM-IV criteria as primarily purpose.

Results: Of the 161 initial sample of patient with SUD related problems, 51 (31.6%) received a diagnosis of unipolar depressive episode. This 51 patients (16 female) constitute our initial cohort. The adherence rate for 12 and 28 week SUD-rehabilitation program of this subgroup was 45% and 0% respectively. This means that all subjects of the cohort was lost and then was asked for a new interview. 40 subjects (80% of the original cohort) was localized and 31 (60.7%) accept a new interview. Nine patients (29%) received a new bipolar diagnosis (one case for type 1 BD and eight for type). Also we reported the data when we modified the diagnostic criteria for hipomanía and when applied the new diagnostic DSM-5 criteria for depressive episode with mixed hipomanic symptoms.

Discussion: When using a DSM-IV approach (our original purpose), a third of patients with SUD and comorbid unipolar depressive episode change to bipolar diagnosis in a 3 year interval. It was a 10% of the original group of subjects with SUD related problems without any affective disorder previously identified. However, applying the DMS-5 criteria a most complex scenario appear, suggesting that SUD has a critical role in the destabilizing process of affective disorder.

Frequency of bipolar spectrum disorder among patients with substance related disorders

SM Samimi Ardestani^a, M Farahzadi^b, M Aminesmaeli^c,
S Sardarpour Gudarzi^d, M Froughi^e

^aPsychiatry, Imam Hossein HP Behavioral Science Research Center
Shahid Beheshti University of Medical Sciences, Tehran, Iran,

^bPsychiatry, Imam Hossein HP Shahid Beheshti University of
Medical Sciences, Tehran, Iran, ^cPsychiatry, Iranian Research
Center for HIV/AIDS Tehran University of Medical Sciences,
Tehran, Iran, ^dPsychiatry, Taleghani HP Shahid Beheshti
University of Medical Sciences, Tehran, Iran, ^ePsychiatry, Imam
Hossein HP Shahid Beheshti University of Medical Sciences,
Tehran, Iran

Introduction: Bipolar and substance related disorders are comorbid in many patients. This comorbidity has negative effects on prognosis of each disorder. Detection and effective treatment of bipolar disorder in patients who are substance abuser or dependent can reduce the substance craving. Majority of researches have been evaluated bipolar type I disorder and bipolar spectrum disorders have been neglected except in a few researches.

Materials and methods: In this study we assessed the frequency of bipolar spectrum in patients came to some of substance outpatients clinics in Tehran. For each patient who has not in the state of intoxication or withdrawal entered the survey. M.M.S.E was used to evaluate the state of consciousness of them and those had number less than 26 do not enter the survey. Bipolar spectrum disorders were assessed by using the MDQ.

Results: Totally 196 patients meet the criteria to enter the study. According to MDQ, 59 (30.1%) patients were diagnosed as bipolar disorder spectrum disorder. The frequency was significantly higher in the young and polysubstance users. In spite of these findings the rate of mood stabilizer prescription was low.

Discussion: This study showed that bipolar spectrum disorders have high frequency among substance abusers /dependents. It seems that bipolar disorder is neglected in patients who are consumers of substance related disorders. On the other hand missing bipolarity in them postpones an essential treatment and increase the possibility of inappropriate medications such as antidepressants.

Psychometric properties of the chinese version of the bipolar spectrum diagnostic scale

K Chou

Graduate Institute of Nursing, Taipei Medical University, Taipei, Taiwan

Aim and objectives: The aim of this study was to test the psychometric properties of the Chinese version of the Bipolar Spectrum Diagnostic Scale (C-BSDS) in a Chinese population to serve as an aid to clinical diagnosis of bipolar disorders.

Background: Bipolar spectrum disorders are often misdiagnosed because of the wide range of symptoms seen in patients. The consequences of delayed diagnoses or misdiagnoses can be devastating.

Design: A cross-sectional research design.

Method: Two hundred patients with affective disorders from a psychiatric outpatient clinic in Taiwan were enrolled. Internal consistency reliability and two week test-retest reliability were performed to evaluate the reliability of the C-BSDS. Expert content validity and factor analysis were used for testing construct validity. To evaluate sensitivity and specificity, the Chinese version of the Mini International Neuropsychiatric Interview (MINI) was used as the gold standard for diagnosis.

Results: The internal consistency coefficient measured by intraclass correlation (ICC) was 0.81, the test-retest reliability coefficient was 0.85, and the expert validity was 0.85. For construct validity, 'irritable and hyper-energetic factors' and 'depressed and lack of

energy factors' were extracted by factor analysis. These two factors reflected the structure of the original scale, and accounted for 33.27% of the variance. The optimal cut off was 12, which yielded a sensitivity of 74 and a specificity of 0.97 for detecting bipolar disorder, and for bipolar II disorder these were 0.79 and 0.68, respectively.

Conclusions: The C-BSDS showed good reliability and validity and the results were consistent with the English version of the BSDS. Therefore, the C-BSDS is an effective tool for evaluation of a Chinese population.

Relevance to clinical practice: The BSDS can further increase the detection rate of bipolar disorders, especially bipolar II disorder, with satisfactory sensitivity and specificity. It can effectively assist with clinical screening of patients for bipolar spectrum disorders.

Keywords: instrument development, mental health nursing, bipolar disorder, screening tools, factor analysis

Bipolarity in medical students at a private university in Lima-Peru

E Galli

Psychiatry, Universidad Peruana Cayetano Heredia, Lima, Peru

Introduction: For over 30 years we have been postulating a new conceptualization of depression and characterize it as a dimensional disease (mono and bipolar) (Galli, 1978, 1994. Lima.). We always had in mind the subvaloration bipolar type (Galli, 1996. Lima; Galli, 2004. Bogotá). With respect to the new concept and spectrum, its brain imaging correlate (Galli, 2005. Egypt) (Galli, 2005. Lima) and mainly to their prevalence (Galli, 2005. Lima) in which we bring up the work of Akiskal and Pinto (2003) where they found a prevalence of 6.2% in a prevalence study with ECA in USA. Depression increases its prevalence in medical students (Valko, 1975; Klaer, 1984, Martin 1986) and gives a fixed point prevalence of between 15% and 30%. We found in our work in 2000 in Lima, in 250 medical students a prevalence of 31%, but no cases of bipolar depression. We found only a 1.41% prevalence of bipolar disorder. To the works of Akiskal and Pinto with ECA (prevalence of 6.2% in the U.S. population) are added Angst works in Switzerland in 2010 (prevalence of 10% of the European population). Having expanded the diagnosis of bipolar disorder and bipolar spectrum and the gradual increase year after year in the patients in our private practice in the Department of Psychiatry at the Ricardo Palma Clinic and Patients from our Social Community Program for 4 months every year have led to us to repeat history with the students of the fifth year of medicine.

Objective: The aim of this work is very simple and consists of: 1. Corroborate the increase of bipolar depression in the world with our own reality. 2. Compare the results with the study in 2000, 2010 and 2012 with the same age group and the same year of studies. 3. Trying to explain it.

Material and methods: For the present study, 100 students of the fifth year of medicine were evaluated. We applied the modified MINI (2010, Lima) for mood disorders either dysthymia, major depression and bipolar depression and MDQ scale (bipolar spectrum).

Lifetime mood spectrum symptoms among bipolar patients and healthy controls

A Ghouse, M Sanches, Z Soares, JC Soares

Psychiatry, University of Texas Health Science Center-Houston, Houston, TX, USA

Background: The "spectrum" model has advantages for the conceptualization of mental disorders, representing a complementary approach to the currently available nosological systems. We carried out a study in order to assess lifetime mood symptoms among

patients with bipolar disorder (BD) and healthy controls from a dimensional perspective.

Methods: The Mood Spectrum Self-Report instrument (MOODS-SR) was administered to 101 bipolar patients (52 BD I, 32 BD II, and 17 BD NOS, 36 males/65 females, mean age + SD = 36.10 ± 13.34 years) and 38 healthy controls (16 males/22 females, mean age + SD = 35.18 ± 13.70 years). The scores of the different MOOD-SR scales and subscales among patients and controls were compared using non-parametric tests (Mann–Whitney and Kruskal–Wallis).

Results: Bipolar patients scored significantly higher than healthy controls on the total MOOD-SR scores (BD: mean ± SD = 98.65 ± 22.17; HC: mean ± SD = 12.92 ± 10.72; $p < 0.01$) and all subdomains. Multiple comparisons revealed lower scores among controls when compared to each one of the subtypes of BD, also regarding the total scores and all subdomains ($p < 0.01$). Comparisons across the different subtypes of BD revealed statistically significant higher scores among BD I patients when compared to BD II and BD NOS patients, only in regard to the total MOOD-SR scores (BD I: mean ± SD = 102.94 ± 22.79; BD II: mean ± SD = 93.53 ± 21.97; BD NOS: mean ± SD = 94.88 ± 18.68; $p = 0.03$ and two subdomains: mood mania and energy mania).

Conclusion: These results suggest that even though the MOODS-SR seems effective in distinguishing BD patients from HC, it is not as good in discriminating different subtypes of BD, especially in respect to lifetime depressive symptoms.

Keywords: bipolar disorder, mood disorder, diagnosis, mood spectrum

Relative frequency of unipolar mania among hospitalized patients with bipolar mood disorder and its associate features: a multicenter study in Iran

F Khodaeifar^a, SS Gudarzi^b, V Mahmoodi^c, A Ghaffarnejad^d, A Mirghiasi^e, M Javanbakht^f

^aDepartment of Psychiatry Psychosomatic Program, Behavioral Sciences Research Center Shahid Beheshti University of Medical Sciences, Tehran, Iran, ^bMelbourne Health, Melbourne VIC, Melbourne, Australia, ^cDepartment of Psychiatry, Behavioral Sciences Research Center Shahid Beheshti University of Medical Sciences, Tehran, Iran, ^dDepartment of Psychiatry, Kerman University of Medical Sciences, Kerman, Iran, ^eDepartment of Psychiatry, Modarres Hospital, Esfahan, Iran, ^fDepartment of Psychiatry, Mashhad Branch Islamic Azad University, Mashhad, Iran

Aims: Considering few studies made in the field of unipolar mania in the world, contradiction of current information, and lack of multi-center studies in this field in Iran, this study could be a manifest of preliminaries of this mood state and a starting point for more studies in this field in Iran. The aim of this study is to investigate the relative frequency of unipolar mania among inpatients with bipolar mood disorder in some mental health centers and to compare demographic and health variables among these patients as well as patients suffering from bipolar mania.

Methods: This multi-center retrospective-descriptive and comparative study was done in four university hospitals in three cities of Iran (Tehran, Mashhad and Kerman). Using available simple sampling method, we reviewed the files of patients suffering from bipolar mood disorder. All patients who were hospitalized during 2000 to 2010 in these centers with the diagnosis of bipolar mood disorder according to DSM-IV or DSM-IV-TR were entered into the study. Exclusion criteria were: duration of illness less than 10 years, diagnosis of schizoaffective disorder, substance induced mood disorder and mood disorder due to medical general condi-

tion. Main variables were the frequency of unipolar mania pattern among patients suffering from bipolar mood disorder, demographic, course and treatment variables which were compared between patients suffering from unipolar mania and patients suffering from bipolar mania. Average comparison of quantitative variables was made between the two groups using Man–Whitney test and comparison of qualitative variables was made between them using Chi-square test. Fischer test was used where necessary and the significant level of $p < 0/05$ was considered.

Results: Finally a number of 697 files were included. Frequency of unipolar mania among patients suffering from bipolar mood disorder was 15.7%. Number of mania attacks, total number of mood episodes, seasonal pattern, psychosis in the first mania attack, mood-congruent psychosis, and record of nicotine use between the two groups showed a significant difference ($p < 0/05$).

Conclusions: Unipolar mania is prevalent among hospitalized patients suffering from bipolar mood disorder in Iran and can be a distinct type of bipolar mood disorder. We recommend prospective studies in this field.

Keywords: unipolar mania, recurrent mania, bipolar disorder, Iran, frequency

The relationship between temperament and residual affective symptoms in clinically stable patients with bipolar disorders

D Lee, JS Jang, JY Kim, TH Ha, M Lim, K Ha

Psychiatry, Seoul National University Bundang Hospital, Seong-Nam Si Gyeonggi-do, Korea

Introduction: Patients with bipolar disorders often report residual symptoms although clinically stable. A growing body of evidence indicates the effects of affective temperament on residual affective symptoms. This study investigated the relationship between temperament and residual affective symptoms in clinically stable patients with bipolar disorders.

Methods: A total of 111 clinically stable outpatients with bipolar disorders (bipolar I, II, NOS) were included in this study. All the participants completed Temperament Evaluation of Memphis, Pisa, Paris, and San Diego (TEMPS-A) short form, Beck's Depression Inventory (BDI), Beck's Anxiety Inventory (BAI), Young Mania Rating Scale (YMRS). Types and frequencies of residual symptoms were analyzed in relation to a predominant temperament.

Results: Twenty one patients were classified into cyclothymic type (Cyc), 15 depressive type (Dep), 21 irritable type (Irr), 27 hyperthymic type (Hyp), and 27 anxious type (Anx). "Sadness", "Negative view for self and future", "Loss of pleasure and energy", "Insomnia" of BDI, "Irritability", "Restlessness", "Fear and Frightened" of BAI, "Irritability" of YMRS were significantly different (p)

Conclusion: Because the management of residual symptoms might be important in preventing relapses, distinct profiles of residual symptoms according to temperament type would be useful for individualized treatment of bipolar disorders.

Keywords: bipolar disorder, residual symptoms, temperament

Verification of usability of the hypomania checklist 32 (HCL-32) for the screening of bipolar disorder in non-clinical adult samples

K Lee^a, H Oh^b, EH Lee^a, JH Kim^a, JH Kim^a, KS Hong^a

^aDepartment of Psychiatry, Samsung Medical Center Sungkyunkwan University School of Medicine, Seoul, Korea, ^bSamsung Biomedical Research Institute, Samsung Medical Center, Seoul, Korea

Background: It is well known that accurate diagnosis of bipolar disorder (BD) is often delayed by many years after the onset of mood symptoms. The hypomania checklist-32 (HCL-32) is a widely used questionnaire developed for identifying hypomanic components in

patients with major depressive episodes. Measuring and screening previous hypomanic symptoms in individuals without any mood episode or general population would be also needed for early detection of BD. This study aimed at testing the usability of the HCL-32 for the screening of BD in non-clinical adult samples.

