

explore how black South Africans diagnosed with schizophrenia experience their illness from their cultural point of view.

**Methods:** The study followed a hermeneutic phenomenological approach. In-depth interviews were conducted with three patients diagnosed with schizophrenia and on medication for their illness. Their stories were analysed using thematic content analysis.

**Results:** Five themes emerged during the study. Theme 1 related to Naming Things. The name given to their illness significantly affected the meanings that were attached to the illness. Theme 2 referred to Being Without. Losses as well as gains became apparent. Participants had lost their roles, independence and intimacy; however, they developed other coping strategies and some relationships became stronger. Theme 3 pertained to Connections and Disconnections. While participants were connected to their families and their community, they also felt disconnected due to the stigma perceived. Theme 4 was the theme of Being Spiritual. Spirituality played a vital role in how participants attached meaning to their illness, and it helped them to cope with challenges. Theme 5 was Rainbow after the Rain. The negative connotation of having a mental illness turned into personal, inter-personal and spiritual growth. The devastating illness became a gift to all participants; they demonstrated immense levels of resilience and they found their own way of being and relating.

**Discussion:** Culture played a crucial role during the initial stages of the illness; all participants sought spiritual help and it determined the meanings attached to the illness. This study proposes a need for mental health workers to explore the challenges that hamper openness within families and communities in order to lessen the perceived stigma experienced by the patients, and to acknowledge and encourage different coping and meaning-making structures, such as spirituality.

## T217. FACTORS RELATED TO SUICIDAL BEHAVIOR IN KOREAN PATIENTS WITH BIPOLAR DISORDER: THE EFFECT OF MIXED FEATURES ON SUICIDALITY

Hye-Jin Seo<sup>\*1</sup>, Hee Ryung Wang<sup>2</sup>

<sup>1</sup>*Yong-In Mental Hospital*; <sup>2</sup>*Yeouido St. Mary's Hospital, The Catholic University of Korea*

**Background:** The aim of the present study was to investigate various risk factors of suicidal behaviors, including mixed feature specifier, in Korean patients with bipolar disorder.

**Methods:** We retrospectively reviewed medical charts from 2005 to 2014. A total of 334 patients diagnosed with bipolar disorder using DSM-IV TR were enrolled. The subjects were categorized into two groups according to history of suicidal behaviors and compared regarding demographic and clinical characteristics including mixed feature specifier. We re-evaluated the index episode using the DSM-5 criteria and classified into index episode with and without mixed feature. Logistic regression was performed to evaluate significant risk factors associated with suicidal behavior.

**Results:** Suicidal behavior had independent relationship with mixed feature at index episode using DSM-5 criteria and number of previous depressive episodes in Korean bipolar patients. The mixed feature specifier was the strongest risk factor in the present study.

**Discussion:** Suicidal behavior had independent relationship with mixed feature at index episode using DSM-5 criteria and number of previous depressive episodes in Korean bipolar patients. The mixed feature specifier was the strongest risk factor in the present study.

## T218. IDENTIFICATION OF FIRST-EPIISODE PSYCHOSIS SUBGROUPS BASED ON POSITIVE SYMPTOM DOMAINS AND THEIR SOCIODEMOGRAPHIC AND CLINICAL CORRELATES

Chiara Galletti<sup>\*1</sup>, Luca Pauselli<sup>2</sup>, Marc Manseau<sup>3</sup>, Alfonso Tortorella<sup>1</sup>, Michael T. Compton<sup>2</sup>

<sup>1</sup>*University of Perugia*; <sup>2</sup>*Columbia University*; <sup>3</sup>*New York University*

**Background:** Although the heterogeneous nature of psychosis is well established in the literature, genetics, neurophysiology, and neuroimaging have not yet succeeded in an unequivocal classification of the diverse clinical presentations. For the time being, the field relies mostly on a symptom-based, descriptive diagnostic system. The purpose of the current study was to use seven previously identified positive symptom domains to identify possible subgroups of first-episode psychosis (FEP), using cluster analysis. In addition, we tested whether possible subgroups differed across a number of sociodemographic and clinical variables.

**Methods:** We analyzed data from a large FEP sample (n=247) to identify possible clinical subgroups of psychosis based on positive symptoms; specifically, delusion and hallucination domains resulting from previous factor analyses of Scale for the Assessment of Positive Symptoms (SAPS) items in this sample. A rigorous methodology was applied to perform cluster analysis and identify FEP subgroups. Kruskal-Wallis tests with pairwise post-hoc comparisons were used to check the differences in each positive symptom domain between the subgroups. Bivariate analyses comparing subgroups on a number of sociodemographic and clinical characteristics were performed.

**Results:** Five FEP subgroups were identified based on the severity of seven domains of delusions and hallucinations. Three of them (Mild Positive Symptoms Subgroup, Moderate Positive Symptoms with Sin/Guilt and Jealousy Delusions Subgroup, Severe Positive Symptoms Subgroup) shared a similar psychopathological profile, with typical psychotic symptoms differing in severity. Another subgroup was characterized by high severity on typical and atypical symptoms (Severe Mixed Atypical Positive Symptoms Subgroup), and the other by high severity in somatic delusions (Somatic Delusions Subgroup). The five subgroups did not significantly differ in terms of gender, age at onset, family history, mode of onset of psychosis, premorbid functioning, and alcohol and non-cannabis drug use disorders, though some potential signals were identified, (but not reaching statistical significance due to small sample sizes in the subgroups). Significantly different prevalence rates of cannabis use disorder were found across the five subgroups.

