

A 1H-MRS study of the auditory cortex in persons with autism spectrum disorder (ASD)

M. S. Brown¹, K. Youngpeter², D. Singel³, S. Hepburn², and D. C. Rojas²

¹Radiology, University of Colorado Denver, Aurora, CO, United States, ²Psychiatry, University of Colorado Denver, Aurora, CO, United States, ³Brain Imaging Center, University of Colorado Denver, Aurora, CO, United States

Introduction

Studies of autism biomarkers have revealed somewhat mixed results. Increased excitatory glutamate+glutamine (Glx) levels have been reported in the hippocampal region of persons with autism using proton magnetic resonance spectroscopy (1H-MRS) measures at 1.5T (1). Shinohe et al. (2) reported increased serum levels of glutamate in persons with autism, consistent with the MRS data. These findings have given rise to a hyperglutamate theory of autism (3), perhaps caused in part by reduced glutamate decarboxylase (GAD) expression in persons with autism (4). Because of our interest in measures of auditory cortical dysfunction in persons with autism spectrum disorders (ASD) (5), we undertook a 1H-MRS of left and right hemisphere auditory cortex to determine if auditory cortex glutamate levels are elevated in subjects with ASD.

Methods

Single-voxel, point resolved spectroscopy (PRESS) data were acquired using a 3T G.E. Signa HDx and 8-channel head coil (TR/TE = 2000/30 ms, 128 averages, voxel size = 3.0 x 1.5 x 2.0 cm) in 11 ASD subjects and 10 age-matched controls. Separate left and right voxels were acquired with the location of the voxel aligned as closely as possible with Heschl's gyrus. One ASD subject did not have left hemisphere data available, so the left ASD N = 10. The primary measures were glutamate (Glu), glutamine (Gln), and the sum of the two (Glx). An additional measure included n-acetyl-aspartate (NAA). Concentrations (in institutional units) were derived from spectra processed using the LCModel software package (6). Metabolite concentrations were correlated with a continuous measure of ASD symptom severity, the Autism Spectrum Quotient (AQ).

Results

The spectroscopic findings are summarized in Table 1. Concentrations are in institutional units.

Metabolite	Control Mean	ASD Mean	Result	p value
Left glutamate	6.96 +/- 1.53	8.19 +/- .75	ASD>Controls	0.04
Left NAA	7.57 +/- 1.54	8.96 +/- 1.12	ASD>Controls	0.035
Right glutamate	7.51 +/- .79	7.68 +/- .95	NS	NS
Right NAA	8.96 +/- 1.22	9.55 +/- .64	NS	NS

The results show higher left side NAA and glutamate concentration in the ASD group versus the controls, with no significant differences on the right side. Within the ASD group, of the 5 subtest scores of the AQ, the communication score was significantly inversely correlated with left glutamate concentration ($r = -.87$, $p = .005$), suggesting that the total score was driven by communication ability. The correlation was also observed in the control group ($r = -.78$, $p < .02$). These correlations would not survive Bonferroni correction for the number of correlations.

Discussion

The elevation in Glu seen in the autism group corresponds well with prior MRS data in the hippocampus (1) and with serum glutamate levels (2), although at least 1 study reported lower Glx and NAA concentrations in a much younger sample (7). Of note, that study also used a significantly longer TE (135 ms) than either the current study (30 ms) or that of Page et al. (1) (35 ms). Several other studies report lower levels of NAA in autism, usually in younger samples than ours (e.g., see 8). Higher NAA has been reported in one prior study (9). The inverse relationship between Glu and symptom severity was unexpected and should be replicated in a larger sample.

References

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Support: This project was supported by NIH/NCRR Colorado CTSI Grant Number 5 UL1 RR025780. Its contents are the authors' sole responsibility and do not necessarily represent official NIH views. Additional support from Autism Speaks!