Methods: Lifetime history of hypomanic symptoms was evaluated using the HCL-32 in 220 patients with BD and 313 non-clinical samples. For measuring discriminatory power, sensitivity, specificity, and the area under the curve (AUC) of the Receiver Operating Characteristic (ROC) were computed. Same analyses were also applied to bipolar subgroups (bipolar I and bipolar II disorders) and two subdomain ("active/elated" and "irritable/risk-taking" factors) scores of HCL-32.

Results: The mean HCL-32 total score was significantly different between the patient and non-clinical groups (p)

Conclusion: The HCL-32 does not seem to be adequate enough to screen BD in non-clinical adult samples. Item selections toward more discriminating items or "irritable/risk-taking" factors might improve its usability especially for the screening of bipolar II disorder.

Clinical characteristics of patients with recurrent mania

S Lee, Y Joo, H Kim, S Park

Psychiatry, Asan Medical Center, Seoul, Korea

Introduction: If bipolar patients with recurrent manic episode only have different clinical characteristics and prognosis compared with whom with depressive episode, it will be meaningful to distinguish recurrent mania as different disease entity. Because psychiatric diagnostic system depends on clinical syndrome based classification. So there is no Korean data about this issue, that it will be valuable to study characteristics and prognosis of recurrent manic bipolar patients in Korea.

Method: This is retrospective chart review based study. Patient who visit Asan Medical Center (AMC) from 2010 to 2012 and diagnosed as bipolar affective disorder were enrolled. Recurrent manic patient should experience more than two admissions for manic episode. And control group should need more than one admission for depressive episode. We compared two groups for clinical variables.

Result: There is no statistical difference in illness-duration and follow-up-years between 38 pure mania patient group and control group. While there is no significant difference in age, sex and education-year, patients with recurrent manic episodes have full time job more and lower family history of mood disorder. Patients in both group experienced similar age of onset, but patients with pure mania had less frequency of episode, admission, longer inter-episodic periods and higher tendency of functional recovery. There's no difference in seasonality of episodes. Within episode, psychotic symptom didn't show significant difference, symptoms like increased sexual interest between two groups, increased consumption and grandiosity, psychomotor agitation emerged frequently in patient who experienced depressive episode.

Conclusion: Patients with recurrent mania have better disease course and outcome. And there are some manic symptoms that observed less frequently in these patients.

Keywords: bipolar affective disorder, recurrent mania, pure mania

A tale of two diatheses: temperament, BIS, and BAS as risk factors for mood disorder

A Van Meter^a, E Youngstrom^b

^aFerkauf Graduate School of Psychology, Albert Einstein College of Medicine, New York, NY, USA, ^bPsychology, University of North Carolina, Chapel Hill, NC, USA

Objective: Two major models of risk for mood disorder focus on affective temperament styles and sensitivity in the behavioral inhibition (BIS) and behavioral activation (BAS) systems. Tempera-

ment and BIS and BAS are important to biological models of mood, and may represent measurable risk that can be assessed regardless of culture or current mood state—two factors that can limit the utility of some diagnostic tools. Learning more about how these traits relate to mood pathology is consistent with the RDoC project goal of investigating mechanisms of risk. Given the potential overlap in temperament, BIS, and BAS, we investigated the association of each with depressed and elevated mood symptoms.

Method: American college students (n = 584), Korean college students (n = 128), and American young adults with depression (n = 23) or bipolar disorder (n = 23) completed a series of self-report questionnaires, including the TEMPS-A, the BIS/BAS Scales, Beck Depression Inventory (BDI), and Hypomanic Checklist (HCL). Linear regression quantified relations between mood symptoms, sample characteristics, temperament, and the BIS/BAS scales.

Results: In total, 49% of the variance in BDI scores was accounted for by the predictors, the majority of which (37%) was explained by the affective temperaments, 1% was uniquely contributed by BIS and BAS, and 9% was a shared contribution of BIS, BAS, and the affective temperaments. Twenty-one percent of the variance in HCL scores was accounted for by the predictors; 5% was uniquely explained by BAS, 7% was explained by the affective temperaments, and 5% was a shared contribution of BAS and affective temperament.

Discussion: Affective temperament and BIS/BAS are partially overlapping, but distinct constructs. Results suggest that some affective temperament styles, particularly cyclothymic temperament, may represent a stronger diathesis for mood pathology than BIS or BAS. Importantly, the diathesis represented by cyclothymic temperament, and associated biological traits, seems to exist irrespective of culture or diagnosis, indicating that assessing temperament may help overcome some of the current challenges of diagnosing mood disorders.

Bipolar affective disorder: constitutional-biological, clinical-dynamic and clinical-prognostic regularities

I Zrazhevskaya, A Israelyan

Psychiatry Narcology & Psychotherapy, Peoples' Friendship University of Russia, Moscow, Russia

Objective: To establish the clinical-prognostic regularities based on the study of constitutional-biological, clinical-psychopathological and clinical-dynamic characteristics of the Bipolar Disorder (BD).

Methods: Clinical (anamnesic, psychopathological, dynamic, catamnestic), statistical, selectively-paraclinical (including experimental-psychological survey, psychometric, pathopsychological; instrumental; laboratory, etc.).

Results: There were developed the new approaches to detection of BD in patients of specialized psychiatric hospital, based on a comprehensive analysis of clinical-biological factors and clinical-dynamic peculiarities of mental disturbances. There were revealed the modifying influence of certain nosological forms of mental and somatic pathology relatives of the patient (the first degree of kinship) on the formation of the type of the course of BD and progression. The dependence the age by the time of the beginning of BD from the presence of burden of heredity psychiatric or somatic pathology, nosologic form of this pathology, type of progressed of BD, gender and premorbid features personality was established. There were allocated the most characteristic and prognostically significant variants of the initial period and syndromal variants of first affective episode. The complexes of clinical-biological factors, which determine the formation of BD with presence or absence of rapid cycles, were scientifically proved and verified by statistical analysis. The dependence of the type of

progression of the course of BD from groups of interrelated indicators of clinical-biological and clinical-dynamic characteristics was revealed.

Conclusions: There was established, that BD is characterized with a complex of interconnected factors: (1) high frequency of burdening of heredity, which is, mainly, represent mental disorders relatives of patient, with the predominance of depressive disorders, alcohol dependence and anxiety disorders; (2) dominance emotionally unstable, mixed and anxiety variants of premorbid peculiarities of the personality; (3) anergic, addictive and affective variants of the initial period; (4) acute onset of the initial period; (5) prevailing syndromic versions of the first affective episode: adynamic depression and simple obsession; (6) predominance of progressive type of the course of BD; (7) an earlier age at the time of the beginning of BD, an earlier age and the greater of the duration of the disease at the time of clinical examination compared with other affective disorders.

Keywords: clinical, prognostic characteristics of bipolar disorder

Qualitative study on characteristics of bipolar disorder and depression in Japan

K Koganei, H Fujiu

Human Sciences Division of Psychology, University of Tsukuba, Tokyo, Japan

Aims: Given the high rate of suicide and the complexed characteristics of bipolar disorder, awareness of these characteristics is critical for clinical therapists. In addition, recent studies have demonstrated depression to be a major feature of bipolar spectrum. Despite these report, clinical research on bipolar and its relation to depression has been limited in Japan. The present preliminary study examined the cognitive and behavioral characteristics of bipolar and depression in Japan.

Methods: Eleven Japanese certified clinical psychologists participated in this study. Participants had more than 5 years of clinical experiences at psychiatry clinics in Tokyo. Those therapists answered three open-ended questions asking characteristics of depression and bipolar as well as significant changes in patients when they became manic from the state of depression. Modified “KJ Hou”, organizing qualitative data by group discussions, was utilized and obtained answers were classified to capture the characteristics of each disorder. Six certified clinical psychologists participated in the discussions.

Results: To the question on characteristics of depression, 72 answers are obtained and they are classified to five categories including relational style and inflexible thoughts. There are 111 answers to the questions on characteristics of bipolar, which are classified to 7 categories such as impulsivity and self-centeredness. Perfectionism and narrow mindedness are listed as the common characteristics of depression and bipolar. However pessimism and self-blame are referred to as unique characteristics of depression. Furthermore, lower motivation for rest and sleep is considered as a significant change with patients entering manic episode. Changes of sleeping patterns are also known as symptoms of depression, therefore both depression and bipolar appear to share sleep problems as their symptoms but the problems manifest differently in the two disorders. Therefore, this study shows that pessimism, self-blame, and the mechanisms of sleep problems are characteristics that can differentiate depression and bipolar.

Conclusions: The implication and the limitation of this study are discussed. The current open-ended questions do not specify the severity of depression and bipolar. Thus, it is suggested that future research applies quantitative method to evaluate differences of the two disorders and the severity of manic and depressive episode.

Keywords: bipolar, depression, self-blame, sleep problems

A comparison of predictive properties of risk measures for bipolar disorder among help-seeking youth

A Ratheesh^a, SM Cotton^a, BN Nelson^a, JK Betts^a, A Chanan^a, PD McGorry^a, M Berk^b, A Bechdolf^c

^aCentre for Youth Mental Health, The University of Melbourne and Orygen Youth Health Research Centre, Parkville Melbourne, Australia, ^bPsychiatry, Deakin University, Geelong, Australia, ^cClinic for Psychiatry Psychotherapy and Psychosomatics, Charité - Universitätsmedizin, Berlin, Germany

Introduction: Short-term prediction of Bipolar Disorder (BD) has great significance in defining prodromal states for this disorder. Previous prospective studies have indicated that young persons have a greater risk of transition to BD. A number of commonly used risk measures were examined for their prospective ability to predict the onset of BD over 1 year among help-seeking youth.

Methods: We interviewed 70 participants aged 15–25 who were seeking treatment for non-psychotic conditions from a young persons mental health service in Melbourne, Australia using a number of measures of bipolar risk. These included continuous measures of manic symptoms (Young Mania Rating Scale- YMRS), depressive symptoms (Montgomery-Asberg Depression Rating scale- MADRS) and temperament (Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego Autoquestionnaire -TEMPS-A). In addition, composite measures of risk factors for bipolar risk such as the Bipolarity Index (BI), Bipolar At-Risk criteria (BAR) proposed by Bechdolf et.al and the criteria for Bipolar Spectrum Disorder (BSD) proposed by Ghaemi et. al. were assessed at baseline. The primary outcome was the development of DSM IV BD I or II using the Longitudinal Interval Follow-up Evaluation interview (LIFE) performed at 12 months. ROC curves and the area under the curve (AUC) were utilized to determine the screening properties of all measures.

Results: Four participants developed BD at 12 months, all of whom were from the BAR sub-group (sensitivity- 100%, specificity-53%, AUC- 0.77 SE- 0.08, $p = 0.07$). The AUC for YMRS, MADRS, TEMPS-A and BI were not statistically significant, but MADRS scores at baseline were associated with the highest AUC (0.70, SE- 0.12). No participant fulfilled the BSD inclusion at baseline.

Discussion: Traditional measures of bipolarity and bipolar risk were not associated with accurate prediction of BD in the short term among youth. The low conversion rate in the entire sample (5.7%) may have limited the statistical predictive ability of these measures. Moreover, the course, treatment, and severity characteristics of a number of these measures may not be applicable to youth. BAR criteria and higher depression severity scores may indicate higher transition risk to BD among help-seeking youth.

The burden of recurrent mood episodes in bipolar I disorder: results from the national epidemiological survey on alcohol and related conditions (NESARC)

A. Peters^a, A. West^a, L. Eisner^b, T. Deckersbach^b

^aPsychiatry, University of Illinois at Chicago, Chicago, IL, USA,

^bPsychiatry, Massachusetts General Hospital, Boston, MA, USA

Aims: Mounting evidence suggests that bipolar disorder is characterized by a progressive course; that with successive episode recurrences, patients experience more severe symptoms and poorer functioning. This link has not been investigated in community-based samples. The aim of this study is to examine the association between number of previous mood episodes and clinical course and functioning in an epidemiological database, the National Epidemiological Survey on Alcohol and Related Conditions (NESARC).

Methods: Subjects (n = 909) meeting DSM-IV criteria for bipolar I disorder who provided data on number of prior episode recurrences were included in our analysis. We evaluated cross-sectional and prospective clinical status and functioning as a function of number of prior mood episodes using Wave 1 and Wave 2 of the NESARC.

Results: Mood episode recurrences accounted for small, but unique variance in outcomes. Greater number of prior recurrences was cross-sectionally associated with poor functioning, more psychiatric co-morbidity, and increased odds of suicidality, disability, and psychiatric hospitalization. Prospectively, individuals with multiple relapses were at greater risk for new onset suicidality, psychiatric co-morbidity, and decline in functioning. Recurrent depressive episodes had a greater impact on clinical status and functioning than manic episodes.

Discussion: The course of bipolar disorder does seem to worsen with progressive mood episodes, but is attenuated in community, relative to clinical samples. Interventions to prevent future depressive episode relapse may be particularly important to implement early in the course of illness.

The relationship between quality of life in elderly patients with bipolar disorder and living in rehabilitation centers or own home

SH Kavari^a, K Nourozi^b

^aRehabilitation Management, University of Social Welfare & Rehabilitation Sciences, Tehran, Iran, ^bNursing, University of Social Welfare & Rehabilitation Sciences, Tehran, Iran

Objectives: Nowadays, the growth of elderly population is a new phenomenon of the major challenges to the developed countries. In Iran, the elderly population has increased over the past two decades there has been a big plus, 60 years from 5.43% to 7.89% in 1986 and increased in 2012. This study was done to assess the relationship between quality of life and with bipolar disorder and living in rehabilitation centers or own home.

Methods: This cross-sectional and descriptive study was undertaken on elderly patients with bipolar disorder. Sampling of elderly patients with bipolar disorder living in rehabilitation centers was (n = 36) and elderly patients living in own house (n = 36). Data obtained using the software SPSS-16 and Chi-square and t tests were analyzed.

Results: A significant difference between the two groups in terms of demographic characteristics was not found. Between elderly patients with bipolar disorder living in rehabilitation centers and living in own house. There was a significant difference in the quality of work life ($P \leq 0/05$). Quality of life of elderly patients with bipolar disorder living in rehabilitation centers ($M = 108/7$ & $SD = 16/8$) was lower than elderly patients with bipolar disorder living in own house ($M = 128/5$ & $SD = 12/4$) ($P = 0/000$).

Conclusions: As the results show a significant difference between staying at home for elderly patients with bipolar and rehabilitation centers have better quality of life in their home and with their relatives to be hospitalized.

