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NAA-NAAG metabolism imbalance associated neuronal damage and socio-communicative impairment correlation in ASD.

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Graphical Abstract

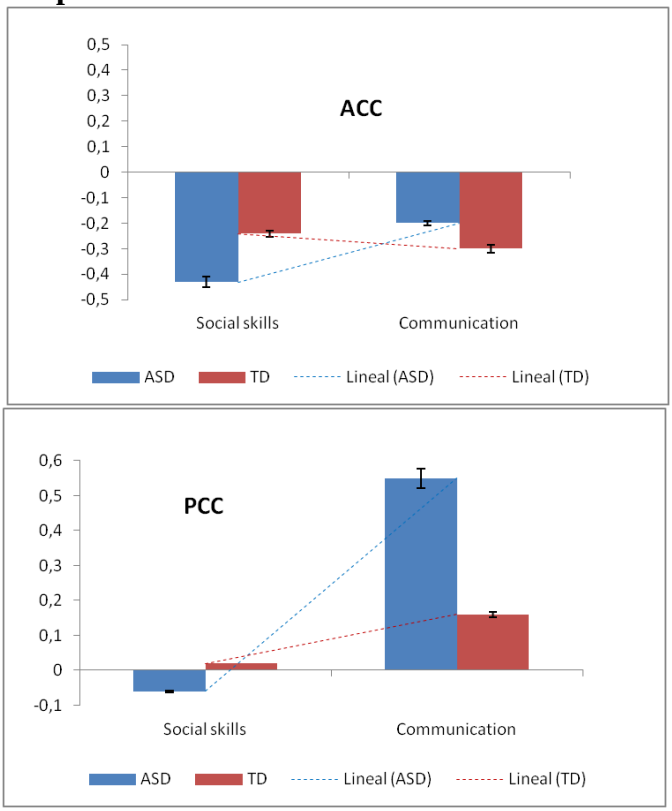
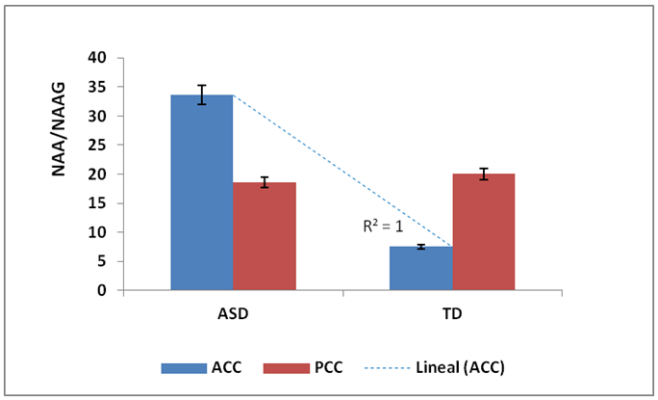
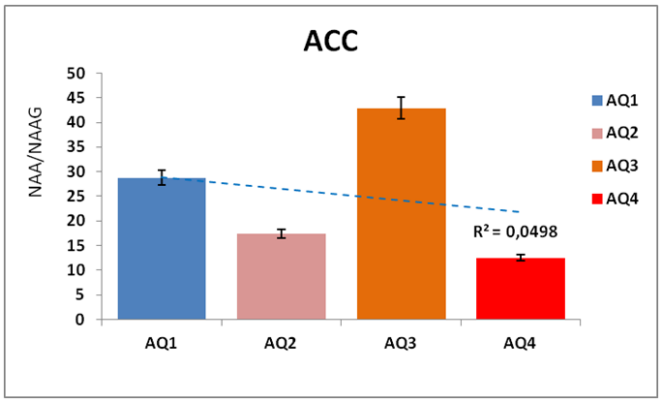


Fig. 1 *Correlation between social skills and communication and NAA/NAAG ratio in ASD and TD groups in cingulated cortices (ACC, PCC).*

Abstract.

Background: *Autism Spectrum Disorder (ASD) is a neurodevelopment disorder characterized by socio-communicative impairments as one of the core symptoms. Autistic symptoms may be seen in the first year of life, they vary in severity from mild to severe, and in a few instances, they may improve over time, even without treatment. The neuropeptide N-acetyl-aspartyl-glutamate (NAAG) modulates glutamate release which has been proposed as a key mechanism underlying symptoms of ASD. NAAG provides one of the components of the proton magnetic resonance spectrum (^{1}H-MRS) in humans. The signal of NAAG, however, largely overlaps with its precursor and degrading product N-acetyl aspartate (NAA) that by itself does not act in glutamatergic neurotransmission. Previously, we described the altered N-Acetyl-aspartyl-glutamate levels found in cingulated cortices by ^{1}H-MRS in individuals with ASD that suggested neuronal damage. Taken together, the findings of this study support our hypothesis and a role*





