

REDUCED BASAL GANGLIA GABA IN ATTENTION DEFICIT HYPERACTIVITY DISORDER

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Target audience - Researchers interested in GABA-edited MRS and attention deficit hyperactivity disorder.

Introduction - Attention deficit hyperactivity disorder (ADHD) is a developmental psychiatric disorder with high persistence, affecting approximately 3% of the adult population.¹ The precise neurobiological mechanisms underlying the disorder remain unclear, although abnormalities in levels of glutamate and gamma-aminobutyric acid (GABA) reflecting a basic neuronal excitation/inhibition imbalance have been implicated in the pathophysiology of ADHD.² Reduced GABA levels in the sensorimotor cortex have recently been reported in children with ADHD.³ The primary purpose of this study was to examine differences in GABA levels between adults with ADHD and healthy control participants in the basal ganglia, a region demonstrating neuroanatomic and functional abnormalities which represent some of the hallmark imaging features of ADHD. A secondary purpose was to evaluate the association between basal ganglia GABA levels and ADHD symptom scores.

Methods - We examined 21 adults with ADHD (13 females, age 37.6 (SD = 10.2)) and 20 age-matched control adults (12 females, age 33.5 (SD = 10)). MR spectroscopy studies were performed with a 3T GE HD.xt TwinSpeed MRI scanner (GE Healthcare, Milwaukee, WI, USA), using an 8-channel receive-only head coil. GABA-edited MR spectra were acquired from a 28x40x25 mm³ voxel in the left basal ganglia (Figure 1) using the MEGA-PRESS method with TE = 68 ms, TR = 2000 ms, 320 averages (160 pairs), and an 8 step phase cycle. GABA to Creatine (Cr) ratios were evaluated from the ratio of the edited GABA signal to the unedited Creatine signal with Gannet (gabamrs.blogspot.com), using a model consisting of a Gaussian fit to the GABA peak and a Lorentzian fit to the Creatine peak, superimposed on a linear baseline. ADHD symptom scores were evaluated with the Wender Utah Rating Scale (WURS)⁴ and Conners⁵ symptom inventories.

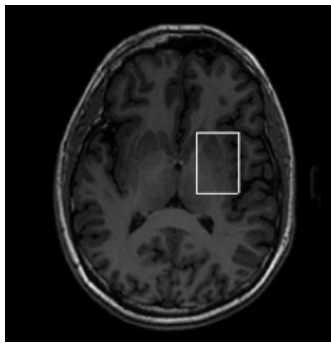


Figure 1: Screenshot showing the position of the basal ganglia voxel

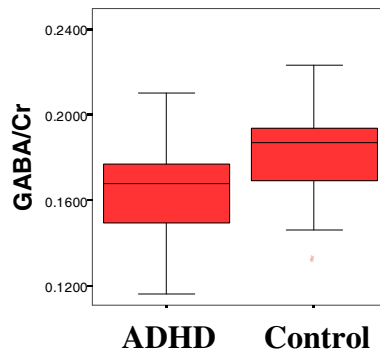


Figure 2: GABA/Cr levels in ADHD and control adults

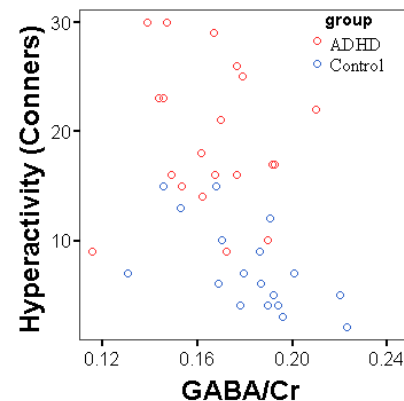


Figure 3: Correlation between hyperactivity and GABA/Cr (across both groups)

Results - GABA/Cr levels in the basal ganglia were lower in ADHD patients relative to healthy controls ($p = 0.03$, 2-tailed t-test, see Figure 2). GABA/Cr ratios were also negatively correlated with WURS hyperactivity scores (Spearman’s rho = -0.32, $p = 0.04$) and Conners hyperactive (Spearman’s rho = -0.48, $p = 0.002$, Figure 3), impulsive (Spearman’s rho = -0.37, $p = 0.02$), and inattentive scores (Spearman’s rho = -0.41, $p = 0.01$). No significant correlation was seen between GABA/Cr levels and depressive or other symptom scores assessed with the Conners and WURS inventories, and no significant differences in fit error were seen between groups (all $p > 0.1$).

Discussion - Our results indicate that patients with ADHD have reduced inhibitory neurotransmitter levels in the left basal ganglia, and that striatal GABA levels correlate with ADHD symptom scores across both groups. The lack of any significant correlations with depressive symptom scores highlights the specificity of this observed link between GABA levels and behavioural dysfunction, and provides further evidence for the neurophysiological basis of ADHD. Future work should clarify the relation of this dysfunction in inhibitory neurotransmitter levels to other measures of basal ganglia function such as perfusion and BOLD.

References

¹Faraone et al., J Atten Disord, 2005; 9(2): 384-91, ²Ferreira et al., J Neural Transm, 2009; 116(5): 623-9, ³Edden et al. Arch Gen Psychiatry. 2012; 69(7):750-753, ⁴Ward M, et al. The Wender-Utah Rating Scale: An Aid in the Retrospective Diagnosis of Childhood Attention Deficit Hyperactivity Disorder. Salt Lake City, UT: 1993. ⁵Conners, CK, et al. Conners’ Adult ADHD Rating Scales (CAARS). North Tonawanda, New York: Multi-Health Systems (1999)