Keywords: quality of life, elderly patients, bipolar disorder, rehabilitation centers

The psychological effects of drama activity on depressed older people: a literature review

WC Wong

School of Science and Technology, The Open University of Hong Kong, Hong Kong, China

Background: Depressed older people always experience low-self esteem, low confidence, unworthiness, loss of interest, and withdrawn from social activities. Drama is regarded as a tool for emotional growth. Researchers applied drama on different population,

including children, young people and elderly, resulting in improving subjects' self-esteem, emotion, and social communication skill. But drama had seldom been used on depressed older people, despite the positive effects.

Purpose: This article aims at reviewing the effects of drama activity on depressed older people.

Method: Criteria were set for searching published studies in databases, including MEDLINE, CINCAHL, PsycINFO, ProQuest, and Springer Link. Both local and overseas research that studied the effects of drama was included. Those studies with keywords, such as "drama", "theater", "acting", "depression", "older people", in titles and abstracts were identified. The studies were limited to articles published between January 2000 and August 2013, in English and Chinese. All kinds of research design and methodology were included.

Results: Seven studies were identified. Drama activities were found to be beneficial to psychological aspects when applying on depressed older people. Older people improved in self-worthiness, strengthened self-esteem, increased sense of control during and after drama activities. Also, older people increased their emotional expression during drama activities, which helped them express positive and negative feelings. Moreover, older people increased their interactions and developed meaningful relationships with other participants, which improved the social withdrawn symptom among depressed older people.

Conclusion: Drama activity has a potential application for depressed older people and may yielded psychological benefits.

Keywords: drama, depression, older people

The relationship of impulsivity and lipid levels in bipolar patients: gender effect

S Kesebir, E Tatlidil Yaylaci, A Demirkan, M Altintas

Psychiatry, Erenkoy Mental and Neurological Disease Training and Research Hospital, Istanbul, Turkey

Objective: The aim of this study was to investigate whether there was a relationship between impulsivity and lipid levels in patients with bipolar disorder (BD) and, if present, to investigate the differences between genders.

Methods: In line with this purpose, one hundred patients who were admitted to our out-patient unit for routine controls that had been in remission for at least 8 weeks and diagnosed as bipolar disorder according to the DSM-IV were evaluated consecutively. Patients completed Barratt Impulsivity Scale (BIS-11). Blood samples were obtained for measuring levels (mg/dL) of lipids, cholesterol, triglyceride (TG), high density lipoproteine (HDL), low density lipoproteine (LDL).

Results: Impulsivity scores were found similar in both genders ($t = 1.2$, $p = 0.273$). A weak correlation was found between impulsivity scores and triglyceride levels ($r = 0.190$, $p = 0.050$). When assessed separately for genders, the relationship between triglyceride levels and impulsivity was detected only in female patients ($r = 0.238$, $p = 0.046$).

Conclusions: Impulsivity and lipid levels are differentially related to gender in bipolar patients.

Keywords: impulsivity, lipid levels, gender, bipolar disorder

Current perspectives of bipolar disorder in women: gender differences or gender bias?

D Ray^a, VG Jhanwar^b, MS Reddy^c, R Nagpal^d

^aPsychiatry, Ruby General Hospital, Kolkata, India, ^bPsychiatry,

Deva Institute of Healthcare & Research, Varanasi, India,

^cPsychiatry, Asha Hospital, Hyderabad, India, ^dPsychiatry,

Manobal Clinic, Delhi, India

Women are not same as men. The difference is objectively quite prominent in bipolar disorder. Bipolar II disorder, depressive

symptoms and rapid cycling course are commoner in women than in men. Menstrual vis-a-vis menopausal, perinatal and post-partum issues also control and modify the course and outcome of bipolar disorders. Irritability is a prominent symptom in the female-specific mood disorders and sometimes becomes serious enough to warrant treatment. Despite a plethora of guidelines in management of bipolar disorders, the literature concerning female-biased gender specific issues and their management is scanty. We attempt to explore female-specific issues in bipolar disorders and bipolar spectrum disorders from both a longitudinal (life-span) and a cross-sectional (dimensional/ categorical) perspective with allusions to their nosological status with respect to DSM 5. Biases that are incorporated in the construct are also examined in the process of this expose.

Self-esteem and self-esteem instability in relation to life events and symptoms in bipolar affective disorder

A Babakhani, M Startup

School of Psychology, The University of Newcastle, Wyoming, Australia

Aims: The relationship between self-esteem and symptoms was studied within individuals with bipolar affective disorder (BAD). Between group comparisons were conducted using t-tests and linear mixed models analysis was used for the longitudinal data.

Methods: Study 1 Method: Individuals with BAD were compared with a healthy control group on Rosenberg's (1965) self-esteem scale and a measure of instability of self-esteem. Study 2 Method: Subsequently, we tested the buffering hypothesis of self-esteem. That is, self-esteem would buffer the individual against occurrence of life events.

Results: It was found that individuals with BAD had lower self-esteem on Rosenberg's positive, negative and total self-esteem scales than the healthy control group. In addition, on positive, negative and total SE instability, individuals with BAD had higher self-esteem instability scores than the healthy control group. We found support for the buffering hypothesis, as individuals with high self-esteem, after experiencing negative life events in the interpersonal domain, had lower levels of BDI and activation (ACT) scores. In contrast, individuals with low self-esteem had higher levels of BDI and ACT scores, after occurrence of interpersonal life events. It was further found that the long-term threat posed by negative interpersonal events, predicted ACT scores in low self-esteem individuals. Also, individuals with low self-esteem instability tended to respond to life events with increased depressive and manic symptoms as compared with individuals with high SE instability.

Conclusions: We suggest that the interactive effects of trait self-esteem and self-esteem instability might provide reasons for the unexpected results.

An exploratory factor analysis of coping inventory for stressful situations (CISS) in Korean adults

YM Choi^a, ES Moon^a, JM Park^{a,b}, BD Lee^{a,b}, YM Lee^a, HJ Jeong^a, YI Chung^b

^aPsychiatry, Pusan National University Hospital, Busan, Korea,

^bPsychiatry, Pusan National University College of Medicine, Yangsan, Korea

Introduction: Given the influence of stress on mood disorder, knowing coping style is very important in treatment of patients with mood disorder. Coping Inventory for Stressful Situations (CISS) is a useful instrument to know a person's coping style consisting of the three factors of Task-/Emotion-/Avoidance-oriented coping skills. In previous study of the CISS in Korean adolescents,

the result was not satisfactory to measure coping styles. However, there has been no research on validity study of CISS in Korean adults. In this study, we regarded there may be some differences between adolescents and adults so that a factor analysis of CISS in adult subjects may be different as well.

Method: 302 adults (153 females and 149 males) who have currently no psychiatric disease completed the CISS-Korean version. Average age was 33.2 (± 9.3 , range 18–60). When performing an exploratory factor analysis, principle component analysis with a promax rotation was used.

Result: High internal consistency reliabilities were shown as Cronbach's alpha coefficients were 0.92 for Task-oriented coping, 0.88 for Emotion-oriented coping, 0.86 for Avoidance-oriented coping. The factor analysis exhibited comparatively clean pattern matrix when we used principal component analysis with a promax rotation. However, three items of avoidance-oriented coping (item 11, 35, 44) didn't loaded on its original factor properly.

Discussion: The result may suggest that the CISS would be a useful tool when gauging a coping style in Korean adults. The oblique rotation might help making the structure clearer, given the correlations between the factors. On the other hand, few items of avoidance-oriented coping style should be ameliorated in further studies. Cross-cultural differences and difference in age may need to be considered when using the CISS.

Keywords: CISS, coping inventory, stress coping, factor analysis

Convergence insufficiency symptom in bipolar disorder and schizophrenia and its association with NES and ICARS

A Chrobak^a, K Siuda^a, A Arciszewska^a, M Siwek^b, M Pilecki^c, D Dudek^b

^aStudents Scientific Association of Adult Psychiatry, Jagiellonian University, Cracow, Poland, ^bDepartment of Affective Disorders, Jagiellonian University, Cracow, Poland, ^cDepartment of Psychiatry, Jagiellonian University, Cracow, Poland

Aims: Some evidence suggests that bipolar disorder (BD) and schizophrenia (SZ) have common neurological symptoms, neurobiological features and genetic components. The aim of this study was to compare neurological and cerebellar soft signs and convergence insufficiency in both diseases.

Methods: 29 patients with SZ, 14 patients with BD and 20 healthy control subjects were examined. The neurological assessment was done with ICARS and NES scales.

Results: The abnormal vergence pattern was observed in 12 out of 29 patients with SZ, 1 out of 20 patients with BD and 0 healthy control subjects. Symptom occurred significantly more often in SZ patients in comparison with BD patients (χ^2 (1, N = 43) = 3.75, $p = 0.05$) and controls (χ^2 (1, N = 49) = 3.75, $p = 0.003$). BD and SZ patients did not differ in NES and ICARS total scores and their subscales. SZ patients with vergence symptom performed significantly worse in oculomotor (t (13.6) = -2.42, $p = 0.03$) and dysarthria ($U = 55$, $z = -2.06$, $p = 0.04$) subscores of ICARS than SZ patients without vergence symptom.

Conclusions: During the neurological assessment an abnormal vergence symptom with unilateral exophoria at near predominantly in nondominant eye was discovered in patients with SZ and BD. To our knowledge this is the first study presenting this symptom in these groups of patients. Due to the lack of differences between neurological assessments' scores between BD and SZ, this abnormal vergence pattern was the only symptom with a potential to distinguish those groups. It is suggested that worsened performance in oculomotor and dysarthria subscales and the abnormal vergence symptom itself may be a marker of possibly greater disturbances in the midbrain and cortico-ponto-cerebellar pathways including fastigial nucleus in SZ, in comparison to BD. Our results shows that

Sixteenth Annual Conference on Bipolar Disorders

despite of similarities between SZ and BD presented in recent reports, differences in physical examination can be found. Evaluation of presented symptom is short and accessible in everyday clinical practice, and brings premise to be supportive in future studies.

Keywords: bipolar disorder, schizophrenia, eye movement disorders, ataxia

Bipolar II disorder in Taiwan: highly prevalent in outpatients presenting with depression?

K Chung, SY Tsai, SH Huang, PH Chen

Department of Psychiatry, Taipei Medical University Hospital, Taipei, Taiwan

Introduction: Bipolar-II Disorder (BP-II) is a common, severe disabling mental illness characterized by recurrent episodes of hypomania and depression, yet it is under-diagnosed and insufficiently investigated especially as far as treatment is concerned. Despite this high burden, research in BP-II has been sparse, particularly in relation to management of the disorder. The aim of this study is to determine the proportion of BP-II in outpatients presenting with depression, in order to provide optimal intervention.

Method: Hypomania check list-32 (HCL-32) was randomly used to survey the first-visit potential bipolar II subjects among clinical population with depressive symptoms from April to December, 2011. The psychiatrist made a final diagnosis based on the DSM-IV through semi-structural interview. Clinical variables of interest were obtained for further analysis.

Results: Among the screening cases of the 107 subjects, 34.6% of them were diagnosed with bipolar II disorder. 25 subjects (men: 44%, women: 56%) with bipolar II disorder had mean age of 32.2 ± 10.3 years. The mean age of onset was 22.7 ± 8.9 years. There was no illegal substance use among the 25 subjects, which was different from data from Western countries.

Discussion: BP-II is estimated as high as one-third in the clinical setting in which depression is the reason for visit. Bipolar depression should be emphasized when facing the patients with chief problem of depression.

Keywords: bipolar II disorder, hypomania, depression, substance abuse and dependence

Difference in psychological resilience between BPD I and BPD II: a preliminary study

E Joo, K Lee, E Kim, J Yi

Psychiatry, Eulji General Hospital Eulji University School of Medicine, Seoul, Korea

Recent studies reported that BPD II has more chronic course of illness and poor prognosis comparing BPD I. Psychological resilience is a dynamic process representing positive adaptive skills and a measure of the ability to cope with stress. Psychosocial stressors are supposed to be important precipitating factors for the onset and recurrence of bipolar disorders. We hypothesized that BPD II has poorer psychological resilience than BPD I. Psychological resilience was investigated using CD-RISC (Korean version) in bipolar disorder comparing between BPD I and BPD II. Higher score of DC-RISC indicates better psychological resilience. We included 35 subjects with BPD I and 17 subjects with BPD II. 86 subjects with recurrent MDD were also included for the additional comparison among mood disorders. The mean total score of CD-RISC was 60.20 ± 20.22 for BPD I, 47.41 ± 19.58 for BPD II, and 54.08 ± 17.77 for recurrent MDD. There is a significant difference in total score of CD-RISC between BPD I and BPD II ($p = 0.035$). BPD II showed the worst psychological resilience among mood disorders. BPD I showed better psychological resilience than recurrent MDD, but the difference was not statistically significant. The small number of subjects is a limitation of this study. In conclusion, BPD II showed poorer psychological resilience than BPD I

and similar level of psychological resilience was found between BPD II and recurrent MDD. Further studies with large number of patients are necessary.

Pooling childhood & adolescent onset attenuates early onset clinical relevance in bipolar disorder

TA Ketter, J Holtzman, S Miller, F Hooshmand, PW Wang, SJ Hill

Psychiatry and Behavioral Sciences, Stanford University, Stanford, CA, USA

Background: Early onset bipolar disorder (BD) has been associated with unfavorable illness characteristics. However, it remains to be determined as to whether childhood and adolescent onset ought to be considered separately or in aggregate.

Methods: BD patients referred to Stanford Bipolar Disorder Clinic during 2000–2011 were assessed with the Systematic Treatment Enhancement Program for BD (STEP-BD) Affective Disorders Evaluation. Patients with childhood and adolescent onset were compared to those with adult onset separately and in aggregate.

Results: Among 502 BD outpatients (mean \pm SD age 35.6 ± 13.1 years; 58.3% female; 48.3% Type I, 51.7% Type II; with illness duration 17.7 ± 13.3 years; Clinical Global Impression for Bipolar Disorder-Overall Severity score 3.9 ± 1.5 , and taking 2.6 ± 1.7 prescription psychotropics), patients with childhood (<13 years, $N = 107$) and adolescent ($13–18$ years, $N = 238$) compared to adult (>18 years, $N = 157$) onset considered separately both had significantly higher rates for six unfavorable illness characteristics: (1) lifetime comorbid anxiety disorders (80.2% and 67.5% versus 54.2%, respectively), (2) lifetime alcohol use disorders (50.0% and 38.7% versus 27.3%), (3) lifetime eating disorders (25.5% and 17.2% versus 6.0%), (4) prior suicide attempt (43.9% and 30.7% versus 20.4%), (5) rapid cycling in the prior year (33.3% and 22.2% versus 18.7%), and (6) at least five lifetime mood episodes (27.4% and 22.1% versus 11.4%). In addition, childhood but not adolescent onset had a significantly higher rate of first-degree relative with mood disorder (69.4% versus 52.6%, $p = 0.0073$; and 53.4% versus 52.6%, $p = 0.29$). Patients with childhood/adolescent (pooled) compared to adult onset had significantly higher rates for five of these seven unfavorable illness characteristics, but not for rapid cycling in the prior year or first-degree relative with mood disorder. Indeed, patients with childhood compared adolescent onset had significantly higher rates for all seven of these unfavorable illness characteristics.