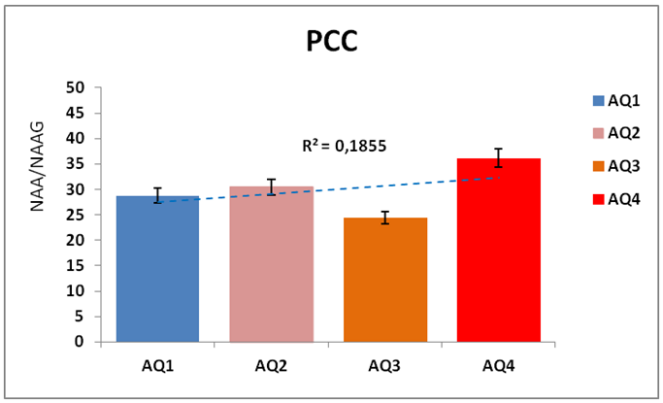


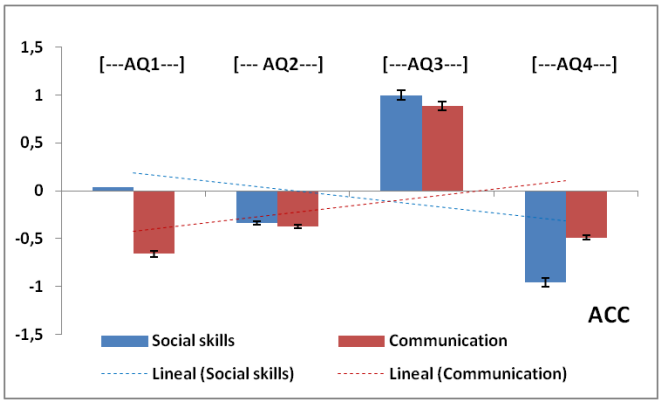
Fig. 2 *NAA/NAAG ratio in ASD, TD, and AQ groups (AQ1, A2, AQ3, and AQ4) in cingulated cortices (ACC, PCC).*

for NAA-NAAG imbalance and impairments in the Social-communication skills in autism, which lead the next step in our investigation to correlate imbalances neurochemistry linked to cingulated cortices in social and communicational skills in the autism spectrum disorders.

Aim: *To study imbalance of NAA-NAAG metabolism role in the cingulated cortices correlated with the AQ domains social skills and communication associated with ASD severity using ^{1}H-MRS.*

Methods: *We quantified NAAG and NAA separately from the ^{1}H-MRS signal in 22 patients with ASD and 44 healthy comparison subjects, matched for age, gender on a 3.0 Tesla MR scanner. Autism quotients (AQ) scores were assessed. Statistic one-way ANOVA and Bonferroni correction was applied. Furthermore, the Pearson correlation hallmarks the goal.*

Results: *The results of the Pearson correlation were represented graphically, where it was observed that there is no correlation between the Socio-communicative skills and the NAA/NAAG ratio in the ACC (r = -0.43, P = .005) in ASD group (See Fig.1). However, when was stratified ASD plus TD groups as AQ1, AQ2, AQ3, and AQ4, there was within groups differences (AQ1, AQ2, AQ3, and AQ4) of NAA/NAAG ratio; was increased significantly (P = .05) in AQ3 (See Fig.2) and, decreased in AQ4. Comparably, there was no differences of (NAAG, NAA, or NAA/NAAG) concentrations in the PCC, but a positive linear correlation with communication (r = .55, P = .049) was observed in ASD group. In addition, in both ACC and PCC, the AQ2, AQ3, and AQ4 groups maintain a different correlation pattern than the AQ1 group (See Fig.3), both in social skills and communication showing the severity level change within AQ domains.*



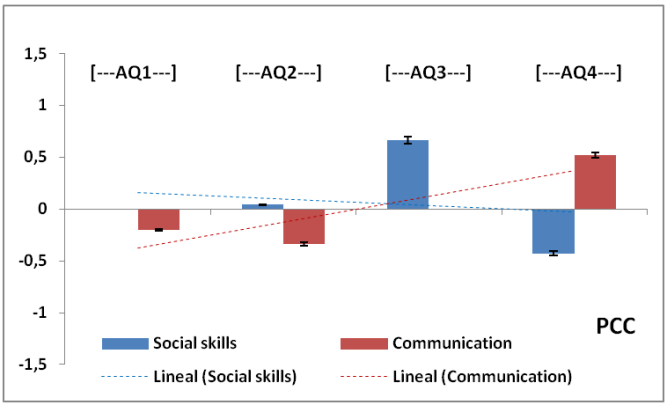


Fig. 3 *Correlation between social skills and communication, and NAA/NAAG ratio in ASD severity by AQ-score by AQ groups (AQ1, A2, AQ3, and AQ4) in cingulated cortices (ACC, PCC).*

These results make us suggest the relation of the deficit socio-communicational with the enlarged relative grey matter volumes (rGMV) of auditory network in ASD adults; in accordance with that described by (Watanabe & Rees, 2016); who demonstrated the relation of the deficits associated with the severity of autistic socio-communicational core symptom. Since NAA is considered a marker of neurons, these results provide stronger support for neuron loss in the posterior cingulated cortex than volume measurements by MRI alone.

Conclusion: *We conclude that the concentrations of NAAG and NAA act differently in ASD. The opportunity to measure NAAG in subjects with ASD creates a new and promising approach for intensified research on the glutamatergic systems and on the effects of novel drug candidates.*

Keywords: *Autism; Biomarkers; N-Acetyl aspartil glutamate; Cingulated cortices; Resonance magnetic spectroscopy.*

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