Glutathione Metabolism in the cingulated cortices related to Autism Quotient Pattern in Adults: Advances in diagnosis

Background: Autism spectrum disorder (ASD) is a neurodevelopmental disorder whose precise etiologic seems to be as heterogeneous as its severity levels. Nevertheless, accumulating evidence suggests that oxidative stress could be a common feature in autism, which may be further exacerbated by inflammatory phenomena, immune deregulation, and certain autoimmune risk factors, that may also contribute to the development and pathogenesis of autism. Following our research line linked to the tripeptide glutathione (GSH) as a key mechanism underlying symptoms of ASD, arise the hypothesis of GSH metabolism imbalance correlates with impairments on the domains of autism quotient (AQ).

Objetives: To study the correlation of glutathione (one of the major antioxidants) to the Autism Quotient (AQ) domains for adults using 1H-MRS *in vivo*.

Methods: We quantified glutathione reduced (GSH), creatine (Cr), and N-acetyl aspartate (NAA) signal in anterior (ACC) and posterior (PCC) cingulated cortices separately by magnetic resonance spectroscopy (MRS) on a 3.0 Tesla MR scanner, to assessed 22 adult patients with ASD and compared with 44 healthy subjects, matched for age, gender. AQ test were applied where the subgroup algorithm, which combines the scores on the five AQ domains (social skills, attention switching/tolerance to change, attention to detail, communication, and imagination) derived the cut off threshold to yield reliable autism subgroups as following: AQ1 (0–10 points) = below average; AQ2 (11–21 points) = average values of the normal population; AQ3 (22–31 points) = above average; AQ4 (32–50points) = very high index of autistic characteristics (Asperger's syndrome or high functioning autism has an average score of 35). Statistic one-way ANOVA was applied. Pearson´s correlation hallmarks our goal.

Results: The Pearson correlation coefficient represented graphically, showed a positive significant correlation between AQ domain 'Communication' to GSH ($r = 0.51$, $p = 0.01$); to GSH/Cr ratio ($r = 0.51$, $p = 0.01$); and GSH/NAA ratio ($r = 0.56$, $p = 0.004$) in AQ2 group (see Fig.1; Fig.2); in AQ3 to GSH negative significant correlation ($r = -0.69$, $p = 0.05$) in the PCC. Contrary in AQ4 to GSH/NAA positive significant correlation ($r = -0.54$, $p = 0.05$) in ACC.

Notably, in AQ1 group is a significant negative correlation between GSH/Cr ratio to ´Attention switching/tolerance to change´ domain ($r = -0.57$, $p = 0.03$); and significative positive correlation between GSH/NAA ratio to ´Attention to details´ domain ($r = 0.52$, $p = 0.05$) in PCC; indicating the intervention of creatine, responsible of cell damage caused by lack of oxygen and protector by preventing the depletion of energy ATP , and N-Acetyl aspartate (marker of density neuronal). AQ2, AQ3, and AQ4 groups maintain a pattern correlation to AQ domains different than the AQ1 group (considered group of healthy subjects) and highlight the differences in the autistic characteristics within ASD, and as hallmark of the ´Communication´ deficit (Bjørklund, G., 2021).

Conclusions: The opportunity to measure the concentration of GSH in cingulated cortices creates a new and promising approach for intensified diagnosis and the effects of a new venue clinical trial in ASD.

Keywords: Autism Spectrum Disorders, Brain, Glutathione, Neuroinflammation, Oxidative stress

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