Conclusions: Childhood compared adolescent onset BD was more robustly related to unfavorable bipolar disorder disease characteristics, so that pooling these groups attenuated such relationships, and was thus less clinically relevant. Further study is warranted to determine the extent to which the adolescent onset group demonstrates an intermediate phenotype between childhood and adult onset.

More liberal “with mixed features” threshold for bipolar depression may be not only more inclusive, but also more clinically relevant

W Kim^a, S Miller^b, F Hooshmand^b, PW Wang^b, SJ Hill^b, TA Ketter^b

^a*Psychiatry, Inje University Seoul Paik Hospital, Seoul, Korea,*

^b*Psychiatry, Stanford University School of Medicine, Stanford, CA, USA*

Aims: Assess prevalence and clinical relevance of “with mixed features” using a more liberal (two opposite pole symptoms) compared to the more conservative DSM-5 (three opposite pole symptoms) threshold in depressed bipolar disorder (BD) patients.

Methods: BD outpatients were assessed with the Systematic Treatment Enhancement Program for BD (STEP-BD) Affective Disorders Evaluation. Prevalence and clinical correlates of baseline depressive episodes “with mixed features” were compared using a more liberal threshold and the more conservative DSM-5 threshold.

Results: Among 503 BD patients (mean \pm SD age 35.6 ± 13.1 years; 58.3% female; 48.3% Type I, 51.7% Type II; with illness duration 17.7 ± 13.3 years; and Clinical Global Impression for Bipolar Disorder-Overall Severity score 3.9 ± 1.5 ; and taking 2.6 ± 1.7 medications), 151 (30.8%) had baseline syndromal major depressive episodes, among whom “with mixed features” occurred in 22.5% (34/151) using a more liberal threshold, but in only 9.9% (15/151) using the more conservative DSM-5 threshold. Hence, the rate of “with mixed features” for depressive episodes using the more liberal compared to the conservative threshold was more than twice (2.3 times) as high (Chi-square = 8.8, $p = 0.004$). Moreover, the more liberal threshold yielded more important statistically significant clinical correlates of “with mixed features” compared to pure depressive episodes, which were not significant using the more conservative DSM-5 threshold. Specifically, using the more liberal threshold, mixed compared to pure depression was associated with more anxiety disorder comorbidity (in 94.1% of mixed, but only 71.7% of pure, Chi-square = 9.307, $p = 0.002$) and alcohol use disorder comorbidity (in 55.8% of mixed, but only 36.2% of pure, Chi-square = 4.218, $p = 0.048$), and less antidepressant use [in only 23.5% of mixed, but 52.1% of pure, Chi-square = 8.688, $p = 0.003$].

Conclusions: Further studies are warranted to assess our preliminary observation that a more liberal “with mixed features” threshold for bipolar depression may be more inclusive and have more clinical relevance.

Education on bipolar affective disorder in Hong Kong

S Law

Department of Family Medicine, University of Hong Kong, Hong Kong, China

The Society for Advancement of Bipolar Affective Disorder (SABAD) in Hong Kong was founded in 2005. The aim of the society is to promote the knowledge of Bipolar Affective Disorder to medical professionals and the public, in order to help diagnose the disorder at an early stage and provide suitable treatment. It has organized many different programs to promote among the medical profession and the community, patients and carers the proper understanding of bipolar affective disorder and its management via appropriate education, scientific research and collaboration with local and international professional bodies. For the medical and allied health profession, the society has been running regular doctors interest group (DIG) to have sharing and discussion on practical issues between psychiatrists and general practitioners, pharmacology seminar in the drug treatment of bipolar disorder and scientific symposia delivered by both local and overseas experts. SABAD has also developed clinical recommendation for different stages of the BAD spectrum as applicable to the local setting. For public education, the society has organized regular public talks and developed educational material including information pamphlets, educational DVD and TV programs on bipolar disorder which is suitable for different categories of persons. The society also developed its website which provides different information to both the professionals and the public. These programs have increased the awareness of the disorder in both the professional and public and the management of the disorder is thus enhanced.

The prestige model of spectrum bipolarity

J Le Bas^a, R Newton^b, D O'Loughlin^c, R Sore^d, D Castle^e

^a*Peninsula Health, University of Melbourne, Melbourne, Australia,*

^b*Austin Health, University of Melbourne, Melbourne, Australia,*

^c*Mental Health, St Vincents Hospital, Melbourne, Australia,*

^d*Statistical Consulting Centre, University of Melbourne, Melbourne, Australia,*

^e*St Vincents Health, University of Melbourne, Melbourne, Australia*

Aims: This paper presents and evaluates a psychosocial model of bipolar spectrum pathogenesis, based on group investment - prestige - and self-esteem.

Methods: A case control study categorised 228 adult participants into a seven node bipolar spectrum. Binary logistic regression was utilised to examine the relationships between strategic prestige (leadership) motivation (MSPM) and bipolar disorder. The correlation of prestige and affective variables was examined, while contour plots of affective change on the plot of MSPM versus prestige were drawn.

Results: MSPM (OR 3.71, 95% CI [1.74, 7.92], $p = 0.001$), along with bipolar family history and childhood relational trauma, predicted categorical and also dimensional bipolarity. Mood elevation in the euthymic/elevated subgroup ($r_s = 0.42$), and depressive symptoms ($r_s = 0.35$) in the bipolar/bipolar “lite” group, were associated with an elevated MSPM. A family history of bipolar disorder predicted a high MSPM “(OR 1.98, 95% CI [1.12, 3.52], $p = 0.019$). The prestige model dynamic was broadly supported in the correlational analysis and MSPM correlated strongly with prestige ($r_p = 0.51$) in the hypomanic group. The pseudounipolar group (with a bipolar family history) had both elevated MSPM and prestige when compared with the unipolar node. The contour maps showed three distinct affective zones—depressive, elevated and euthymic.

Conclusions: Social, genetic and prestige variables appear to be etiologically related to the bipolar spectrum, while MSPM dynamically covaries with mood state and prestige - consistent with evolutionarily stable strategies for prestige resource competition. Mood disorders may have arisen in ancestral time through the risk of social marginality in the context of prestige competition; depression being a means of ostracism avoidance and hypomania serving to raise prestige through mood elevation and prestige motivation. The propensity toward prestige enhancement appears to be under genetic influence, being associated with bipolar inheritance. Genetic factors, interacting with (epigenetic) childhood relational trauma may lead to a bipolar phenotype, which has several features in common with vulnerable narcissism. The prestige model offers a new conceptualisation of affective disorders and has received preliminary support.

Keywords: bipolar disorder, prestige, self-esteem, MSPM, evolution

Characteristics of coping style in bipolar patients

E Moon^a, JM Park^b, BD Lee^b, YM Lee^a, HJ Jeong^a, JJ Lee^a, Y Choi^a, YI Chung^b

^a*Department of Psychiatry, Pusan National University Hospital,*

Busan, Korea, ^b*Department of Psychiatry, Pusan National University College of Medicine, Busan, Korea*

Objective: Coping style for stressful situation may influence on the course of bipolar disorder. This study aimed to examine coping styles in bipolar patients compared to healthy controls.

Methods: Eighty five patients who met DSM-IV criteria for bipolar disorders and 343 healthy controls were included. Coping styles were measured by Coping Inventory for Stressful Situations (CISS). We compared coping styles between bipolar patients and healthy controls using independent t-test and analysis of covariance (ANCOVA) to adjust the influence of age.

Results: Emotion-oriented coping score was significantly higher in bipolar patients than controls ($t = -2.556$, $p = 0.012$). Meanwhile, Task- and avoidance-oriented coping scores were not significantly different between two groups (independent t-test, Task-oriented coping $t = 1.188$, $p = 0.0237$; avoidance-oriented coping $t = -0.009$, $p = 0.993$). Emotion-oriented coping was still significantly different after adjustment of age (ANCOVA, covariate = age, $F = 7.649$, $p = 0.006$).

Conclusion: This study results suggested that bipolar patients may have maladaptive coping styles for stressful situation. Psychosocial intervention might be necessary to improve coping strategies for stressful situation in the treatment of bipolar disorder.

Evolutionary anthropological hypotheses of bipolar disorder

H Park^{a,c}, J Choi^b, E Woo^c, S Park^c

^aDepartment of Psychiatry, St. Andrew's Hospital, Seoul, Korea,

^bDepartment of Child and Adolescent Psychiatry, National Seoul Hospital, Seoul, Korea, ^cDepartment of Anthropology, Seoul National University, Seoul, Korea

Evolutionary anthropological approaches based on ultimate causation principle is resolving the inter-disciplinary conflicts between different fields of study for human mind. Evolutionary anthropology is the multidisciplinary field of social and natural sciences about the physiology and behavior of Homo sapiens, and the relationship between human and other hominoids like primates or ancient human species. This evolutionary approaches is useful for attempting as to why mood disorders have been evolved in spite of harmful effects on individual level. The conditions labeled as disorders may simply be extreme forms of naturally occurring human psychological traits. Some psychiatrists and anthropologists regard depressive and elated mood as one of adaptive social strategy of Hominin. There is evidence of some genetic basis to bipolar disorder, and some patients and their close relatives seem to possess good creativity, high energy, uniqueness, intuition and high performance. For clinicians, it is not uncommon to see bipolar patients who show high creativity and excellent performance in the field of art and literature. This anthropological and evolutionary perspectives could open the new way to discover the true meaning of bipolar disorder. We would like to summarize the previous and recent hypotheses about evolution of bipolar disorder. And we compare the pros and cons of several competing evolutionary explanations of bipolar disorder.

Keywords: homo sapiens, evolution, hominin, bipolar disorder

Clinical profile of people with bipolar disorder who die by self-poisoning

A Schaffer^a, L Weinstock^b, M Sinyor^a, BI Goldstein^a, AJ Levitt^a

^aPsychiatry, Sunnybrook Health Sciences Centre, Toronto, Canada,

^bPsychosocial Research Program, Alpert Medical School of Brown University, Providence, RI, USA

Background: Bipolar disorder (BD) is associated with elevated rates of suicide. Developing a better understanding of suicide among people with BD, and determining who is more likely to die by a specific method, is one key aspect of potentially improving suicide prevention strategies. This study aimed to elucidate differences between people with BD who died by suicide via self-poisoning versus other methods of suicide.

Methods: Data on all 170 BD suicide deaths in the City of Toronto from 1998–2010 were extracted from the Office of the Chief Coroner of Ontario, including demographics, clinical variables, recent stressors, and details of the suicide. Comparisons of suicides by self-poisoning to suicides by other methods were conducted using univariate analyses and a logistic regression inputting all variables with a $p < 0.1$.

Results: Death by self-poisoning accounted for 57/170 (33.5%) of all BD suicide deaths. Those who died by self-poisoning were significantly more likely to be female (59.6% versus 35.4%, $p = 0.003$), had higher rates of a past suicide attempt (59.6% versus 40.7%, $p = 0.02$), comorbid substance abuse (38.6% versus 20.4%, $p = 0.01$), and had a trend towards higher rates of a bereavement stressor (10.5% versus 3.5%, $p = 0.07$). Each of these variables, including female sex (OR = 3.37, $p = 0.001$), past suicide attempt (OR = 2.08, $p = 0.04$), comorbid substance abuse (OR = 3.16, $p = 0.004$), and bereavement stressor (OR = 5.13, $p = 0.027$), were found to account for unique variance in death by self-poisoning when evaluated in the multivariate logistic model.

Conclusions: Self-poisoning is a common method of suicide in people with BD. Differences identified in the demographic and clinical profile of BD suicide deaths by self-poisoning warrant further prospective study in order to ultimately develop more targeted suicide prevention approaches.

Suicide in bipolar disorder: characteristics and subgroups

A Schaffer, M Sinyor, C Reis, BI Goldstein, AJ Levitt

Psychiatry, Sunnybrook Health Sciences Centre, Toronto, Canada

Objectives: The development of more sophisticated models for understanding suicide among people with bipolar disorder (BD) requires diagnosis-specific data. This study aimed to elucidate differences between people who die by suicide who have BD as compared with those who do not, and to identify subgroups within those with BD.

Methods: Data on all suicide deaths in the City of Toronto from 1998–2010 were extracted from the Office of the Chief Coroner of Ontario, including demographics, clinical variables, recent stressors, and details of the suicide. Comparisons of person- and suicide-specific variables between suicide deaths among those with BD ($n = 170$) to those without ($n = 2716$) were conducted using univariate analyses and logistic regression. A two-step cluster analysis was performed among the BD suicide group only.

Results: BD was recorded in 5.9% of all suicide deaths. People with BD who died by suicide were more likely to be female (OR = 1.75 [1.27–2.42], $p = 0.001$), to have made a past suicide attempt (OR = 2.01 [1.45–2.80], $p < 0.0001$) and to have had recent contact with psychiatric or emergency services (OR = 1.59 [1.00–2.52], $p = 0.049$). Five clusters were identified within the BD group, with differences between clusters in age, sex, marital status, living circumstances, past suicide attempts, substance abuse, interpersonal, employment/financial and legal/police stressors, and rates of death by fall/jump or self-poisoning.

Conclusions: The present findings identified differences between BD and non-BD suicide groups, providing support to the utilization of an illness-specific approach to better understand suicide in BD. Subgroups of BD suicide deaths, if replicated, should also be incorporated into the design and analysis of future studies of suicide in BD.

Socio-demographic characteristics of admitted manic episode of bipolar mood disorder patients in a tertiary psychiatric hospital in Bangladesh

MMJ Uddin^a, HU Ahmed^b, MT Alam^b, MF Alam^b, MA Hamid^b, WA Chowdhury^b, MG Rabbani^b

^aPsychiatry, National Institute of Neurosciences and Hospital, Dhaka, Bangladesh, ^bPsychiatry, National Institute of Mental Health and Hospital, Dhaka, Bangladesh

Introduction: Manic episode of bipolar mood disorder is a public health problem that causes enormous personal and economic cost

in a developing country like Bangladesh. Bangladesh is a south Asian country with 167 million population in her 147,570 square kilometers area. Among them 0.4% have bipolar mood disorder out of 16.01% adult mental patients in this country

Aims: This study was done to assess the socio- demographic characteristics of manic patients admitted in tertiary level mental hospital.

