Methods: Male C57BL/6 mice were given mixed cuprizone (CPZ, a copper chelator, 0.2 %, w/w) rodent chow for six successive weeks to induce demyelination. During the last two weeks, mice were given an oral gavage of saline, or SZAST of three different doses (a low dose of 5.5g·kg⁻¹·d⁻¹, a medium dose of 8.24g·kg⁻¹·d⁻¹, or a high dose of 10.98 g·kg⁻¹·d⁻¹), or quetiapine, respectively. Behavioral tests were conducted after the last treatment. Meanwhile, the expression of myelin basic protein (MBP) and neuregulin-I (NRG1) in the brain was tested by immunohistochemistry staining or Western Blot.

Results: Mice exposed to CPZ for six weeks showed obvious schizophrenia-like behaviors, including lower nest-building activity, sensory gating activity, and higher locomotor activity. CPZ-fed mice also displayed a lower myelin density in the corpus callosum, hippocampus, and cerebral cortex and a reduction of MBP and NRG1 protein in the hippocampus compared with controls. Both quetiapine and SZAST significantly alleviated the abnormal schizophrenia-like behaviors and the impairment of myelin sheath in CPZ-fed mice, however, SZAST with medium dose showed better neuroprotective effect than the low dose or the high dose of SZAST. Furthermore, the expression of NRG1 protein in the hippocampus was slightly, but not significantly increased in all SZAST-treated and quetiapine-treated groups.

Discussion: These results indicate that the neuroprotective effect of SZAST in demyelinated mice might partially relate to remyelination in the hippocampus in CPZ-fed mice.

M212. A SYSTEMATIC REVIEW AND META-ANALYSIS OF CLINICAL VARIABLES ASSOCIATED WITH RESPONSE TO CLOZAPINE IN TREATMENT RESISTANT SCHIZOPHRENIA

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Background: Approximately one third of patients with schizophrenia display suboptimal response to two trials of non-clozapine antipsychotic medication and may be termed treatment resistant. Clozapine is the only licensed pharmacotherapy for treatment resistant schizophrenia, but response to clozapine is variable and can only be determined through a trial of treatment. Understanding demographic and clinical sources of varied response to clozapine may be useful in the optimisation of clinical treatment algorithms and stratification of patient groups for clinical trials of early use of clozapine.

Methods: We systematically reviewed literature to investigate clinical and demographic factors associated with variation in clozapine response. Articles were eligible for review if they reported differences in clozapine response as a function of baseline variables within patient samples of schizophrenia spectrum disorders. In a second step, a random-effects meta-analysis to study group mean differences in age, age of onset and duration of illness between clozapine responders and non-responders was performed.

Results: Thirty-one articles were eligible for qualitative review. The systematic review found that a poorer response to clozapine was associated with older age at clozapine initiation, younger age at illness onset and longer delay in clozapine initiation. A higher number of previous hospitalisations and antipsychotic trials prior to treatment with clozapine were also associated with poorer outcomes. Both systematic review and meta-analysis identified that longer durations of illness before clozapine initiation were associated with worse clinical outcomes. In a total sample of 313 participants (n = 158 responders), clozapine responders had a significantly shorter duration of illness than non-responders (g = -0.31; 95% CI, 0.06 - 0.56; p = 0.02). Analysis was then limited to studies with a minimum follow-up period of 12 weeks to align with the recommended amount of time to monitor clozapine response. The difference in duration of illness between responder versus non-responder groups remained significant and overall effect size increased (g = -0.42; 95% CI, 0.17 – 0.67; p < 0.001). Between study heterogeneity was low (Q = 3.59, I² = 0%, P = 0.61).

Discussion: The results imply that delay in clozapine treatment is associated with worse response and support the view that initiation of clozapine earlier in illness may be beneficial. Although we cannot make causal assertions from the data presented, poor response to clozapine when prescribed after a longer delay is likely due to a combination of factors; including the effects of sustained active symptoms on neurobiological integrity, social functioning and self-care. Given evidence that early non-response to conventional antipsychotics predicts a later diagnosis of treatment resistance and poorer outcomes, identifying treatment resistance and prescribing clozapine earlier in the illness course would prevent unnecessary loss of time in the treatment of refractory psychosis. Current research into clinical variables associated with clozapine response is limited to few studies but future investigation into the predictive value of these variables is warranted. This is important given the relative ease and low-cost clinical information can be obtained from acutely unwell patient groups who may poorly tolerate more invasive research and clinical procedures.

