

GLUTAMATERGIC DYSFUNCTION IN THE ANTERIOR CINGULATE CORTEX IN ADULTS WITH ATTENTION-DEFICIT / HYPERACTIVITY DISORDER: A PROTON MAGNETIC RESONANCE SPECTROSCOPY STUDY

Jochen Bauer¹, Anne Werner¹, Waldemar Kohl¹, Anya Pedersen², Harald Kugel³, and Patricia Ohrmann¹

¹Department of Psychiatry, University Hospital Münster, Münster, Germany, ²Psychology, University of Münster, Münster, Germany, ³Institut for Clinical Radiology, University Hospital Münster, Münster, Germany

Introduction: Attention-deficit/hyperactivity disorder (ADHD) including symptoms of impulsivity, hyperactivity and inattention, is a neurodevelopmental disorder with app. 65% of affected children showing persistent symptoms into adulthood. Glutamate is the major excitatory neurotransmitter in human brain and plays a pivotal role in cognitive functioning. A recent study⁴ highlighted the relevance of glutamate in ADHD by demonstrating that the norepinephrine reuptake inhibitor atomoxetine, which is effective against ADHD symptoms, is also an NMDA receptor antagonist. So far, studies with magnetic resonance spectroscopy (MRS) studies of glutamate/glutamine revealed controversial results⁵. We used an optimized ¹H-MRS technique to reliably quantify glutamate in the anterior cingulate cortex (ACC) and the dorsolateral prefrontal cortex (DLPFC) in adult patients with ADHD.

Methods 28 adult patients (mean age 30.82 SD 8.8 years, 12 female), meeting DSM-IV criteria for ADHD, and 29 age, gender and education matched healthy controls (mean age 28.9 SD 8.6 years; 11 female) were included in our study. Diagnosis were confirmed with DIVA and comorbidity was assessed using SCID-I. Clinical evaluations included WURS-K, ADHS-SB, AProF und PHQ-D. ¹H magnetic resonance spectroscopy was performed with a 3T scanner (Philips Gyroscan Intera 3T) using a Point Resolved Spectroscopy Sequence (PRESS) with the following parameters: TE 32ms, TR 2000ms, 2048 datapoints, bandwidth 2000Hz, an iterative shim procedure and water suppression. Volumes of interest VOIs (3.375 ml) were investigated in the dorsolateral prefrontal cortex (DLPFC) and the anterior cingulate cortex (ACC), two brain regions important for cognitive functioning, esp. working memory and cognitive control. A high resolution T1 weighted 3D dataset was acquired used for segmentation of the VOIs. Spectroscopic data were analyzed with LCModel and corrected for CSF.

Results: In the ACC, glutamate levels were significantly higher in patients than controls, all other metabolites revealed no difference. Also, there were no differences in metabolite levels in the DLPFC.

Conclusion: Our finding of increased levels of glutamate in the ACC supports the hypothesis of a glutamatergic dysfunction in patients with ADHD and is in line with a previous study in ADHD patients⁶, although other MRS studies revealed decreased levels of glutamate/glutamine in the ACC⁶ or no differences¹. Interestingly, increased glutamate in the ACC has also been found in bipolar patients², and has been related to impulsivity in patients with borderline personality disorder³. Pursuing analyses of clinical characteristics and metabolites in our patients are underway.

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