Methods: This was a cross sectional study done in inpatient department of National Institute of Mental Health, Dhaka, Bangladesh during the period of January 2012 to December 2012. 107 manic episode of bipolar mood disorder patients were taken as sample according to the DSM-IV-TR diagnostic criteria. A semi structured questionnaire was used to collect the socio- demographic characteristic of the respondents. Ethical considerations were maintained accordingly.

Result: 107 manic episode of bipolar mood disorder patients were the sample of the study. Among the respondents 77 (71.96%) were male and 30 (28.04%) were female, most of them 71 (66.36%) were in age group of 20–40 years. Regarding education of the patients most of them 43 (40.19%) passed secondary or higher secondary school, graduate or above graduate were 14 (13.08%), on the other hand illiterate or completed primary level comprises 23 (21.5%). Majority of the respondents 36 (33.64%) were unemployed, 24 (22.43%) were self employed, 22 (20.56%) were student. Most of the respondents 87 (81.30%) were poor or lower middle class. In this study 21 (19.63%) of the patients were admitted for their first episode of manic illness, 62 (57.94%) of the patients had history of previous one or two episodes and 24 (22.43%) had history of previous more than two manic episodes. Among the respondents 18 (16.82%) of the patients have family history of mental illness either bipolar mood disorder or other major mental illness.

Conclusion: Socio-demographic profile is an important tool for understanding a disease, its aetiology or risk factors, and effect on patient as well as family. These findings will help to understand the needs of our country in respect of mental health service and planning for preventive and rehabilitation program.

Elevated levels of urinary markers of oxidatively generated DNA and RNA damage in bipolar disorder

K Munkholm^a, HE Poulsen^b, LV Kessing^a, M Vinberg^a

^aPsychiatric Center Copenhagen, Rigshospitalet, Copenhagen, Denmark, ^bLaboratory of Clinical Pharmacology Q7642, Rigshospitalet, Copenhagen, Denmark

Background: Bipolar disorder is associated with an increased medical burden and shortened lifespan. The pathophysiological mechanisms underlying the disorder and its multisystem nature are unclear. Oxidatively generated damage to nucleosides has been demonstrated in metabolic disorders; however the extent in bipolar disorder in vivo is unknown. We investigated oxidatively generated damage to DNA and RNA in bipolar disorder patients and their relationship with affective phase compared with healthy control subjects.

Methods: Urinary excretion of 8-oxo-7, 8-dihydro-2'-deoxyguanosine (8-oxodG) and 8-oxo-7, 8-dihydroguanosine (8-oxoGuo), markers of oxidatively generated DNA and RNA damage, respectively, was measured using ultraperformance liquid chromatography with tandem mass spectrometry (UPLC/MS-MS) in 37 rapid cycling bipolar disorder patients and in 40 age- and gender matched healthy control subjects. A longitudinal design was employed, evaluating repeated measurements of urinary levels of oxidatively generated nucleoside damage in various affective phases (depression, mania and remission) in bipolar disorder patients during a 6–12 months period and compared with repeated measurements in healthy control subjects.

Results: In linear mixed model analysis, adjusting for multiple demographical, metabolic and- lifestyle factors, excretion of both the urinary DNA oxidation marker 8-oxodG and the RNA oxida-

tion marker 8-oxoGuo was significantly elevated in euthymic bipolar disorder patients compared with healthy control subjects, with substantial increases of 40% ($p < 0.0005$) and 43% respectively ($p < 0.0005$). The increased levels of oxidatively generated nucleoside damage were present through all affective phases of the illness, with no significant difference between affective states.

Conclusions: Our results indicate that bipolar disorder is associated with increased oxidatively generated damage to nucleosides. The findings could suggest a role for oxidatively generated damage to DNA and RNA as a molecular mechanism contributing to the increased risk of medical disorders, shortened life expectancy and the progressive course of illness observed in bipolar disorder.

Comparison of different creativity between bipolar disorders and normal control and correlate with functional connectivity in the brain: preliminary findings

T Su, Y Kuan

Institute of Brain Science, National Yang-Ming University, Taipei, Taiwan

Background: Creativity is one of our most valued human traits. Bipolar disorders are emotionally unstable, yet they are exceptionally highly creative in many fields.

Specific aims: To distinguish the difference of creativity among four groups of bipolar disorders, highly creative bipolar disorders, normal controls, and highly creative normal controls.

Method: The study utilized a 2×2 between-subject design to investigate the difference between subjects with high/normal creativity and subjects with/without bipolar disorders. There are 30 subjects in each group, two variables are fixed: age and gender. In order to measure our subjects' creativity, in this study, all subjects will take Abbreviated Torrance Test for Adult (ATTA), Remote Associates Test (RAT) and Creative Personality Scale (CPS). First, we analyzed the behavioral data of different creativity. Next, we analyzed the brain network connections of creativity in resting-state. Finally, we adopted ROI approach and two-way ANOVA statistical analysis to evaluate between-group differences between bipolar disorders and normal controls, as well as highly creative normal people and highly creative bipolar disorders.

Results: Our preliminary results showed that highly creative bipolar disorders have greater creativity in ATTA measures than comparable normal controls. The CPS measures correlated significantly with the total ATTA creativity test score. But no significant correlation was uncovered between ATTA and RAT scores. Resting fMRI disclosed less functional connectivity (FC) between medial prefrontal cortex (mPFC) and striatum in bipolar disorders than normal controls, and higher creativity was with lower FC of this network.

Discussion: Consistent with the behavioral data, which showed greater creativity in highly creative bipolar disorders, the imaging data showed deficit in PFC and striatum network, which was negative with higher creativity. These creativity networks would have some differences/similarities among persons with special creative talents. By understanding the extraordinary creativity of bipolar disorders, and the difference between bipolar disorders and highly creative normal people, we might help bipolar disorders clinically in eliminating their emotional disturbance and at the same time preserving or uplifting their positive cognitive functions.

Keywords: bipolar disorders, brain, creativity, functional connectivity (FC), neuroimage

The monarca project- electronic daily self-monitoring of subjective and objective symptoms in bipolar disorder

M Faurholt-Jepsen^a, MV Vinberg^a, AS Jacoby^a, EM Christensen^a, M Frost^b, J Bardram^b, LV Kessing^a

^aPsychiatric Centre Copenhagen, Rigshospitalet Copenhagen University Hospital, Copenhagen, Denmark, ^bPIT Lab, IT University of Copenhagen, Copenhagen, Denmark

Introduction: Bipolar disorder is associated with a high risk of relapse and hospitalization. Major reasons for the decreased effect of interventions in clinical practice are delayed intervention for prodromal depressive and manic symptoms. Electronic self-monitoring of affective symptoms using cell phones is suggested as a practical and inexpensive way to monitor illness activity and identify early signs of affective symptoms. Nevertheless, so far the electronic devices have been rather simple not including a bi-directional feedback loop between patients and providers. It has never been tested in a randomized clinical trial whether electronic self-monitoring improves outcomes in bipolar disorder. Aim of the study: to investigate in a randomized controlled trial whether the use of an online monitoring system in patients suffering from bipolar disorder reduces symptoms of affective disorder.

Methods: We developed the MONARCA application for Android based Smartphones, allowing patients suffering from bipolar disorder to do daily self-monitoring - including an interactive feedback loop between patients and clinicians through a web based interface. Design: the effect of the application was tested in a parallel-group single-blind randomized controlled trial including 78 patients suffering from bipolar disorder age 18–60 years. Patients were allocated to using a Smartphone with the MONARCA application (intervention group) or to using a Smartphone without the application (placebo group) during a 6 months study period. The study ended in September 2013. The outcomes were: changes in affective symptoms (primary), social functioning, perceived stress, self-rated depressive and manic symptoms, quality of life, adherence to medication, stress and cognitive functioning (secondary and tertiary).

Analysis: Results will be presented at the conference, since analyzes is ongoing.

Conclusions: Awaiting results.

The effects of distance learning (by mobile) on the anxiety & depression level of nursing care patients with bipolar disorder

SH Kavari^a, K Nourozi^b

^aRehabilitation Management, University of Social Welfare & Rehabilitation Sciences, Tehran, Iran, ^bNursing, University of Social Welfare & Rehabilitation Sciences, Tehran, Iran

Introduction and objectives: Distance learning provides access to learning when the source of information and the learners are separated by time and distance, or both.

Methodology: This research is interventional. In this study one questionnaire was distributed to nursing staff working in bipolar disorders ward. The questionnaire was to assess the knowledge of the nurses with regards to essential information required for; nursing care for patients with bipolar disorders problems, Anxiety Disorders, and Depression etc. Their knowledge was then re-assessed following forward of eight E-Newsletter via SMS mobile phone to the same nursing staff during a 1 month. The two results, before and after sending the information, was compared.

Results: The findings of this study showed there was significant improvement in awareness and knowledge of the nurse in the bipolar disorders ward of Tehran Psychiatry Hospital before and after sending E-newsletter containing the required information, via SMS. ($p < 0.0/05$).

Conclusion: According to the results of this research, development of Distance learning by mobile in all parts of our country can be used to forward the latest information to medical, paramedical professionals and to all employees and workers in these sectors, even in remote areas using this technology. The information can even be expanded based on request based on their needs.

Keywords: Distance learning-anxiety and depression level-nursing care patients-bipolar disorder

Ketamine modulates behavioral and neurochemical alterations induced by stress: novel evidence for treatment of mood disorders

G Reus^a, MP Nacif^a, H Abelaira^a, F Dal Pizzol^b, E Streck^c, J Quevedo^a

^aLaboratório de Neurociências, University of Southern Santa Catarina, Criciúma, Brazil, ^bLaboratório de Fisiopatologia Experimental, University of Southern Santa Catarina, Criciúma, Brazil, ^cLaboratório de Bioenergética, University of Southern Santa Catarina, Criciúma, Brazil

Introduction: A growing body of evidence is pointing towards an association between glutamatergic system within depression and bipolar disorder (BD).

Objective: The present study was aimed to evaluate the behavioral and molecular effects of the ketamine, an antagonist of NMDA receptor of glutamate in maternally deprived adult rats.

Results: In deprived rats treated with saline, it was observed an increase in the immobility time, but ketamine treatment reversed this effect. In the amygdala and nucleus accumbens (NAc) of deprived rats there was a decrease on BDNF, however, ketamine was able to reverse this alteration. The complex I was reduced in the prefrontal cortex (PF) and amygdala of deprived rats, the complex II-III was reduced in the PF and hippocampus of deprived rats. The ketamine treatment increased the complex IV in the PF and amygdala of deprived rats. The creatine kinase was decreased in the PF and amygdala of deprived rats, but ketamine treatment reversed this effect in the amygdala. Ketamine reduced TNF- α , IL-1 and -6 in the serum and CSF of deprived rats.

Conclusion: In conclusion, these findings further support a relationship between immune activation, alteration on neurotrophins, energy metabolism, and depression, and considering the action of ketamine, it is suggested that antagonists of NMDA receptor could exert their effects by modulating of immune system, BDNF and energy metabolism.

Effects of assertive community treatment after two years of treatment of patients with severe mental illness

J Aagaard^a, S Skadhede^b, J Achton Nielsen^c

^aDepartement Q Anxiety and Depression, Aarhus University Hospital, Risskov, Denmark, ^bDepartement M, Aarhus University Hospital, Risskov, Denmark, ^cDepartement S, Aalborg University Hospital, Aalborg, Denmark

Introduction: Effects of Assertive Community Treatment (ACT) for patients suffer Severe Mental Illness (SMI) have been highlighted in several studies, including two Cochrane reviews. The fact that the very positive results from the older studies conducted in the United States not to the same extent have been able to be replicated in later European and especially UK studies, have given rise to some controversy and some new studies.

Method: The study was conducted in North Jutland Region, settled by approx. 400,000 people, 20 <80 years. Patients with SMI were identified from the Psychiatric Central Research Register. Three ACT teams were established, they covered the entire region. The study deals with the first 240 patients who were attached to one of the three ACT teams. Data included standardized questionnaire /

interview data at inclusion, 1 and 2 years of follow-up, and register data not only for the ACT patients, but for all patients throughout the region.

Results: Use of psychiatric bed days for the 240 patients attached to ACT decreased from 2 years before to 2 years after inclusion from an average of 141 days to 65 days. The number of psychiatric consultations increased significantly. Consultations were now predominantly as home visits. Consultations in general hospital also increased significantly. No changes in psychopathology were found, but some improvements in function and satisfaction. By logistic predictor analyses were found that the most significant predictors to explain the reduction in consumption of admissions and bed days were the consumption before inclusion. The ACT patients fewer bed days seem only slightly to affect the region's total use of psychiatric bed days.

Perspectives: The results indicate that the establishment of Region-wide ACT teams has significant positive effects on these severe mentally ill patients. It is argued that the principles with ACT might be nationwide.

Keywords: assertive community treatment, severe mental illness, observational clinical study

Needs assessment of community families to patients with severe mental illness (SMI)

J Aagaard^a, P Kølbaek^b, ULLA Væggesøse^c, PIA Vedel Ankersen^c

^aDepartement Q nxiety and Depression, Aarhus University Hospital, Risskov, Denmark, ^bDepartement M, Aarhus University Hospital, Risskov, Denmark, ^cCentral Region Quality Institute, CFK, Skejby Aarhus, Denmark

Introduction: Psychiatric patients and especially the most severely mentally ill may have significant difficulties concerning social inclusion. Studies indicate that poor social inclusion is of important of the course of the disease, including enlarged use of social and psychiatric services. One way to promote social inclusion is that the civil society established Community Families for individual patients. The patient attached to such a family has the possibility of acute and agreed day contacts and when needed an overnight stay in the family. Prior to the establishment of a casus-control study of effects of Community Family in Denmark, the present study of need assessment was performed.

Methods: The study was conducted in the seven municipalities with a total of approx. 500,000 aged 20 <80 years inhabitant, where the case-control study should be established. Patients with Severe Mental Illness (SMI) were identified through the Psychiatric Central Research Register. Patients with SMI got their suitability for Community Family assessed by their primary contact persons.

Results: The point prevalence of SMI was 1.9/1,000. The point prevalence was significantly correlated with the population density in the seven municipalities. About 1/3 of the patients were found suitable for the Community Family offers. Patients settled in municipalities with less population density, where the prevalence of SMI was lowest, were more frequently rated as suitable for a Network Family offers than patients from municipalities with higher population density. Further, it was found that significant predictors of suitability for Network Family offers included gender (female), age (younger), relatively few admissions and no compulsory admissions in the 2 years before suitability assessment, i.e. the healthiest fraction of the patients suffering SMI.

