

Outcome Scales (HoNOS) and Liverpool University Neuroleptic Side Effect Rating Scale (LUNERS).

**Results** Of 32 completers who experienced a beneficial effect of memantine 23 patients continued memantine for one year. Memory improvement was sustained, verbal recognition memory improved even further between  $t=26$  weeks and  $t=52$  weeks. Continued treatment with memantine add-on to clozapine was associated with significantly improved PANSS positive, negative and overall score, CGI-S and HoNOS scores.

**Conclusions** In the extension phase the positive effect of memantine add-on therapy on verbal memory sustained and positive, negative and overall symptoms of schizophrenia, clinical global status and psychosocial functioning significantly improved. Memantine was well tolerated without serious adverse effects.

**Disclosure of interest** The authors have not supplied their declaration of competing interest.

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## FC95

### Decreased interhemispheric resting state functional connection in schizophrenic patients with auditory hallucinations

H. Wang<sup>1,\*</sup>, G. Wang<sup>2</sup>

<sup>1</sup> Renmin Hospital of Wuhan University, Wuhan, China

<sup>2</sup> Renmin Hospital of Wuhan University, Department of Psychiatry, Wuhan, China

\* Corresponding author.

**Introduction** Auditory hallucination (AH) has been always concerned as a main core symptom of schizophrenia. However, the mechanisms of AH are still unclear.

**Objectives** The aim of this study is to further explore the complicated neuroimaging mechanism of AHs from a new insight by using voxel-mirrored homotopic connectivity (VMHC).

**Methods** Forty-two patients with AH (APG), 26 without AHs (NPG) and 82 normal controls (NC) participated in resting state fMRI scan. Correlation analyses were used to assess the relationships between VMHC and Hoffman scores. Additionally, ROI analysis was used to further know about the functional connectivity between the brain areas with changed interhemispheric FC and the whole brain.

**Results** APG showed reduced VMHC in the parahippocampus, fusiform gyrus, rolandic operculum, insula, heschl's gyrus and superior temporal gyrus (STG). Hoffman score of APG group had negative correlation with VMHC in these regions. Besides, ROI analysis supported decreased interhemispheric FC in schizophrenia with AH and verified functional connectivity abnormalities in schizophrenia.

**Conclusions** These findings suggest impairment of interhemispheric coordination and whole brain FC in schizophrenia with AH, which may be implicated to the neuroimaging mechanism of auditory hallucination. Furthermore, this research highly support dysconnectivity hypothesis that schizophrenia related to abnormalities in neuronal connectivity.

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## FC96

### Efficacy and safety of brexpiprazole in schizophrenia: Meta-analysis of three double-blind, randomized, placebo-controlled phase 3 studies

C. Weiss<sup>1,\*</sup>, P. Zhang<sup>2</sup>, M.J. Hakala<sup>3</sup>, A. Skuban<sup>4</sup>, E. Weiller<sup>5</sup>

<sup>1</sup> Otsuka Pharmaceutical Development & Commercialization Inc., Global Medical Affairs, Princeton, USA

<sup>2</sup> Otsuka Pharmaceutical Development & Commercialization Inc., Biostatistics, Princeton, USA

<sup>3</sup> H. Lundbeck A/S, ICR Psychiatry, DK, Valby, Denmark

<sup>4</sup> Otsuka Pharmaceutical Development & Commercialization Inc., Global Clinical Development, Princeton, USA

<sup>5</sup> H. Lundbeck A/S, Medical Affairs, Valby, Denmark

\* Corresponding author.

**Introduction** Brexpiprazole is a serotonin-dopamine activity modulator that is a partial agonist at 5-HT1A and dopamine D2 receptors at similar potency, and an antagonist at 5-HT2A and noradrenaline alpha1B/2C receptors.

**Objectives** To evaluate the efficacy, safety, and tolerability of brexpiprazole in patients with acute schizophrenia in a meta-analysis of three phase 3 studies with brexpiprazole.

**Aim** The primary endpoint was change from baseline to week 6 in PANSS total score.

**Methods** Data from the 3 clinical studies in patients with acute schizophrenia were combined and analyzed using individual patient data meta-analysis. In two similarly designed studies (NCT01396421; NCT01393613), patients with acute schizophrenia were randomized to fixed-doses of brexpiprazole 2 mg/day, 4 mg/day or placebo (a low-dose treatment group was included in each study [0.25 mg and 1.0 mg]; not included in the meta-analysis). In the third study (NCT01810380), patients were randomized to flexible dosing of brexpiprazole (2 to 4 mg/day), placebo, or an active reference (quetiapine extended release). Changes from baseline for brexpiprazole vs. placebo were analyzed using an MMRM approach.

