Quality Index global score (PSQI-global). Pearson correlation analyses were performed between DB baseline to Week 26 change in Cogstate composite and subscale scores and Week 26 change in the psychotic scale scores.

**Results:** Small improvements, from DB baseline to Week 26, were observed in standardized scores on the Cogstate composite (+0.29), Identification task (+0.19), Detection task (+0.28); One Card learning task (+0.33); and One Back task (+0.33). Improvement from OL baseline at Week 26 was also observed on the mean [SD] UPSA-B total score (+6.2 [11.6]). At DB baseline, there were no correlations between CogState composite score and individual test scores with any of the psychiatric scales. Week 26 improvement in the following Cogstate composite and subscale tasks were correlated with Week 26 improvement in the following psychiatric scale scores: Cogstate composite score (PANSS total, r=-0.26; BNSS total, r=-0.31; CGI-S, r=-0.30; MADRS total, r=-0.23; PSQI-global, r=-0.23); Identification task (PANSS total, r=-0.30; BNSS total, r=-0.30). Detection task (BNSS total, r=-0.30; CGI-S, r=-0.28; PSQI-global, r=-0.23); One Card learning task (MADRS total, r=-0.29); and One Back task (PANSS total, r=-0.26).

**Discussion:** During 6-months of open-label extension treatment with SEP-363856, improvement in overall functioning was observed on the UPSA-B scale; and small but consistent improvement in cognition was noted in the Cogstate composite and subscale task scores. Endpoint reduction in the severity of schizophrenia-related symptomatology (eg, on the PANSS, BNSS, MADRS, and insomnia) was associated with modest correlations, in the range of 0.2 to 0.3, in cognitive performance as measured by the Cogstate composite and subscale task scores.

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M210. GRIN2B METHYLATION IS RELATED TO PANSS EXCITED COMPONENT (PANSS-EC) IN SCHizophrenia

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**Background:** Among the adversities found in schizophrenia, the dysfunctions in the glutamatergic system, specifically the N-methyl-D-aspartate receptor (NMDAR) are apparent. GRIN2B (coding a NMDAR subunit) has a critical role in synaptic plasticity and important participation in CNS neurodevelopment, this gene is closely associated with both global and cognitive impairments. One of the mechanisms that may underlie these abnormalities is DNA methylation which is known to regulate gene expression. As part of a major study investigating the relationship of DNA methylation with schizophrenia, we determined whether methylation of the GRIN2B promoter region was associated with specific symptoms of schizophrenia determined by the Positive and Negative Syndrome Scale (PANSS).

**Methods:** Blood samples were collected from schizophrenia patients (n = 79) over a 2-year period. Bisulphite conversion and pyrosequencing were used to determine methylation levels in 5 CpG sites in the GRIN2B promoter region. PANSS score and the five factor subscores (Wallwork et al, 2012) were used to determine methylation levels in 5 CpG sites in the GRIN2B promoter region and the five factor subscores (Wallwork et al, 2012) at baseline and at 6 weeks was collected, and the change in PANSS following treatment was determined.

**Results:** Mean methylation at the five CpG sites was not associated with overall PANSS score or with the change in PANSS. However, a highly significant positive correlation of mean methylation with the baseline excited factor score (r=0.342, p=0.002), but with no other PANSS subscore, was found. No significant correlation with changes in PANSS, or in changes in subscores, over the treatment period was found.

**Discussion:** This is the first evidence showing GRIN2B methylation correlated with the excited component (EC) of schizophrenia symptoms. PANSS-EC is used to assess agitation in patients (Lindenmayer et al., 2008, Montoya et al., 2011), and is valuable in identifying risks associated with agitation and aggression related to primary psychiatric disturbances. This result suggests that this GRIN2B epigenetic signature may relate to agitation and aggressive behaviour in schizophrenia.

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M211. NEUROPROTECTIVE EFFECT OF SHI-ZHEN-AN-SHEN-TANG, A CHINESE HERB FORMULA ON MICE EXPOSED TO CUPRiZoNE

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**Background:** There is a growing interest in the potential use of traditional Chinese herbal medicine for the treatment of psychiatric disorders. Shi-Zhen-An-Shen-Tang (SZAST) is a traditional Chinese herbal formula consisting of five constituents (Sang, Shen, An, and Tang). This study aimed to evaluate the neuroprotective effects of SZAST on 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced nigrostriatal degeneration in mice.

**Methods:** Male ICR mice were divided into four groups: control, MPTP, MPTP + SZAST low, and MPTP + SZAST high. Mice were treated with SZAST for 4 weeks starting 1 week before the MPTP injection and for 2 weeks after the MPTP injection. The mice were sacrificed at 2 weeks after the MPTP injection, and the striatum was analyzed for the expression of tyrosine hydroxylase (TH) and the number of TH-positive neurons in the substantia nigra. The mice were also assessed for their motor behavior using the rotarod test.

**Results:** The mice treated with SZAST had significantly higher levels of TH expression and a greater number of TH-positive neurons in the substantia nigra compared to the MPTP-treated group. The rotarod test also showed improved motor performance in the mice treated with SZAST.

**Discussion:** These findings suggest that SZAST has neuroprotective effects in mice exposed to MPTP and may have potential for use in the treatment of Parkinson's disease.
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 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).

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. 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 Disability Inventory (SDI). A systematic review and meta-analysis were performed to identify factors which might be associated with CRS.

Results: A total of 158 participants were enrolled into the study. The primary outcome was the development of CRS after 12 weeks of clozapine treatment. Both univariate and multivariate analyses identified a number of factors associated with CRS, including older age at illness onset, longer duration of illness, lower dose of clozapine, and comorbid substance use.

Discussion: The results suggest that early identification and intervention may be crucial in preventing the development of CRS. Future research should focus on developing targeted interventions to reduce the incidence of CRS.