Perspectives: The results indicate that it is possible to estimate the dimension of the Community Family offer and describe characteristics of potential service users.

Keywords: community family, severe mental illness, epidemiological study

The efficacy of psychoeducation with home visit in patients with bipolar affective disorder

TA Batista, C Baes, MF Jurruena

Department of Neuroscience and Behavior, University of Sao Paulo, Ribeirão Preto, Brazil

Background: Recent evidences for Bipolar Disorder (BD) treatment demonstrated that only medication is not enough to stabilize mood. The clinical complexity of this disease, the presence of several comorbidities and the different degrees of adherence to pharmacotherapy, demands the use of diverse therapeutic options. Among the alternatives to meet this demand, we have combined the pharmacological treatment psychoeducational (PE) approach as an effective option in the treatment of individuals with BD. The use of PE in group format has often been used in several studies with good applicability, however PE in home visits to our knowledge have not been evaluated in controlled trials yet. Our aim is to evaluate the efficacy of PE in home visits in bipolar patients in pharmacological treatment and their clinical course, medication adherence and functionality.

Methods: This was a randomized controlled trial with 30 patients with bipolar I or II, according to the DSM-IV criteria. The experimental group consisted of 15 patients received pharmacological treatment and home visits with structure PE intervention reduced version of the PE program created by the Group of Barcelona. The control group consisted of 15 patients received, in addition to pharmacological treatment, home visit without PE. Both groups received weekly visits (8 sessions) with 90 minutes of duration. The assessment instruments to assess depression, mania and medication adherence were administered at baseline (week 0), 4th week and at the end of interventions (8th week).

Results: The experimental group, after received PE, showed a significant reduction in depression score in Hamilton Depression Rating Scale during the treatment phase ($p < 0.01$). Furthermore, compared to the control group, the PE group showed a significant improvement in medication adherence ($p < 0.01$).

Discussion: The method of PE with home visit provide to be effective as adjunctive treatment for patients with bipolar affective disorder, reducing the risk of symptomatic recurrence and significantly improving adherence to medication. Superiority of home visits with PE in medication adherence demonstrated improvement and impact of PE home visit.

Keywords: Psychoeducation, bipolar affective disorder, psychosocial approach, medication adherence

Nursing care for hospitalized patients with acute mania: a descriptive study

TH Daggenvoorde, B Geerling, PJJ Goossens

Centre Bipolar Disorder, Dementia, Almelo, Netherlands

Aims: When patients diagnosed with a bipolar disorder are suffering from acute mania (forced) admission in a psychiatric hospital is often necessary. Scientific research about the nursing care of patients with an acute mania in a hospital is scarce. To enlarge the body of knowledge a description of the patients' problems, goals and interventions from a nursing perspective is important.

Methods: This qualitative study is carried out in the Netherlands. In total 29 patient reports were examined and 22 nurses from four institutions were individually interviewed on the above mentioned topics. Later on these nurses participated in focusgroup interviews to deepen the findings of the individual interviews. Member checks were carried out to increase the trustworthiness of the findings.

Findings: The data-analysis of the interviews was done by qualitative content analysis, a Top 5 of mentioned nursing problems, goals and interventions per interview was made. Thereafter each topic on 1 got 5 points, on 2 four points etc. So an overall Top 5 was made. This Top 5 was used as input for the focus group inter-

views. Top 5 of problems: 1. Disturbed day-night rhythm, 2. Agitation, 3. No or poor awareness of or insight in the disease, 4. Verbal aggression, 5. Too much physical activity. Top 5 of goals: (1) Stable functioning despite the disease; (2) Increasing awareness of the disease; (3) A stable day-night rhythm; (4) Prevention of injuries; (5) Autonomous functioning despite the disease. Top 5 of interventions: (1) Limit setting; (2) Motivating appropriate use of medication; (3) Administration of medication; (4) Structuring day-night rhythm; (5) Supporting communication.

Conclusions: This study presents what nurses actually do while taking care of patients who are admitted with acute mania in a mental health institution in the Netherlands. We provide rich descriptions of the signs and symptoms per problem, the indicators nurses use to evaluate the goals and the activities nurses do while carrying out the interventions.

The first randomized controlled trial evaluating the impact of genetic counseling for serious mental illnesses

C Hippman^a, A Ringrose^a, A Inglis^a, J Cheek^a, A Albert^b, WG Honer^a, JC Austin^a

^aPsychiatry, University of British Columbia, Vancouver, Canada,

^bWomen's Health Research Institute, BC Women's Hospital and Health Centre, Vancouver, Canada

Importance: Serious mental illnesses (SMI) are complex, highly heritable conditions that affect 1–4% of the population and are associated with social stigma that impairs quality of life and engagement in treatment. Genetic counseling (GC) for diseases such as cancer has been shown to increase patient knowledge and adaptation to illness. Individuals with SMI express interest in GC, however, the potential benefits of GC for those with SMI are uncertain.

Aims: To study the outcomes and potential benefits of GC for people with SMI.

Methods: A three arm, parallel group, randomized controlled trial. Individuals with schizophrenia, bipolar disorder, or schizoaffective disorder (confirmed by the Structured Clinical Interview for Diagnosis), referred by self or psychiatrist, were randomized to one of three groups (each $n = 40$): GC, a control intervention involving an educational booklet, or a waitlist group. Participants completed a purpose-designed measure of knowledge and risk perception, the Internalized Stigma of Mental Illness scale, and the Illness Perception Questionnaire (mental illness version), at baseline (T1) and one month later (T3); those in the GC and educational booklet groups also completed measures immediately post-intervention (T2). The Brief Symptom Inventory was administered at T1 and T3 to control for current symptoms. Missing data were imputed using a multiple imputation method in an intent-to-treat analysis. Analyses included ANCOVAs for between-group effects for continuous variables and chi-squared tests for risk perception accuracy.

Results: Knowledge increased for GC compared to waitlist at T3 ($p = 0.0001$). Risk perception accuracy increased at T3 for GC compared to waitlist ($p = 0.001$) and educational booklet ($p = 0.002$). There were no definitively significant differences between groups for stigma scores or perceived control scores, however, effect sizes for the difference between GC and waitlist group scores on the stigma stereotype endorsement subscale and the perceived control consequences subscale were moderate ($d = 0.67$, $d = 0.43$ respectively).

Conclusions and relevance: GC improves knowledge and risk perception accuracy for this population, and has potential to decrease internalized stigma and increase perceived control. GC should be considered for all patients with serious mental illness.

Keywords: genetic counseling, randomized controlled trial, internalized stigma, perceived control, knowledge

Addressing suicide and self-harm in young people with bipolar disorder

ML Inder^a, MT Crowe^a, S Moor^a, PR Joyce^a, J Carter^b

^aPsychological Medicine, University of Otago, Christchurch, New Zealand,

^bPsychology, University of Canterbury, Christchurch, New Zealand

Rates of attempted and completed suicide are high in Bipolar Disorder (BD). In contrast to the considerable research on suicide and suicide attempt in BD, there is very little data on self-harm, and on the likelihood of "repeat" suicide attempt and self-harm after people with BD undergo treatment. This paper presents the impact of age of onset of BD and comorbidity on self-harming and suicide attempts on young people (15–36 years) participating in a Psychotherapy for Bipolar study and reports on the pattern of suicide attempts and self-harm over the intervention and follow up period. The SCID was used to confirm bipolar diagnosis and identify lifetime comorbidity. Exclusion criteria were minimal. Patients received 18 months of psychotherapy plus medication with 18 month follow-up. One hundred adolescents and young adults (aged 15–36 years) participated with the majority BDI (78%) and female (76%). Previous self-harm occurred in 50 participants and 47 participants had previous attempts at suicide. Co-morbid conditions were very common with comorbidity increasing as the age of onset decreased. Greater comorbidity significantly increased risk of having self-harmed and attempted suicide. Self-harm was predicted by having a lifetime diagnoses of Borderline Personality Disorder and Panic Disorder and an early age of onset. In contrast, suicide attempts were predicted by greater comorbidity but not age of onset. At the conclusion of the three year period the number of suicide attempts and self-harm were markedly reduced with rates of suicide attempts dropping from 11% to 1.3% and self-harm dropping from 15% to 6.7%. This study of young people with BD confirms the presence of high rates of suicide attempts, self-harm and comorbid conditions. Those who have their first episode of BD in childhood and adolescence experience the highest burden and greater of rates of self harming behaviour and suicide attempts. It is important to find effective ways of reducing the burden of BD in adolescents and young adults and mitigating the long term effects of this illness. Given the decline in suicide attempts and self-harm, access to adjunctive psychotherapy may have an important role in contributing to reducing the burden.

The internalized stigma and its correlates in patients with bipolar I disorder in Korea

WJ Kim^a, YJ Song^a, V Ryu^b, JM Kim^a, RY Ha^a, SJ Lee^c, KR Kim^a, HS Cho^a

^aPsychiatry, Yonsei University College of Medicine, Seoul, Korea,

^bPsychiatry, Konyang University College of Medicine, Daejeon,

Korea, ^cInstitute of Behavioral Science in Medicine, Yonsei University College of Medicine, Seoul, Korea

Aims: We aimed to look at the internalized stigma of Korean patients with bipolar I disorder, together with some other mental illness, and to identify the contributing factors to it, among the demographic, psychosocial, and clinical variables.

Methods: A total of 160 subjects (102 patients with bipolar I disorder, 53 with schizophrenia, and five schizoaffective disorder) were recruited from the bipolar disorder clinic in a university mental hospital. We collected the socio-demographic data, clinical variables, and the self-report scales for the internalized stigma, self-esteem, hopelessness, social support, and social conflict.

Results: The internalized stigma was determined in 8 percent of whole participants (9.8% of bipolar I disorder). The scale of internalized stigma itself was not significantly different between diagnostic groups. The education, number of hospitalizations, insight, self-esteem, hopelessness, and social conflict were contributing

factors for internalized stigma in our sample. Divided by diagnostic group, the gender (female) and self-esteem were predictive of internalized stigma in schizophrenia, whereas the education, insight, self-esteem, and social conflict were predictive of it in bipolar I disorder.

Conclusions: The internalized stigma in bipolar disorder might be explained by “psychosocial” factor, such as social conflict, insight, and education, more than in schizophrenia. The active psychosocial intervention (e.g., building-up of the coping strategy for social conflict) can be helpful to overcome the internalized stigma in patients with some mental illness, especially with bipolar disorder. In addition, we added evidence on the need for the program developing personal character such as self-esteem to manage for the patients’ internalized stigma.

Keywords: internalized stigma, psychosocial factors, mental illness, bipolar disorder, Korea

Comprehensive rehabilitation program in bipolar disorder (prisma): a multimodal approach

C Lopez Jaramillo^a, C Vargas^a, S Saldarriaga-Gomez^a, JD Palacio^a, J Ospina-Duque^a, S Ospina^b

^aPsychiatry, Universidad de Antioquia, Medellin, Colombia,

^bEpidemiology, San Vicente Foundation University Hospital, Medellin, Colombia

Patients with bipolar disorder (BD) represent a high social and economic burden to their families and health system. A multimodal approach to this condition needs to be studied to identify potential benefits for both social environment and health system and to establish further treatment guidance. Characterize actual situation of BD, associated conditions such as violence and suicide, and then apply a multimodal approach that can become a national health politic to reduce social and economic burden; analyze the clinical, neurocognitive, neurofunctional, psychologic, occupational and social effect in short-mid-long term of a multimodal approach in patients with BD and to determine if it affects clinical functionality, biomarkers and brain activation. This is a longitudinal randomized controlled trial in which we made an initial evaluation of 200 BD patients, ages 18 to 65, including psychiatric (DIGS, HRSD, YMRS), psychologic (AQ-12, TEMPS-A, FAST, BIS-11, SAI-E), neuropsychologic (Winston card sorting test, CVLT-II, WAIS III, TMT, WMS III, Rey-Osterrieth complex figure), occupational (Social skills inventory, EMES-M, EMES-C, assertiveness test, SAD scale), familiar (FEICS, FACES-III, ECF) and general practitioner (BRIAN, MMSE, Practices and beliefs about health styles questionnaire) evaluations (Multimodal group); samples for biomarkers (NT-3, IL6, 10, 17, BDNF, NT-3, TNF-alpha, Carbonylation of proteins, Nitration of proteins and TBARS) were obtained and fMRI studies were made in 90 patients defined randomly. Patients were then randomly assigned into one of both groups: Control or intervention group. In this last one, participants are going to be enrolled in a multimodal approach based in needs identified by the multimodal group, ranging from 12 to 18 specific interventions including functional remediation and 10 psychoeducation sessions compared to control group, evaluated only by psychiatry and general practitioner as usual. Once intervention is finished, all instruments will be applied again to all participants to compare data before and after intervention. Our study will allow to know the importance of multimodal intervention in BD and targeting intervention goals to functional rehabilitation and not only to the symptomatic improvement. We are planning a second phase to reproduce the multimodal approach intervention in other cities expecting better outcomes and life quality in all participants.

Overcoming stigma: a new psychoeducational and behavior modification course

R Milev^a, H Stuart^b, C Petznick^c

^aPsychiatry, Queen's University, Kingston, Canada, ^bPublic Health, Queen's University, Kingston, Canada, ^cCentre for Neuroscience Studies, Queen's University, Kingston, Canada

Bipolar Disorders are common and associated with significant disability. Stigma because of Bipolar Disorders is also ubiquitous in the society. We have created a new course for people with mood disorders to help them learn more and be able to practice ways to overcome stigma in their lives and themselves. The course is a closed group with five to eight participants, co-led by a mental health professional and a person with lived experience. The course consists of seven 2 h sessions and focus on the following topics: Introduction and orientation; Depression, Anxiety and Recovery; Self-Stigma; Social Stigma—Family, Friends and Medical settings; Stigma in Education, Housing and the Workplace; Disclosure; and Conclusion. There is a homework assigned between sessions. A pilot running of the course has just completed. It was used for a fine-tuning of the course and finalizing the course content. Feedback was encouraged and was used for these purposes. The course: “Overcoming Stigma in Mood Disorders” may have a significant role in helping people with those disorders to achieve recovery.

