

EPP328

Neurological Soft Signs in Patients with Schizophrenia May be Related to Treatment Resistance

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Introduction: Motor abnormalities in schizophrenia are important as they are measurable objective parameters. Neurological soft signs (NSS), which are one of the primary motor abnormalities, are minor motor and sensory abnormalities that cannot be localised to a specific brain region, reflect the areas of sensory integration, motor coordination and motor sequencing. Instrumental measures of motor abnormalities have the potential to improve detection, early intervention and treatment strategies in psychotic disorders.

Objectives: Our aim in this cross-sectional study was to compare NSS in patients with treatment-resistant schizophrenia (TRS) and treatment responsive schizophrenia (non-TRS) and healthy controls (HC), and to examine the relationship of NSS with socio-demographic and clinical variables, premorbid adjustment, functioning, negative and cognitive symptoms.

Methods: 30 TRS patients, 30 non-TRS patients and 30 HC were included in the study between November 2021 and November 2022. The inclusion criteria for the TRS group were to meet the criteria for resistance to antipsychotic treatment. Neurological Evaluation Scale (NES) was applied to all participants to evaluate NSS. The scale assesses impairment in four different functional areas: "sensory integration", "motor coordination", motor sequencing" and "other signs". Brief Psychiatric Rating Scale (BPRS), Brief Negative Symptom Scale, General Assessment of Functioning (GAF), Clinical Global Impression-Severity Scale (CGI-S), Premorbid Adjustment Scale-Childhood (PAS), and a cognitive battery were applied to patients with schizophrenia. The authors declare that all methods used in this study adhere to the ethical guidelines of the corresponding national and institutional review boards for human research and are in alignment with the 1975 Helsinki Declaration, as updated in 2008. All participants provided written informed consent to participate in this study.

Results: We found significant differences in the NES-Total score and all subscale scores between patients with schizophrenia and HC (all comparisons $p < 0.001$). NSS in patients with schizophrenia were found to be higher than in HC. TRS had higher NES-Total ($p = 0.002$), NES-Sensory Integration ($p = 0.001$), and NES-Other Signs ($p < 0.001$) scores than non-TRS. NES-Total score was negatively correlated with GAF score and positively correlated with BPRS, CGI-S and PAS-childhood scores. Poor performance on cognitive tests was associated with more NSS. Only the sensory integration deficits were found to be associated with negative symptoms.

Conclusions: Our findings suggest that NSS examination in patients with schizophrenia may indicate treatment resistance or response. NSS are associated with severity of illness, lower functioning, poor premorbid adjustment, and poor cognitive performance. Longitudinal studies involving larger samples are needed to understand the course of NSS at different stages of the illness.

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EPP328

Cariprazine in multiple-episode dual schizophrenia: post-hoc analysis of an observational study

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Introduction: Schizophrenia frequently coexists with substance use disorders, especially cannabis use disorder (CUD). Importantly, cannabis use is known to further exacerbate symptoms, leading to more frequent and severe psychotic episodes, longer hospital stays and poorer overall treatment outcomes. The lifetime risk of relapse is around 60%. Therefore, the treatment of patients with multiple episodes is even more challenging

Objectives: To evaluate the effectiveness of cariprazine in schizophrenia patients with multiple episodes and comorbid cannabis use disorder.

Methods: This was a 6-month, multi-centre, observational study conducted at six institutions in Spain. The study included adult outpatients aged 18 to 65 years, diagnosed with schizophrenia and cannabis use disorder according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria, who were receiving cariprazine treatment based on medical judgment. Exclusion criteria included pregnant or breastfeeding women and patients with co-existing medical conditions that could potentially skew the study results.

The study evaluated changes in schizophrenia symptoms using the Positive and Negative Syndrome Scale (PANSS) and the Clinical Global Impression-Schizophrenia (CGI-SCH), as well as changes in CUD symptoms based on the Cannabis Abuse Screening Test (CAST) and the Severity of Dependence Scale (SDS). This post-hoc analysis focused on patients with multiple episodes. Patient characteristics were summarized using descriptive statistics. Least squares (LS) means were calculated for the change from treatment start to treatment end for PANSS, CGI-SCH, CAST, SDS using a mixed model for repeated measures. All analyses were conducted using SAS.

Results: From the cohort, 38 (65%) patients had multiple episodes. The mean age of these patients was 36.5 and 65.8% of them was male. Most patients received 4.5 mg/day cariprazine at baseline (60.5%). Half of the patients also took concomitant antidepressants and/or antipsychotics. Throughout the 6-month observational period significant improvement was detected in both schizophrenia (LS mean change in PANSS Total score: -46.2, $p < 0.001$, CGI-SCH Total score: -8.0, $p < 0.001$) and CUD symptomatology (LS mean change in CAST Total score: -6.6, $p < 0.001$, SDS Total score: -8.0, $p < 0.001$).

Conclusions: Cariprazine seem to be an effective treatment option for schizophrenia patients with multiple episodes and comorbid CUD.

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