M213. COMPARISON OF LONG-TERM ANTIPSYCHOTIC USE DATA FROM MEDICAL RECORDS AND NATIONAL PRESCRIPTION REGISTER

Abstract not included.

M214. NALTREXONE INDUCED VISUAL HALLUCINATIONS: A CASE REPORT

Abstract not included.

M215. FACTORS ASSOCIATED WITH CLOZAPINE RESPONSE AND RESISTANCE IN SCHIZOPHRENIA

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Background: Clozapine remains the only antipsychotic with unique efficacy in treatment resistant schizophrenia (TRS). Considerable ongoing research and clinical efforts have focused on reducing barriers to clozapine use in a bid to increase rates of clozapine use to improve outcomes in TRS. However, less than half of individuals with TRS respond to clozapine, with the remainder categorised as clozapine resistant (CRS) or Ultra-resistant. It is important to deepen understanding on the development of CRS so we can identify them early, attempt to prevent/delay its onset and also explore novel treatments. In the present study, we sought to compare clozapine responders from CRS and identify factors which might be associated with CRS.

Methods: This study was conducted at the Institute of Mental Health, the only psychiatric facility with clozapine services in Singapore. Individuals with TRS on clozapine for at least 12 weeks and the capacity to give informed consent were enrolled into the study. Each participant underwent a clinical assessment on the Structured Clinical Interview DSM-IV-TR (SCID), Positive and Negative Syndrome Scale (PANSS) and Social
Occupational Functioning Assessment Scale (SOFAS). We applied the Treatment Response and Resistance In Psychosis consensus criteria to define clozapine response and resistance. Brief Neurocognitive Assessment was done using the digit sequencing and symbol coding tasks from the Brief Assessment of Cognition in Schizophrenia (BACS). A fasting sample of blood was collected; assays for clozapine and norclozapine were performed using high performance liquid chromatography. To be classified as CRS, a participant must meet the below criteria: (i) not meeting symptom remission criteria on the PANSS using the Remission in Schizophrenia Working Group criteria, (ii) moderate and lower level of functioning on the SOFAS, and (iii) at least 12 weeks of clozapine treatment and plasma clozapine levels ≥ 350 ng/ml.

Results: A total of 91 participants were enrolled in this study and 67 (73.6%) met criteria for CRS. 1 in 4 clozapine responders had plasma clozapine levels not exceeding 350 ng/ml. There were no significant differences in age, sex, smoking status, age at onset of illness, clozapine adherence, antipsychotic polypharmacy rates and duration of clozapine use between clozapine responders and CRS. Compared to clozapine responders, individuals with CRS had statistically significantly lower BMI (26.4 vs. 23.4, p=0.008) lower rates of employment (79.2% vs. 35.8%, p<0.001), and poorer cognitive function in both digit sequencing (−0.86 vs. −1.60, p=0.011) and symbol coding (−1.09 vs. −1.88, p=0.002) tasks. In a multivariate logistic regression model with age, sex, age at onset, BMI and cognition, only BMI (OR=0.88, p=0.043) and symbol coding (OR=0.48, p=0.019) were significant variables predicting clozapine resistance.

Discussion: Our study highlighted a high rate of CRS and suggests that poorer cognitive function, specifically in processing speed, might be associated with the development of clozapine resistance in schizophrenia. Additionally, it was interesting to note that a higher BMI was associated with clozapine response; this lends weight to existing metabolic and lipid hypotheses of schizophrenia.

M216. ASSOCIATIONS OF EXTRAPYRAMIDAL SYMPTOMS WITH PSYCHOTIC SYMPTOMS IN A COHORT OF HOMELESS OR PRECARIOUSLY HOUSED PERSONS WITH OR WITHOUT SCHIZOPHRENIA

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Background: There is considerable evidence supporting the association between extrapyramidal symptoms (EPS) and psychotic symptoms in patients with schizophrenia (SCZ). However, it is not well understood whether such an association exists in individuals without SCZ and how the association differs from those with SCZ. Our aim was to examine the associations of EPS with psychotic symptoms and compare them between SCZ and non-SCZ individuals.

