N-acetyl aspartate and glutamate levels of the anterior cingulate predict symptom severity in schizophrenia: a magnetic resonance spectroscopy (1H-MRS) study

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Abstract

The anterior cingulate cortex (ACC) is important for executive functioning, and in schizophrenia, alterations of the neuronal marker N-acetyl aspartate (NAA) and the neurotransmitter glutamate are repeatedly found in this region. However, less is known about the functional consequences of these changes. Using proton magnetic resonance spectroscopy (1H-MRS), NAA and glutamate were measured bilaterally in the ACC of 19 schizophrenia patients and 17 healthy controls. Schizophrenia patients were assessed with the Positive and Negative Syndrome Scale (PANSS) and analysed according to the five factor model (Negative, Positive, Cognitive/Disorganized, Excitation and Depression symptoms). Spearman's Rank correlations revealed a negative correlation between right ACC glutamate and negative symptoms (r=-0.51, p=0.02), while right ACC NAA correlated with cognitive/disorganized symptoms (r=0.48, p=0.04). Also, schizophrenia patients showed significantly lower levels of glutamate in the left hemisphere (p=0.01) and lacked the interhemispheric glutamatergic correlation found in healthy controls (r=0.65, p=0.004). The present results show that while left ACC glutamate is lower in the schizophrenia group, the degree of negative symptoms is related to glutamate in the right hemisphere. The lack of an interhemispheric glutamatergic correlation in schizophrenia also points towards an interhemispheric imbalance as part of the negative symptom pathology. Additionally, increased NAA levels in this cognitive region together with the commonly found NAA reduction in other brain regions, appear to interfere with cognitive processes and result in disorganized cognition. Our results indicate that the perturbation of metabolites such as glutamate and NAA influences normal brain functioning and contributes to the clinical manifestation of schizophrenia.

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