**Discussion:** In our analysis, five possible FEP subgroups were identified based on the severity of seven domains of delusions and hallucinations: three of them shared a similar psychopathological profile differing in severity, and two were characterized by different atypical symptoms. Despite several acknowledged limitations, our results highlight the potential to identify clinical phenotypic subgroups of FEP, which may be helpful in future research aimed at filling the gaps between clinical, neuropathological, and genetic explanations of psychosis etiology. Such an approach may also lead to better targeted preventive interventions and more individualized and effective treatments.

## T219. THE ROLE OF MELATONIN AND MELATONIN AGONISTS IN COUNTERACTING ANTIPSYCHOTIC-INDUCED METABOLIC SIDE EFFECTS: A SYSTEMATIC REVIEW

Won-Myong Bahk<sup>\*1</sup>, Young Joon Kwon<sup>2</sup>, Bo-Hyun Yoon<sup>3</sup>, Sang-Yeol Lee<sup>4</sup>, Kwanghun Lee<sup>5</sup>, Duk-In Jon<sup>6</sup>, Moon Doo Kim<sup>7</sup>, Eunsung Lim<sup>8</sup>

<sup>1</sup>*Catholic University of Korea*; <sup>2</sup>*Soonchunhyang University*; <sup>3</sup>*Naju National Hospital*; <sup>4</sup>*Wonkwang University, School of Medicine*; <sup>5</sup>*College of Medicine, Dongguk University*; <sup>6</sup>*College of Medicine, Hallym University*; <sup>7</sup>*School of Medicine, Jeju National University*; <sup>8</sup>*Shinsegae Hospital*

**Background:** Melatonin administration to high cholesterol-treated and high fat-treated rats has been shown to suppress body weight and visceral adiposity. In addition, in various animal models related to obesity, metabolic syndrome, and diabetes, melatonin has beneficial efficacy in ameliorating various metabolic symptoms, including attenuating weight gain, lowering blood pressure (BP), and improving insulin resistance. This systematic

review aims to investigate whether melatonin or melatonin agonists significantly attenuate metabolic side effects among psychiatric populations treated with atypical antipsychotics.

**Methods:** Four randomized controlled trials were identified through a comprehensive literature search using MEDLINE, EMBASE, and the Cochrane Library on 22 October 2015. These four trials (including three melatonin studies and one ramelteon study) included 138 patients, of whom 71 were treated with melatonin or ramelteon and 67 were treated with a placebo. Because of high heterogeneity, we did not carry out a meta analysis.

**Results:** Melatonin was beneficial in lowering blood pressure among bipolar disorder patients; this blood pressure-lowering effect was not prominent among schizophrenic patients. Melatonin appeared to improve lipid profiles and body composition and attenuated weight gain among both schizophrenic and bipolar disorder patients. Ramelteon showed a significant efficacy in lowering total cholesterol level.

**Discussion:** Despite the few studies included, this systematic review provided promising evidence of the potential benefits of melatonin and its agonists in attenuating one or more components of metabolic syndrome among psychiatric patients using atypical antipsychotics.

## T220. THE GLUTAMINASE INHIBITOR EBSELEN PREVENTS AMPHETAMINE SENSITIZATION IN MICE

Lior Heffetz-Giterman<sup>1</sup>, Sharon S. Lander<sup>1</sup>, Reut Cohen<sup>1</sup>, Amit Gross<sup>1</sup>, Inna Gaisler-Salomon<sup>\*1</sup>

<sup>1</sup>University of Haifa

**Background:** Dysregulated glutamatergic neurotransmission has been strongly implicated in the pathology of schizophrenia (SZ). Glutaminase 1 (GLS1) plays a critical role in the recycling of glutamate. GLS1 deficient mice were previously shown to display an attenuated response to the acute and chronic effects of the dopamine-releasing psychotomimetic drug amphetamine and have a pro-cognitive profile. A recent large-scale drug screening study identified ebselen as a potent CNS-available GLS1 inhibitor. Here, we asked whether ebselen (10 mg/kg) would attenuate sensitization to amphetamine (4 mg/kg) and induce pro-cognitive behavior.

**Methods:** Sensitization to amphetamine (4mg/kg) was tested in the open field. Mice received either saline, amphetamine or amphetamine+ebselen (10mg/kg) i.p. on 4 consecutive days. Seven days later, mice were challenged with amphetamine, amphetamine+ebselen or saline. We further assessed the effect of ebselen administration on Glsl mRNA in the hippocampus, prefrontal cortex and striatum, and on dopamine receptor expression in the striatum. Finally, we measured social preference and recognition in genetically modified GLS1 deficient mice and in ebselen (10mg/kg)-treated wild-type mice.