A new CBT-treatment for bipolar disorder - results from a pilot-study and plan for further testing of the model including an internet-mediated support system

SV Pankowski^a, C Svanborg^a, M Adler^a, G Andersson^b, N Lindefors^a

^aDepartment of Clinical Neuroscience, Karolinska Institute, Stockholm, Sweden, ^bDepartment of Behavioural Sciences and Learning, Linköping University, Stockholm, Sweden

Cognitive-behavioral therapy (CBT) can be used as an adjunctive treatment to medication for persons with bipolar disorder in order to decrease recurrence rate and duration of mood episodes. However, recent meta-analyses show that these treatments have a limited effect on important aspects such as recurrence rate. Thus, new CBT strategies are needed to increase and enrich the impact of CBT. Since 2010 we have developed a new 12-session manual based on Acceptance and Commitment (ACT) for group-treatment of bipolar disorder and co-existing anxiety symptoms. The objective of the pilot-study was to gain knowledge about the needs of persons with bipolar disorder when it comes to treatment interventions and adjustments. Twenty-five adult patients with bipolar disorder were recruited from a specialist mental health service for affective disorders in Stockholm, Sweden. The treatment manual consisted of psychoeducation, mindfulness, identification of values, learning about emotions and how to handle them by acceptance-based tasks. An open trial within-subject design was used for quantitative measures, which patients repeatedly self-assessed. Patients also participated in a semi-structured interview for a qualitative assessment of the treatment effects. Results and earned experiences from the pilot-study have led to a new CBT-model for bipolar disorder and a need to include an internet-mediated support system to enhance learning. In a further study we will compare this new CBT-intervention to treatment as usual on 100 patients with bipolar disorder in a randomized controlled study. The intervention will include skill training, since cognitive and social functions are known to be frequently impaired in persons with bipolar disorder. It will also include treatment of residual symptoms, since they are highly prevalent in bipolar disorder and have been shown to have serious negative impacts on the course of illness. Finally, it will include acceptance and mindfulness practice, since experiences from our pilot study as well as other studies show this is effective

when it comes to treating lifelong severe conditions. The model of a modulated CBT-treatment including an internet-mediated support system may be applied on similar psychiatric diagnoses, such as schizophrenia.

Keywords: bipolar disorder, psychotherapy, outcome, quality of life

Simple psychoeducation conducted in a clinic for patients with bipolar II disorder

Y Saito-Tanji^a, A Nishikawa^b, E Tsujimoto^a, R Taketani^a, A Maruyama^b, H Ono^a

^aDepartment of Psychological Science Graduate School of Humanities, Kwansei Gakuin University, Hyogo, Japan,

^bMaruyama Clinic, Hyogo, Japan

Background and objectives: It has been reported that psychoeducation is one of the effective treatments for maintenance of bipolar disorder. However, in general, it has been too difficult to practice psychoeducation in Japanese clinics. Therefore, we developed a simple method of psychoeducation for use in Japanese clinics and investigated its effectiveness.

Methods: A retrospective review of medical charts from 1st February 2012 to 31st July 2013 was conducted at a psychiatric clinic in Japan. The inclusion criteria for the study were: (1) diagnosis of bipolar II disorder; (2) treatment with a simple psychoeducation procedure that consisted of a patient individually reading a textbook together with a therapist; (3) assessment of knowledge of bipolar disorder using a self-produced questionnaire and (4) Clinical Global Impression-Severity Scale (CGI-S) to evaluate disease severity. This study was approved by Kwansei Gakuin University Regulations for Research with Human Participants.

Results: Five female patients (56.8 ± 20.6 years old, mean ± SD) fulfilled the four criteria. After the simple psychoeducation, comprehensive knowledge of bipolar disorder 19.4 ± 11.2% (mean ± SD), knowledge of its symptoms 31.3 ± 37.1%, knowledge of its managements 21.2 ± 7.3%, and knowledge of its mechanisms 36.2 ± 27.1%, all increased. Moreover, the severity of the disease improved as CGI-S score changed from 4.8 ± 1.1 at baseline to 2.6 ± 0.9 after psychoeducation (mean ± SD).

Conclusion: This study suggests that the simple psychoeducation conducted in a clinic could be effective in bipolar II disorder for improving understanding about the disorder, as well as for reducing its severity.

Group psychoeducation to bipolar patients from South Korea

S Won, T Koo, J Kim, D Kim

Psychiatry, Kyungpook National University Hospital, Daegu, Korea

The evidence for the use of psychoeducation and family-focused therapy as prophylactic adjuncts to medication in patients with stabilized bipolar disorders. There are some elements that are common and hurdles across cultures to implementing psychoeducation in my clinical setting. Korea is one of the few countries in which ethnicity and nationality coincide. Social stigma and poor insight to their illness is the main factor that difficulties in maintaining medical treatments. Most Koreans are highly educated and parents have initiatives to their children economically and emotionally in later years. So psychoeducation program focused to patients and their main care providers for bipolar disorder is very useful in our society. How to manage patients' parents is an important factor in successful psychoeducation program. We conducted modified western developed psychoeducation program for patients with bipolar disorder since 2007. Some experiences to implementing group psychoeducation is discussed in a view of cross-cultural issues.

Relationship management functionality sub-threshold depressive symptoms in bipolar disorder

B Erkek^a, E Ozalp^b, EH Karslioglu^b, S Peker^b, N Sevil^b

^aPsychiatry, State Hospital, Usak, Turkey, ^bPsychiatry, Ankara Oncology Training and Research Hospital, Ankara, Turkey

Aims: Bipolar disorder, which is frequently encountered and has a chronic course, is one of the most common causes of disability. Sub-threshold symptoms that continue even in periods of recovery are one of the important reasons for the prediction of relapse and decreased levels of functioning.

Method: Seventy-three patients with bipolar disorder (bipolar disorder I, bipolar disorder II, bipolar disorder not otherwise specified) were recruited for this study. Patients were grouped according to the phase of their disorder (acute phase, sub-threshold symptoms and remission) during the intake process and they were followed up at the third and sixth months longitudinally. The Young Mania Rating Scale, the Hamilton Depression Scale and the Bipolar Disorder Functionality Scale were administered to all patients.

Results: The bipolar patients who had sub-threshold depressive symptoms were found to score lower on the bipolar disorder functionality scale than the patients who were in remission. These areas are examined subscales: emotional functioning, cognitive functioning, sexual functioning, feelings of stigmatization, social withdrawal, household relations, relationships with friends, participation in social activities, daily activities and hobbies were areas ($p < 0.01-0.05$). Furthermore, it was found that the length of the last episode, age, the first episode, gender, the number of hospitalizations, alcohol use, the length of remission, the severity of depression and having an occupation had effects on some aspects of functioning.

Conclusion: Our study showed that the group of patients with sub-threshold symptoms had more negative results in many aspects of functioning than the group of patients who were in remission. These results indicate that functional recovery should be targeted rather than syndromal recovery, and that sub-threshold symptoms significantly affect levels of functioning. Therefore, it is important to treat sub-threshold symptoms effectively.

Keywords: bipolar disorder, functionality, sub-threshold symptoms

Clinical and neurocognitive predictors of psychosocial functioning in euthymic bipolar II patients

R İlhan, V Senturk Cankorur

Psychiatry, Ankara University School of Medicine, Ankara, Turkey

Aim: There are limited studies investigating psychosocial functioning and its correlates in euthymic bipolar II patients (I). The aim of this study was to investigate psychosocial functioning and its associations with clinical features and neurocognitive functions in euthymic BB-II patients.

Method: Thirty eight euthymic patients with a diagnosis of DSM-IV TR bipolar II disorder participated in this study. Functioning Assessment Short Test (FAST) was used to assess psychosocial functioning. All participants were assessed for psychomotor speed, working memory, executive functions, verbal learning and visuospatial ability, as well as the residual symptoms of depression and mania. The cognitive battery included the Wechsler Memory Scale-R, Wisconsin Card Sorting Test and three subtests of the Wechsler Adult Intelligence Scale Revised, Trail Making Test, Stroop Test, Auditory Consonant Trigram Test, and Wechsler Memory Scale- Revised. All statistics were carried by SPSS.

Results: The mean age was 37.3 (10.5) and the mean education level was 11.6 (3.1). The mean duration of illness was 11.3 (8.0) years. The mean number of depressive and hypomanic episodes were 3.3

(2.1) and 2.2 (1.8), respectively. Most of them were treated with mood stabilizers and atypical antipsychotics. The mean scores of HAM-D, HAM-A, and YMRS were 4.6 (2.0), 7.4 (3.9), and 0.6 (1.5), respectively. There was no significant impairment in psychosocial functioning according to FAST scores, 7.0 (3.5) (1). Psychosocial functioning was only associated with subclinical depressive ($p < 0.01$) and anxiety ($p < 0.01$) symptoms whereas no significant correlations were found between FAST scores and other sociodemographic and clinical variables. Regarding neurocognitive functions, there was no significant association between FAST scores and neurocognitive functions except the categories completed on WCST ($p = 0.04$).

Conclusions: In this study psychosocial functioning was only associated with subclinical depression, anxiety symptoms, and the concept formation. These results suggest that subclinical symptoms and cognitive impairment may have effect adversely psychosocial functioning in euthymic bipolar II patients.

Reference(s): 1. Rosa AR, Bonnin CM, Vazquez GH et al (2010). Functional impairment in bipolar II disorder: Is it as disabling as bipolar I? *Journal of Affective Disorders* 127, 71–76.

Relationship between perceived criticism and emotional social support to depressive symptoms, and social functioning in Japanese patients with bipolar disorder: a preliminary study

M Naruse^a, S Horiuchi^b, Y Sakano^b

^aGraduate School of Psychological Science, Helth Science Univesity of Hokkaido, Sapporo, Japan, ^bSchool of Psychological Science, Helth Science Univesity of Hokkaido, Sapporo, Japan

Introduction: Patients diagnosed with bipolar disorder can show high levels of depressive symptoms and poor social functioning. Perceived criticism from important others such as parents or romantic partners has been shown to influence how severely depressed patients are (Miklowitz et al., 2005). The availability of social support has been shown to reduce depressive symptoms (Johnson et al., 1999). However, no study has been conducted on Japanese patients diagnosed with bipolar disorder. Additionally, no study has been carried out to examine the relationship between perceived criticism from important others and social functioning in this population. Therefore, the purpose of this study was to examine the relationship of perceived criticism from important others and emotional social support to depressive symptoms and social functioning in Japanese patients with bipolar disorder.

Method: Five patients with bipolar disorder participated in this study. After giving informed consent, they completed the following scales: (1) Perceived Criticism Measure (Hooley & Teasdale, 1989); (2) Beck Depression Inventory-II (Beck et al., 1996); (3) Sheehan Disability Scale (Sheehan, 1983); and (4) Emotional Social Support Scale (Munakata et al., 1986). The Perceived Criticism Scale, a one-item scale, assesses the severity of an important other's criticism toward the participant using a 10-point Likert scale. The survey was conducted between June and August 2013.

Results: The severity of perceived criticism showed a significant positive correlation with depressive symptoms ($r = 0.92$, $p = 0.03$) and social functioning ($r = 0.90$, $p = 0.04$), respectively. The magnitudes of the correlations were strong. Emotional social support did not correlate significantly with either depressive symptoms ($r = 0.86$, $p = 0.06$) or social functioning ($r = 0.79$, $p = 0.11$) thereby exhibiting moderate magnitudes. From the findings of this study, it was found that perceived criticism from important others can influence the levels of both depressive symptoms and social functioning, while social support has a weaker influence. Perceived criticism can be modified by providing psycho-education to patients. We suggest that reducing perceived criticism from

important others could buffer depressive symptoms in Japanese patients with bipolar disorder.

Profile of disability in bipolar affective disorder and interplay of social factors: policy and treatment design relevance in a developing context

AT Olagunju^{a,b}, DA Adegbaaju^c, R Uwakwe^d

^aDepartment of Neuropsychiatry, Lagos University Teaching Hospital, ^bCollege of Medicine University of Lagos, Lagos, Nigeria, ^cDepartment of Neuropsychiatry, Federal Neuropsychiatric Hospital Yaba, Lagos, Nigeria, ^dDepartment of Neuropsychiatry and Mental Health, Nnamdi Azikiwe University Teaching Hospital Nnewi, Nnewi, Nigeria

Objectives: Individuals with Bipolar Affective Disorder (BAD) often contend with disability in spite of symptoms remission; making overall outcome unpredictable. This study is aimed at assessing the profile of disability among individuals with BAD and investigates the associated factors.

Methods: A total of one hundred consecutively enrolled study participants, made up of adult outpatients with BAD attending a Lagos based health facility were interviewed. The participants were subjected to questionnaire to inquire about demographic and illness related variables. Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID) was used to confirm diagnoses of BAD in them. Both *Young Mania Rating Scale (YMRS)* and *Hamilton rating scale for depression (HDRS)* were used to rate the severity of symptoms and lastly the *World Health Organisation Disability Assessment Schedule II (WHODAS II)* was used to assess disability in participants.

Results: The mean WHODAS score and range for the participants were 24.93(± 2.2) and 21.11–32.20 respectively. The WHODAS mean score in domain 3[self care, 2.39 \pm 0.30] was least, while domain 6 [participation in the society, 7.55 \pm 1.18] had the highest mean score. Participants that were single ($t = -2.016$, $p = 0.047$) and unemployed ($t = -2.306$, $p = 0.023$) were more disabled, while those that earned money were less disabled ($t = -2.898$, $p = 0.005$).

Conclusions: This study finds varied levels of disability among people with BAD, with participation in the society being the most affected area. The single and unemployed were more likely to be disabled, while those having a source of income seem less disabled. Thus, proactive interventions with incorporation of relevant social policy(s) to address disability in people with BAD to ensure better overall outcome are implied.

Relation between depression, anxiety, self-esteem, demographical factor and maternal complications with fear of childbirth in marital satisfaction, nulliparous women

F Akhlaghi^a, N Mokhber^b, F Shamsa^c

^aObstetrics & Gynecology, Mashhad University of Medical Sciences, Mashhad, Iran, ^bPsychiatry and Behavioral Sciences, Mashhad University of Medical Sciences, Mashhad, Iran, ^cFaculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Introduction: In the present study, the relation of depression, anxiety, self-esteem, marital satisfaction, demographical factor and early maternal complications with Fear of childbirth in primiparous women have been analyzed.

Materials and methods: This study which was done on 100 term primiparous women who referred for caring in last month of pregnancy to prenatal clinic of Omolbanin hospital. Women who had inclusion criteria and consented for participation in this study, filled the questionnaires include personal, demographic, and social

characteristics. Fear of childbirth was assessed by a research designed questionnaire, satisfaction from matrimonial life, self-esteem, anxiety, and depression in participants were determined by using Enrich marital satisfaction questionnaire, Rosenberg scale, Spiel-berger test, Beck depression inventory. After delivery outcomes of their childbirth were recorded and data were analyzed by using SPSS software (version 13) and statistical tests (Pearson correlation, Spearman rating, Man-Whitney, Kolmogorov-Smirnov).

