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Introduction: Schizophrenia (SZ) is a leading cause of global disability that affects about 1% of people and typically develops in early adulthood [1] profoundly affect an individual's cognitive and social functioning.The First-Episode Psychosis (FEP) is a critical period for preventing deterioration and attaining recovery. Determining the neurobiological underpinnings that might predict treatment outcomes is important for precision medicine and the development of better treatments.

Gamma-aminobutyric acid (GABA) is the primary inhibitory neurotransmitter in the human brain. GABA levels in the visual cortex have been associated with processing of facial emotional expressions related to social communication skills [2].Several studies have suggested alterations of the GABAergic system in SZ and related psychotic disorders relative to healthy individuals [3].Additionally patients with schizophrenia show highly significant deficits in use of visual scanning of naturalistic social scenes to inform Social Cognition (SC) [4] and SC deficits contribute significantly to disability in schizophrenia patients [5].

Driven by the hypothesis that disrupted GABAergic activity is associated with social cognition impairments in SZ spectrum disorders since the FEP, our approach combined proton magnetic resonance spectroscopy (1H-MRS) with fMRI to explore the role of frontal eye fields (FEFs) GABAergic activity in social cognition and symptom prediction and explore the connectivity patterns between FEFs and brain regions of face emotional expression processing.

Methods: Prospective cohort study in a sample of 20 patients (18 males, mean age 26 y.o., range 20-46) with SZ-spectrum FEP acutely ill, minimally treated (taking antipsychotic medication for two weeks or less). Symptom severity was assessed with the Positive and Negative Syndrome Scale (PANSS) and social cognition with the Reading the Mind in The Eyes Test (RMET), at treatment baseline (T1) and after 6 months (T2). GABA + macromolecules (GABA+) levels were measured at T1 from a 3x3x3 cm voxel comprising the right FEF and the premotor cortex, using 1H-MRS HERMES sequence and the Osprey software. fMRI was performed atT1 during an oculomotor paradigm (prosaccade, antisaccade, no-go) with facial expression cues. ROI-to-ROI functional connectivity analysis was performed in CONN software, using the right FEF as seed and visuospatial brain regions involved in social cognition as targets. Statistical analyses were performed using SPSS Statistics (Version 27).

Results: Mean PANSS Total score was 92,5 at T1 and 58,3 at T2. Mean RMET score was 24,05 at T1 and 24,88 at T2. Right FEF GABA+ levels at T1 negatively correlated with the RMET score at T1 (rho=-0.694, p=0.012, n=12) and PANSS Total score at T2 (rho=0.532, p=0.050, n=14).Functional connectivity between the right FEF and right pSTS showed a negative correlation (t=-3,08, p-FDR=0.024).

Discussion: Our results suggest that higher GABAergic activity in FEFs is associated with worse SC and therefore may be related with SC deficits occurring in SZ. In addition, T1 GABA levels correlated with symptom severity at 6 months of antipsychotic treatment and could be investigated in the future as putative biomarker of treatment response. Finally, functional connectivity between the right FEF and right pSTS supports the existence of networks that allow integration of visual information to drive oculomotor activity during sociocognitive processing.

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Conflict of interest

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EVENT-RELATED POTENTIALS CORRELATE WITH MAGNETIC RESONANCE SPECTROSCOPY MEASURES OF EXCITATORY NEUROTRANSMISSION AND SYMPTOM SEVERITY IN OBSESSIVE-COMPULSIVE DISORDER

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Background. Obsessive-Compulsive Disorder (OCD), a highly debilitating condition affecting circa 1-3% of the population, is linked to dysfunction in the cortico-striato-thalamo-cortical (CSTC) circuitry. Two brain regions, the anterior cingulate cortex (ACC) and the supplementary motor area (SMA), have been strongly implicated in key OCD-related cognitive and motor deficits. Brain imaging and electroencephalographic (EEG) findings converge in revealing an overactivation of these regions in OCD. For example, magnetic resonance spectroscopy (MRS) shows increased levels of the excitatory neurotransmitter glutamate in these regions, which correlate with OCD symptomatology and overreliance on habitual behaviour [1]. Enhanced amplitudes of event-related potentials (ERPs), including the error-related negativity (ERN), representing error-monitoring and generated in the ACC, and the readiness potential (RP), representing motor preparedness and generated in the SMA, have also been found in OCD [2]. Nevertheless, the precise relationship between changes in excitatory and inhibitory neurotransmission (glutamate-Gamma-Amino-Butyric Acid (GABA) ratio) and EEG markers in OCD is not yet known

Aims. We aimed to investigate the relationship between increased glutamate levels in the ACC and SMA with the amplitudes of the ERN and the RP, respectively.

Methods. Twenty-one individuals with DSM-5 OCD and 22 matched healthy volunteers selected from a larger sample reported by Biria and colleagues [1] underwent 128-channel EEG alongside 7-Tesla proton MRS (measuring glutamate and GABA) of the ACC and SMA. During the EEG, participants performed a combined Stop-Signal/Go-No Go task to measure the amplitudes of the ERN and the RP. Participants also completed a battery of clinical and self-report questionnaires that investigated OCD symptomatology and habitual behaviour.

Results. Independent-sample t tests indicated ERN amplitudes were increased in OCD vs controls (p=0.013), but RP amplitudes were not. Correlational analyses indicated significant associations between the amplitudes of the ERN and the RP and the glutamate-GABA ratio in the ACC (p=0.03), and SMA (p=0.027), respectively. Furthermore, higher self-reported symptomatology as measured by the Obsessive-Compulsive Inventory (OCI) correlated significantly with both the increased ERN amplitudes (p=0.04), and the glutamate-GABA ratio in the ACC (p=0.03).

Discussion. Perhaps the first of its kind, this study utilised two high resolution brain imaging techniques and showed an association between the amplitudes of the ERN and the RP and the glutamate-GABA ratios in the ACC and SMA, respectively, representing increased excitatory over inhibitory neurotransmission in these critical OCD-related brain regions. Moreover, the amplitude of the ERN correlated with OCD symptom severity. These findings suggest that specific EEG markers involving ERPs, namely the ERN and possibly the RP, hold potential as markers of increased excitatory neurotransmission in OCD-related corticostriatal nodes. Furthermore, ERPs may have utility as affordable and well tolerated proxy biomarkers of MRS neurotransmitter measures of OCD symptomatology. Further research is indicated to corroborate and strengthen these findings in larger datasets.

References

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