

## **The Role of Glutamate and GABA in Autism Spectrum Disorders: Pilot Results from a Proton Magnetic Resonance Spectroscopy Study**

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**Objectives:** To measure the levels of glutamate, a major excitatory neurotransmitter; glutamine, a metabolite of glutamate; and  $\gamma$ -aminobutyric acid (GABA), a major inhibitory neurotransmitter; in a pilot study of proton magnetic resonance spectroscopy ( $^1\text{H}$ -MRS) findings in adolescents with Autism Spectrum Disorders (ASD).

**Methods:** The subjects were assessed with the Autism Diagnostic Observation Schedule (ADOS), the Reading the Mind in the Eyes test (RMET) and the Social Responsiveness Scale (SRS).  $^1\text{H}$ -MRS measures of the anterior cingulate cortex were conducted using a Philips 3.0 T scanner.

**Results:** To date, we have completed the data analysis on 18 subjects, 8 with ASD and 10 healthy control (HC) subjects. There was no significant difference between the combined glutamate + glutamine concentrations as measured by  $^1\text{H}$ -MRS (ASD =  $12.0 \pm 0.9$  IU, HC =  $11.6 \pm 0.8$  IU,  $p = 0.37$ ). However, there was a higher than average glutamine level in the ASD group compared to healthy controls (ASD =  $2.4 \pm 0.2$  IU, HC =  $1.9 \pm 0.3$  IU,  $p = 0.01$ ). This was accompanied by a trend toward lower GABA/Cr levels in the ASD group (ASD =  $0.073 \pm 0.010$ , HC =  $0.082 \pm 0.010$ ,  $p = 0.06$ ). Glutamine levels in the ACC were correlated positively with deficits of social cognition across groups (higher SRS, lower RMET scores). Those with higher glutamine levels made more errors when identifying emotions in the RMET task ( $r(10) = -0.77$ ,  $p = 0.009$ ), and also had more clinically significant scores on the SRS ( $r(10) = 0.87$ ,  $p = 0.001$ ).

**Conclusions:** Our results present evidence that glutamine levels measured within the ACC region are higher for adolescent males with ASD than age-matched HC males, and signal that GABA levels may also be decreased in this region. These changes are correlated with deficits in social cognition.