**Results** Brexpiprazole 2–4 mg ( $n=868$ ) was superior to placebo ( $n=517$ ) in change from baseline in PANSS total score ( $-20.1$  vs.  $-14.3$ ; estimated treatment difference to placebo:  $-5.8$  [95% CI:  $-8.0$ ;  $-3.6$ ];  $P<0.001$ ). The proportions of patients reporting TEAEs were similar between the brexpiprazole and placebo treatment groups (57.9% vs. 57.5%). No unexpected safety concerns were observed.

**Conclusion** This meta-analysis supports evidence from three individual trials that brexpiprazole is efficacious and safe in treating patients with acute schizophrenia.

**Disclosure of interest** The authors have not supplied their declaration of competing interest.

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## Sleep disorders and stress

### FC97

#### Sleep disturbances and substance use disorders: An international study of primary care and mental health specialty care patients

L. Fortuna<sup>1,\*</sup>, N. Noyola<sup>2</sup>, B. Cook<sup>3</sup>, A. Amaris<sup>2</sup>

<sup>1</sup> Boston Medical Center, Psychiatry, Child and Adolescent Psychiatry, Boston, USA

<sup>2</sup> Massachusetts General Hospital, Disparities Research Unit, Boston, USA

<sup>3</sup> Cambridge Health Alliance and Harvard Medical School, Health Equity Research Lab, Cambridge, USA

\* Corresponding author.

**Introduction** There is no comprehensive evidence on the influence of sleep disturbances (SD) on substance use disorders (SUD) or treatment use patterns of individuals with comorbid disturbances.

**Objective/aim** To better understand comorbidities and treatment use patterns of individuals with SD and SUD.

**Methods** We combine 2010–2012 electronic health record (EHR) data from healthcare system in Boston ( $n = 131,966$  person-years) and Madrid, Spain ( $n = 43,309$  person-years). Patients with sleep disturbances (SD) were identified in the EHR through ICD-9 codes and medical records and substance use disorders (SUD) identified by documented treatment for drug or alcohol abuse or dependence. Rates of SUD are compared between individuals with and without SD. Among those with both, adequacy of mental health treatment (defined as eight or more outpatient visits or four or more outpatient visits with a psychotropic prescription) and ER use is compared.

**Results** Among the individuals, 21.1% with SD also report SUD, compared to only 10.6% of individuals without SD ( $P < .01$ ). Those with comorbidities were more likely than their specialty care counterparts without comorbidities to be seen in the ER (57.1% vs. 36.6%, respectively,  $P < .05$ ). Limiting the sample to only those with both SD and SUD in specialty mental health care ( $n = 268$  in Boston and  $n = 28$  in Madrid), 49.2% of Boston patients received adequate care compared to 38.5% of Madrid patients, and 57.8% of Boston patients had any ER use in the last year vs. 50% of Madrid patients.

**Conclusions** SD is correlated with SUD and comorbid patients are more likely to use emergency services.

**Disclosure of interest** The authors have not supplied their declaration of competing interest.

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## FC98

### Sensory hypersensitivity predicts reduced sleeping quality in patients with major affective disorders

G. Serafini<sup>1,\*</sup>, B. Engel-Yeger<sup>2</sup>, X. Gonda<sup>3</sup>, M. Pompili<sup>4</sup>, Z. Rihmer<sup>3</sup>, M. Amore<sup>1</sup>

<sup>1</sup> University of Genoa, Neuroscience DINOGMI, Genoa, Italy

<sup>2</sup> Faculty of Social Welfare and Health Sciences, University of Haifa, Occupational Therapy, Haifa, Italy

<sup>3</sup> Kutvolgyi Clinical Center, Semmelweis University, Clinical and Theoretical Mental Health, Budapest, Hungary

<sup>4</sup> Sant'Andrea Hospital, Sapienza University of Rome, Neuroscience, Rome, Italy

\* Corresponding author.

**Introduction** Major affective disorders ranging from subthreshold affective temperaments to severe affective diseases and anxiety, are frequently associated with sleep–wake dysregulation. Interestingly, recent studies suggested an active role of Sensory Processing Disorders (SPD) in the emergence of sleep disturbances.

**Objectives** The objective of this study was to investigate the relationship between SPD and sleep quality in subjects with major affective disorders and specific affective temperaments.

**Aims** This study aimed to examine the sensory profile (expressed in hypersensitivity or hyposensitivity) of patients with major affective disorders and its relative contribution to the prediction of sleep quality while also considering affective temperaments and depression, known as factors that may impact sleep quality.

