Elevated Levels of Myo-inositol and Choline in the Associative Striatum of Antipsychotic-Naïve Patients with First Episode Psychosis

Eric Plitman[1,2], Camilo de la Fuente-Sandoval[3], Pablo León-Ortiz[3], Francisco Reyes-Madrigal[3], Gladys Gómez-Cruz[3], Shinichiro Nakajima[1,4], Philip Gerretsen[1,5], M Mallar Chakravarty[6,7], Sofia Chavez[1,5], Jun Ku Chung[1,2], Fernando Caravaggio[1,2], Yusuke Iwata[1,4], Danielle Uy[1], Gary Remington[1,5], and Ariel Graff-Guerrero[1,5]

[1]Centre for Addiction and Mental Health, Toronto, Ontario, Canada, [2]Institute of Medical Science, University of Toronto, Toronto, Ontario, Canada, [3]Instituto Nacional de Neurología y Neurocirugía, Mexico, [4]Neuropsychiatry, Keio University School of Medicine, Japan, [5]Psychiatry, University of Toronto, Toronto, Ontario, Canada, [6]Douglas Mental Health University Institute, Montreal, Quebec, Canada, [7]Psychiatry, McGill University, Montreal, Quebec, Canada

TARGET AUDIENCE: Individuals researching neurometabolite levels in schizophrenia, clinicians searching for a biomarker in schizophrenia, and persons studying therapeutic compounds, would all benefit from this information.

PURPOSE: Current findings reporting upon levels of myo-inositol (mI) and choline compounds (Cho) are inconsistent and include confounding variables,[1-3] necessitating further investigation of these neurometabolites. The present study limited confounds by comparing mI and Cho levels in the associative striatum between a sample of antipsychotic-naïve patients experiencing their first non-affective psychosis episode and a group of healthy controls, effectively providing insight towards how levels of these neurometabolites deviate in schizophrenia.

METHODS: 58 first episode psychosis (FEP) patients and 58 age- and sex-matched healthy controls were included in this study. Proton magnetic resonance spectroscopy (^{1}H-MRS) was obtained in a 3T GE scanner using point-resolved spectroscopy, with the voxel centered on the right dorsal-caudate nucleus. The Positive and Negative Syndrome Scale (PANSS) was used to assess patient symptoms. ^{1}H-MRS acquisitions were analyzed with LCModel and corrected for CSF composition within the voxel. mI and Cho levels were compared between groups using a general linear model. Pearson correlations were used to examine the relationship between metabolite levels and PANSS subscale total scores.

RESULTS: mI levels in the associative striatum were higher in patients with FEP in comparison to healthy controls ($p<0.05$). Cho levels in the associative striatum were also higher in patients with FEP compared to healthy controls ($p<0.01$). A trend level positive correlation existed between mI levels and PANSS Positive subscale total score ($r=0.250$, $p=0.059$). Exploratory investigations controlling for multiple comparisons identified a significant correlation between mI levels and PANSS P5 score (Grandiosity) ($r=0.401$, p-corrected<0.05). The relationship between mI levels and PANSS P3 score (Hallucinatory Behavior) approached significance ($r=0.319$, p-corrected>0.05).

DISCUSSION: mI has been reported to be a marker of glial activity, and elevated mI is believed to represent glial activation, hypertrophy, and gliosis.[4] Cho is related to cell membrane metabolism and myelination, and elevated levels of Cho are understood to reflect phospholipid disturbances, increased membrane turnover, and demyelination.[5] The parallel increase in both of these neurometabolites may be representative of an attempt to compensate for neuronal damage by improving glial proliferation to modulate vascular and metabolic activities, and may also provide evidence for early neuroinflammation in schizophrenia.

CONCLUSION: mI and Cho levels appear to be concomitantly elevated in the associative striatum of antipsychotic-naïve patients with FEP, likely indicative of glial cell disruption within the patient group. The relationship between mI levels and positive symptoms warrants further investigation. Future research should continue to investigate potential glial cell abnormalities in schizophrenia, which may additionally explain irregularities in dopaminergic and glutamatergic systems.

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