Results: The average age was 22.54 ± 3.7 within the range of 16–36 years. There was a positive and significant correlation between the level of individual's covert and overt anxiety and fear of childbirth ($P < 0.05$). There also was a negative and significant correlation between the level of knowledge about the process of natural childbirth, the rate of cooperation in childbirth, and Apgar score of the neonate with fear of childbirth ($P < 0.05$). There was no significant relationship between the rate of self-esteem, depression, satisfaction from matrimonial life, age, education, income, and early maternal complications with fear of childbirth ($P > 0.5$).

Conclusion: Fear of childbirth in primiparous had a positive and significant correlation with covert and overt anxiety but a negative and significant relationship with level of knowledge about the process of natural childbirth, rate of cooperation in childbirth and Apgar score.

Mania and depression in the perinatal period among women with a history of major depressive disorders

A Inglis, C Hippman, P Carrion, WG Honer, JC Austin

Psychiatry, University of British Columbia, Vancouver, Canada

Background: Women with a history of major depressive disorder (MDD) have increased risks for postpartum depression, but the risk for postpartum mania in this population is unknown.

Aims: To prospectively determine the frequency with which mania occurs in the postpartum among women who have a history of MDD, and to explore temporal relationships between onset of mania/hypomania and depression.

Methods: We administered the Structured Clinical Interview for DSM IV disorders (SCID) to pregnant women with a self-reported history of MDD to confirm diagnosis and exclude women with any history of mania/hypomania. Participants completed the Edinburgh Postnatal Depression Scale (EPDS) and Altman Self-Rated Mania scale (ASRM): once during the pregnancy (~26 weeks), and 1 week, 1 month, and 3 months postpartum.

Results: Among women ($N = 107$) with a SCID-confirmed diagnosis of MDD, 34.6% ($n = 37$) experienced mania/hypomania (defined by an ASRM score of ≥ 6) at ≥ 1 timepoint during the postpartum: and for just over half (20/37, 54%), onset was during the postpartum. The highest frequency of mania/hypomania (26.4%, $n = 26$) was at one week postpartum. Women who experienced mania/hypomania at one week postpartum were not more likely to experience depression later in the postpartum, but were more likely to experience mania/hypomania.

Conclusions: A substantive proportion of women with a history of MDD may experience first onset of manic symptoms in the early postpartum. Confirmatory studies involving diagnostic interviews with this population are needed, but these findings suggest a rationale for screening women with a history of MDD for mania/hypomania during the early postpartum period.

Keywords: mania, hypomania, perinatal, postpartum depression, risk

Maintenance ECT for bipolar disorder

O Koh, H Habil

Psychological Medicine, University Malaya medical Centre, Kuala Lumpur, Malaysia

Electroconvulsive therapy (ECT) is used to treat major mental illnesses. However, it's often seen as controversial. ECT is indicated for mood and psychotic illnesses for rapid and short-term improvement of severe symptoms after adequate trial of other treatment options have proven ineffective and/or when the condition is considered potentially life threatening. A retrospective descriptive study of patients who received ECT in UMMC from 1st January 2007 till 31st December 2007. A total of 157 cases were identified, traced and analyzed. Mean age was 39.9 SD 13.8 range (13–78 years old). Of these 77 (49%) were males and 80 (51%) of them were females. Of those analyzed, 42.7% were diagnosed as having bipolar mood disorder, while almost a third had schizophrenia (32.5%) and the remaining had major depressive disorder. There were 12 patients undergoing maintenance ECT. Majority of them have a mood disorder diagnosis. Most were maintaining well. 2 patients defaulted. Normally, it is only considered when a patient is resistant to all anti-depressants and combination treatments and he or she may benefit from indefinite maintenance ECT, e.g. every 7, 10 or 14 days for a few years.

Conclusion: Maintenance ECT seems to be effective in reducing relapses and enhancing quality of life for bipolar disorder.

Maintenance treatment in patients with BDII misdiagnosed as RDD in Russia

SN Mosolov, AV Ushkalova, EG Kostukova, AA Shafarenko

Department for Therapy of Mental Disorders, Moscow Research Institute of Psychiatry, Moscow, Russia

Background: BD II is frequently misdiagnosed as recurrent depressive disorder (RDD). The consequences of misdiagnosis and inappropriate treatment with antidepressants include a higher risk of rapid cycling, suicide, alcoholism, substance use, sexually transmitted infections, criminal activity, and increased costs of care.

Objective: To assess maintenance therapy during 12 months prior to study enrollment in patients with BDII misdiagnosed as RDD in Russia.

Participants: 409 patients with a current diagnosis of RDD. The mean age of the participants was 48.4 years ($SD = 11$); the ratio of males to females was 21.6%/78.4%. Mean duration of illness was 13 ($SD = 11$) in both groups. There were no statistically significant differences between the two diagnostic groups in the main demographic features.

Methods: The diagnosis was re-established by a qualified psychiatrist and confirmed by the validated Russian version of the Mini International Neuropsychiatric Interview (MINI). The maintenance therapy during previous 12 months was analyzed.

Results: After clinical verification of the diagnosis patients were allocated to 2 groups: (1) with a confirmed diagnosis of RDD ($n = 242$; 59.2%); (2) with a change in diagnosis to BD II ($n = 147$; 35.9%). Patients with other diagnostic categories ($n = 20$) were excluded from further analysis. 29 (20%) of 147 BD II patients misdiagnosed as RDD had received any maintenance therapy for 3 months or more in the previous year in comparison with 78 (32.2%) patients with confirmed diagnosis of RDD. Antidepressants were the most frequently prescribed medications in both groups: 27 (93.3%) of BD patients and 100% of RDD patients had received any of them. The BD group had received 9 (33.3%) TCAs and 16 (5.3%) SSRIs, and 2 (7.4%) SNRIs. Only 3 patients (10.3%) in BD group had received mood stabilizers.

Conclusions: A small number of BDII misdiagnosed as RDD patients in Russia receive any maintenance therapy. Among those who received medical treatment, the majority had antidepressants. Very few patients in spite of RDD diagnosis received mood stabilizers.

The efficacy of psychoeducation with home visit in patients with bipolar affective disorder

TA Batista, C Baes, MF Jurueña

Department of Neuroscience and Behavior, University of Sao Paulo, Ribeirão Preto, Brazil

Background: Recent evidences for Bipolar Disorder (BD) treatment demonstrated that only medication is not enough to stabilize mood. The clinical complexity of this disease, the presence of several comorbidities and the different degrees of adherence to pharmacotherapy, demands the use of diverse therapeutic options. Among the alternatives to meet this demand, we have combined the pharmacological treatment psychoeducational (PE) approach as an effective option in the treatment of individuals with BD. The use of PE in group format has often been used in several studies with good applicability, however PE in home visits to our knowledge have not been evaluated in controlled trials yet. Our aim is to evaluate the efficacy of PE in home visits in bipolar patients in pharmacological treatment and their clinical course, medication adherence and functionality.

Methods: This was a randomized controlled trial with 30 patients with bipolar I or II, according to the DSM-IV criteria. The experimental group consisted of 15 patients received pharmacological treatment and home visits with structure PE intervention reduced version of the PE program created by the Group of Barcelona. The control group consisted of 15 patients received, in addition to pharmacological treatment, home visit without PE. Both groups received weekly visits (8 sessions) with 90 min of duration. The assessment instruments to assess depression, mania and medication adherence were administered at baseline (week 0), 4th week and at the end of interventions (8th week).

Results: The experimental group, after received PE, showed a significant reduction in depression score in Hamilton Depression Rating Scale during the treatment phase ($p < 0.01$). Furthermore, compared to the control group, the PE group showed a significant improvement in medication adherence ($p < 0.01$).

Discussion: The method of PE with home visit provide to be effective as adjunctive treatment for patients with bipolar affective disorder, reducing the risk of symptomatic recurrence and significantly improving adherence to medication. Superiority of home visits with PE in medication adherence demonstrated improvement and impact of PE home visit.

Keywords: Psychoeducation, Bipolar affective disorder, Psychosocial approach, medication adherence

Lurasidone in bipolar I depression: a 24 week, open-label extension study

TA Ketter^a, K Sarma^b, R Silva^a, H Kroger^b, J Cucchiaro^b, A Loebe^b, F Grossman^b, A Pikalov^a

^aPsychiatry, Department of Psychiatry and Behavioral Sciences Stanford University School of Medicine, Stanford, USA, ^bClinical Development, Sunovion Pharmaceuticals Inc, Fort Lee, NJ, USA,

^cClinical Development, Sunovion Pharmaceuticals Inc, Stanford, CA, USA

Aims: To evaluate the longer-term safety and tolerability of lurasidone in bipolar I depression.

Methods: Patients completing 6 weeks of double-blind, placebo-controlled treatment with either lurasidone monotherapy (1 study) or lurasidone adjunctive therapy with lithium (Li) or valproate

(VPA; 2 studies), were treated for 6 months with once-daily flexible doses of lurasidone, 20–120 mg/day in this open-label extension study (N = 817; monotherapy, 39%; adjunctive therapy, 61%). Safety endpoints were analyzed as change from double-blind baseline for study completers who had initially been randomized to lurasidone in the initial 6 week study (30 weeks of total exposure; monotherapy, n = 154; adjunctive, n = 104). Efficacy endpoints were secondary, and included the MADRS and the CGI-BP-Severity of depression score.

Results: A total of 68% of patients completed the extension study. Adverse events (AEs, incidence $\geq 5\%$) were akathisia (8.1%), headache (7.7%), nausea (7.6%), insomnia (6.4%), and anxiety (5.8%). Discontinuation due to an AE occurred in 7.0% of monotherapy patients and 8.7% of adjunctive therapy patients. Mean change in weight at month 6 was +0.45 kg in the monotherapy group and +0.90 kg in the adjunctive group. Median changes observed at month 6 were: total cholesterol (monotherapy, 0.0 mg/dL; adjunctive, -1.5 mg/dL); triglycerides (monotherapy, +6.0 mg/dL; adjunctive, +8.0 mg/dL); glucose (monotherapy, 0.0 mg/dL; adjunctive, +1.0 mg/dL); and prolactin (monotherapy, +1.3 ng/dL; adjunctive, +1.3 ng/dL). The incidence of protocol-defined treatment-emergent mania was 1.3% in the monotherapy treatment subgroup and 3.8% in the adjunctive subgroup; the incidence of “any suicidal ideation or behavior” on the Columbia Suicide Severity Rating Scale was 2.1%. The following mean changes were observed at month 6 (observed case) for the MADRS (monotherapy: -6.9; adjunctive: -6.5), CGI-BP-S (monotherapy: -0.87; adjunctive: -0.85), and Young Mania Rating Scale (monotherapy: -0.8; adjunctive: -0.5).

Conclusions: Long term treatment with lurasidone 20–120 mg/day for 6 months was safe and well tolerated with minimal effect on weight and metabolic parameters. There were minimal differences in tolerability or safety outcomes in patients who received lurasidone monotherapy or adjunctive therapy with lithium or valproate. Treatment with lurasidone was associated with sustained improvement in MADRS. Sponsored by Sunovion Pharmaceuticals Inc.

Efficacy and safety of lurasidone in bipolar depression: results from two, double blind, placebo-controlled studies

A Loebe^a, J Cucchiaro^a, R Silva^a, K Sarma^a, H Kroger^a, J Calabrese^b, G Sachs^c, F Grossman^a, A Pikalov^a

^aClinical Development, Sunovion Pharmaceuticals Inc, Fort Lee, NJ, USA, ^bPsychiatry, University Hospitals Case Medical Center Case Western Reserve University, Cleveland, OH, USA, ^cBipolar Clinic and Research Program, Massachusetts General Hospital, Boston, MA, USA

Aims: To evaluate the efficacy of lurasidone as monotherapy, or adjunctive therapy with lithium (Li) or valproate (VPA), in treating bipolar I depression.

Methods: Patients with bipolar I depression were randomized, in 2 double-blind trials, to 6 weeks of once-daily treatment with lurasidone (20–120 mg/day) vs. placebo, each adjunctive with Li or VPA (N = 346); or monotherapy treatment with lurasidone (fixed-flexible doses of 20–60 mg/day or 80–120 mg/day) vs. placebo (N = 505) compared with placebo. The primary outcome was change in depressive symptoms, assessed by the MADRS; the key secondary outcome was change in the Clinical Global Impression Bipolar Severity of Illness (CGI-BP-S) depression score in both the studies.

Results: In the adjunctive therapy study, treatment with lurasidone significantly reduced mean MADRS scores compared with the placebo group (-17.1 vs. -13.5; $p = 0.005$; effect size = 0.34) with a significantly greater endpoint reduction in CGI-BP-S depression

Sixteenth Annual Conference on Bipolar Disorders

scores compared with placebo (-1.96 vs. -1.51 ; $p = 0.003$; effect size = 0.36) at week 6. In the monotherapy study, treatment with lurasidone significantly reduced mean MADRS total scores for the lurasidone 20–60 mg/day (-15.4 ; $p < 0.001$; effect size = 0.51) and 80–120 mg/day (-15.4 ; $p < 0.001$; effect size = 0.51) groups compared with placebo (-10.7) with a significantly greater endpoint reduction in CGI-BP-S depression scores (lurasidone 20–60 mg/day 1.8 ; $p < 0.001$; effect size = 0.61) and 80–120 mg/day groups (-1.7 ; $p < 0.001$; effect size = 0.50) compared with placebo (-1.1) at week 6. Significantly greater improvement in anxiety symptoms, and in patient-reported measures of quality of life (Q-LES-Q) and functional impairment (SDS), were observed in both studies. In the adjunctive therapy study, adverse events more frequently reported

on lurasidone were nausea, somnolence, tremor, akathisia, and insomnia. In the monotherapy study, adverse events more frequently reported on lurasidone were nausea, headache, akathisia, and somnolence. In both studies minimal changes in weight, lipids, and measures of glycemic control were observed during treatment with lurasidone.

Conclusions: Treatment with lurasidone 20–120 mg/day, either as monotherapy, or adjunctive with Li or VPA, significantly improved depressive symptoms in patients with bipolar I depression. Lurasidone was well-tolerated with few changes in weight or metabolic parameters. Sponsored by Sunovion Pharmaceuticals Inc.