**Methods** We recruited 176 participants (mean age = 47.3) of which 56.8% have unipolar depression and 43.2% bipolar disorder. Reduced sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI) whereas affective temperaments were assessed using the Temperament Evaluation of Memphis, Pisa, Paris and San Diego (TEMPS).

**Results** Sensory hypersensitivity, assessed using Adolescent/Adult Sensory Profile (AASP), significantly distinguished between poor and good sleepers. Sleep quality was mainly predicted by the Beck Depression Inventory-II total score and anxious temperament. Yet, sensory hypersensitivity contributed to this prediction mainly in regard to sleep efficiency and related daytime dysfunctions.

**Conclusions** The careful assessment of the unique sensory profile and its behavioral/functional influence on patients' quality of life may help clinicians and health providers in developing targeted treatment interventions.

**Disclosure of interest** The authors have not supplied their declaration of competing interest.

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## FC99

### Association between circadian rhythm, sleep disturbances and temperament in major depression, bipolar disorder and schizophrenia

S. Tunç<sup>1,\*</sup>, İ. Yağcı<sup>1</sup>, Y. Yenilmez Bilgin<sup>2</sup>, Ö. Canbek<sup>3</sup>, M.İ. Atagün<sup>4</sup>, N. Hüseyinoğlu<sup>5</sup>, S. Ardic<sup>6</sup>

<sup>1</sup> Kafkas University School of Medicine, Psychiatry, Kars, Turkey

<sup>2</sup> Istanbul Kanuni Sultan Süleyman Research and Training Hospital-Formerly Kafkas University School of Medicine, Psychiatry, Istanbul, Turkey

<sup>3</sup> Istanbul Bakırköy Research and Training Hospital for Psychiatry, Psychiatry, Istanbul, Turkey

<sup>4</sup> Ankara Yıldırım Beyazıt University School of Medicine, Psychiatry, Ankara, Turkey

<sup>5</sup> Kafkas University School of Medicine, Neurology, Kars, Turkey

<sup>6</sup> Kafkas University School of Medicine, Chest Diseases, Kars, Turkey

\* Corresponding author.

**Introduction** Circadian rhythms and quality of sleep have been associated with temperament characteristics in healthy populations. Since temperaments are personality traits concerning the behavioral, motivational and emotional responses, adaptive capacity for sleep and circadian rhythm may also be related with temperament traits.

**Aims** To identify the determinants of sleep quality (SQ) and biological rhythm (BR) in bipolar disorder, schizophrenia and depression among temperament measures.

**Methods** Patients with bipolar disorder (BD,  $n = 49$ ), major depression (MD,  $n = 35$ ), schizophrenia (SZ,  $n = 30$ ) and a healthy control group (HC,  $n = 36$ ) were enrolled. Pittsburgh Sleep Quality Index (PSQI), Biological Rhythms Interview of Assessment in Neuropsychiatry (BRIAN) and the Temperament and Character Inventory (TCI) were the measures. One-way ANOVA, Spearman Correlation Test and Linear Regression analyses were the other comparisons.

**Results** Determinants of sleep quality were self-directedness in MD [ $F(1,26) = 6.10$ ,  $P = 0.020$ ] and BD [ $F(1,31) = 10.88$ ,  $P = 0.002$ ] groups. Self-transcendence ( $P = 0.004$ ), self-directedness ( $P = 0.038$ ) and persistence ( $P = 0.05$ ) were the determinants of sleep quality in schizophrenia group [ $F(3,21) = 9.71$ ,  $P < 0.001$ ]. Harm-avoidance was the determinant of sleep quality in the HC group [ $F(1,28) = 7.97$ ,  $P < 0.001$ ]. Determinants of biological rhythms were harm-avoidance in the BD group [ $F(1,32) = 9.65$ ,  $P = 0.004$ ] and self-directedness in the SZ group [ $F(1,23) = 11.09$ ,  $P = 0.003$ ] and harm-avoidance ( $P < 0.001$ ) and self-transcendence ( $P = 0.039$ ) in the HC group [ $F(2,27) = 15.81$ ,  $P < 0.001$ ].

**Conclusions** Self-Directedness was associated with circadian rhythm and sleep quality in MD, BD and SZ groups. Extreme temperament features may contribute to emotional and behavioral dysfunction, which may lead to abnormal sleep patterns in psychiatric disorders.

**Keywords** Sleep; Circadian rhythm; Temperament; Bipolar disorder; Schizophrenia; Depression

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