**Results:** We found decreased sensitization to amphetamine in mice that received pre-treatment with ebselen. Gene expression studies revealed reduced Glsl expression in hippocampus, and altered expression of dopamine markers in the striatum of ebselen-treated mice. Finally, ebselen-treated mice show enhanced social recognition, similarly to GLS1 deficient mice.

**Discussion:** Similarly to genetically modified GLS1 deficient mice, ebselen-treated mice demonstrate resilience to the sensitizing effects of the pro-psychotic drug amphetamine and a pro-cognitive phenotype. These findings provide evidence for the potential of GLS1 inhibition in addressing some of the central clinical features of SZ and related pathology.

## T221. LURASIDONE DISPLAYS ANTIDEPRESSANT AND PRO-COGNITIVE EFFECTS IN THE CHRONIC MILD STRESS MODEL: A ROLE FOR REDOX MECHANISMS AND PARVALBUMIN EXPRESSION

Andrea Carlo Rossetti<sup>1</sup>, Maria Serena Paladini<sup>1</sup>, Paola Brivio<sup>1</sup>, Giulia Sbrini<sup>1</sup>, Mariusz Papp<sup>2</sup>, Francesca Calabrese<sup>1</sup>, Raffaella Molteni<sup>1</sup>, Marco Andrea Riva<sup>\*1</sup>

<sup>1</sup>University of Milan; <sup>2</sup>Polish Academy of Sciences, Krakow

**Background:** Exposure of rodents to chronic stress is able to recapitulate a number of functional alterations that are associated with psychiatric disorders, including anhedonia and cognitive impairment. Stress-based experimental models are also useful to investigate the ability of pharmacological intervention in normalizing such defects as well as the molecular alterations associated with the behavioral phenotype. On these bases, the aim of the present study was to investigate the ability of a chronic treatment with the multi-receptor modulator lurasidone in normalizing behavioral changes produced by chronic mild stress (CMS) in rats. Moreover, we investigated the potential contribution of parvalbumin expression and of redox mechanisms in the alterations brought about by CMS exposure.

**Methods:** Adult male Wistar rats were exposed to CMS for 2 weeks and sucrose consumption was used to identify rats that were susceptible to the stressful manipulation. Control and CMS-susceptible rats were then randomized to receive chronic vehicle or the multi-receptor modulator lurasidone (3 mg/kg/day) for 5 more weeks, while continuing the stress procedure. Animals were tested for anhedonia, using the sucrose intake test, and for cognitive impairment, using the novel object recognition (NOR) test. Rats were sacrificed at the end of the procedures and the brain regions of interest were dissected and used for the molecular analyses.

**Results:** Exposure to CMS produced a persistent anhedonic phenotype as well as a significant deficit in the NOR test. Both behavioral abnormalities were normalized by chronic lurasidone treatment. Rats exposed to CMS display a marked and selective reduction in the expression of parvalbumin, which identifies a subpopulation of GABAergic interneurons, in dorsal (but not ventral) hippocampus, an effect that was normalized by chronic lurasidone administration. CMS rats also show a significant up-regulation of (NADPH) oxidase 2 (NOX2), which is critically involved in oxidative stress, as well as a down-regulation of Nrf-2, a master regulator of antioxidant defense. These alterations in dorsal hippocampus were normalized in animals that received chronic lurasidone treatment that was also capable of reducing the levels of Keap-1, an important player that exerts a repressive control over Nrf-2.

**Discussion:** Our results demonstrate the ability of lurasidone in normalizing anhedonia and cognitive deficits associated with CMS exposure, suggesting its effectiveness on different 'domains' (RDoC) that characterize psychiatric disorders. Lurasidone was also able to normalize the effects produced by CMS exposure on parvalbumin expression, possibly through its ability in promoting anti-oxidative mechanisms within the dorsal hippocampus. All in all, these effects may promote resilience toward the alterations produced by adverse environmental conditions, such as stress, which represents a major vulnerability element in the etiology of psychiatric disorders.

## T222. EARLY TREATMENT RESISTANCE IN A LATIN-AMERICAN COHORT OF PATIENTS WITH SCHIZOPHRENIA

Cristian Mena<sup>1</sup>, Alfonso Gonzalez-Valderrama<sup>1</sup>, Barbara Iruetagoiena<sup>2</sup>, Juan Undurraga<sup>1</sup>, Nicolas Crossley<sup>\*2</sup>  
<sup>1</sup>J. Horwitz Psychiatric Institute; <sup>2</sup>Universidad Católica de Chile

**Background:** Failure to respond to antipsychotic medication in schizophrenia is a common clinical scenario with significant morbidity. Recent studies have highlighted that many patients present treatment-resistance from disease onset. We here present an analysis of clozapine prescription patterns, used as a real-world proxy marker for treatment-resistance, in a cohort of 1195 patients with schizophrenia from a Latin-American cohort, to explore the timing of treatment resistance during the course of the disease and possible subgroup differences.

**Methods:** We used survival analysis from national databases of clozapine monitoring system, national disease notification registers, and discharges from an early intervention ward.