Methods: We used data from a 10-year community-based study of homeless or precariously housed persons from Vancouver, Canada. Diagnosis of SCZ was made according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR). Severity of psychotic symptoms was rated using the Positive and Negative Syndrome Scale (PANSS). Severity of parkinsonism, dyskinesia, and dystonia was rated using the Extrapyramidal Symptom Rating Scale (ESRS), and akathisia using the Barnes Akathisia Rating Scale (BARS). Presence of EPS was defined as having at least moderate severity on the ESRS (i.e., ≥24 out of 8) or BARS (i.e., ≥23 out of 5) Clinical Global Impression-Severity (CGI-S) scale. Absence of EPS was defined as scoring ≤2 on the ESRS or ≤1 on the BARS CGI-S scale. Two-way analysis of covariance was performed using SCZ and EPS as independent variables and PANSS five factors (i.e., positive symptoms, negative symptoms, disorganization, excitement, and depression) as dependent variables, controlling for age, antipsychotic users, and cocaine- or methamphetamine-dependent individuals. Multiple linear regression analysis was performed for both SCZ and non-SCZ groups, controlling for the same confounding variables, to examine 1) associations of the severity of EPS subtypes with PANSS factors and 2) whether the presence of multiple EPS subtypes would be associated with increased SCZ symptoms relative to the presence of a single subtype.

Results: A total of 223 participants were included in this study (mean age: 44.1 ± 12.0 years; 76.1% male). Eighty-four participants met the diagnosis of SCZ, of whom 39 met our criteria for having EPS and 32 for not having EPS. The remaining 139 participants were not diagnosed with SCZ, of whom 50 had EPS and 72 did not. None of the participants had clinically significant dystonia. Overall, significant main effects of EPS were found for total symptoms (F1,182 = 24.4, p < 0.001), negative symptoms (F1,182 = 16.3, p < 0.001), disorganization (F1,181 = 16.6, p < 0.001), and excitement (F1,182 = 15.8, p < 0.001), but not positive symptoms or depression. The presence of EPS was associated with greater total symptoms and disorganization in both SCZ and non-SCZ groups. Significant interaction effects between SCZ and EPS were found for negative symptoms (F1,182 = 6.0, p = 0.015) and excitement (F1,182 = 3.9, p = 0.050), where the presence of EPS was associated with greater negative symptoms and excitement in SCZ participants, but not in non-SCZ participants. Consistent in both SCZ and non-SCZ groups, there were significant positive associations of the severity of 1) parkinsonism with negative symptoms, 2) dyskinesia with disorganization and total symptoms, and 3) akathisia with excitement. The presence of multiple EPS subtypes, relative to a single subtype, was not associated with significant increases in any SCZ symptoms, except a significant increase in excitement in non-SCZ participants.

Discussion: The presence of EPS is clearly associated with greater symptoms of SCZ, even in individuals without SCZ. People with SCZ may experience greater negative symptoms and excitement as a result of EPS than those without SCZ. Subtypes of EPS are distinctly associated with factors of SCZ symptoms. Future studies should elucidate the mechanisms underlying these associations.

M217. EFFICACY OF PALIPERIDONE PALMITE ON PSYCHIATRIC SYMPTOMS AND ATTITUDES TOWARD MEDICATION IN SCHIZOPHRENIA

Abstract not included.

M218. RELATIONSHIP BETWEEN JUMPING TO CONCLUSIONS AND OTHER COGNITIVE BIASES AND SOCIAL COGNITION IN PEOPLE WITH SCHIZOPHRENIA

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Background: Deficits in jumping to conclusions and social cognition have been described in people with schizophrenia. The aims of the study are to relate jumping to conclusions with social cognition and other cognitive biases in people with schizophrenia attended in rehabilitation services.

Methods: A descriptive study was performed. The subjects of our study were persons from 18 to 65 years old, attended in rehabilitation services, with schizophrenia diagnoses and other diagnoses with presence of psychotic symptoms (depression, bipolar disorder, borderline disorder, delusional disease, schizoaffective, and schizotypal personality). The variables included were JTC considered three beads tasks with different proportions: 85:15%, 60:40% and 60:40% salient task. Moreover, cognitive