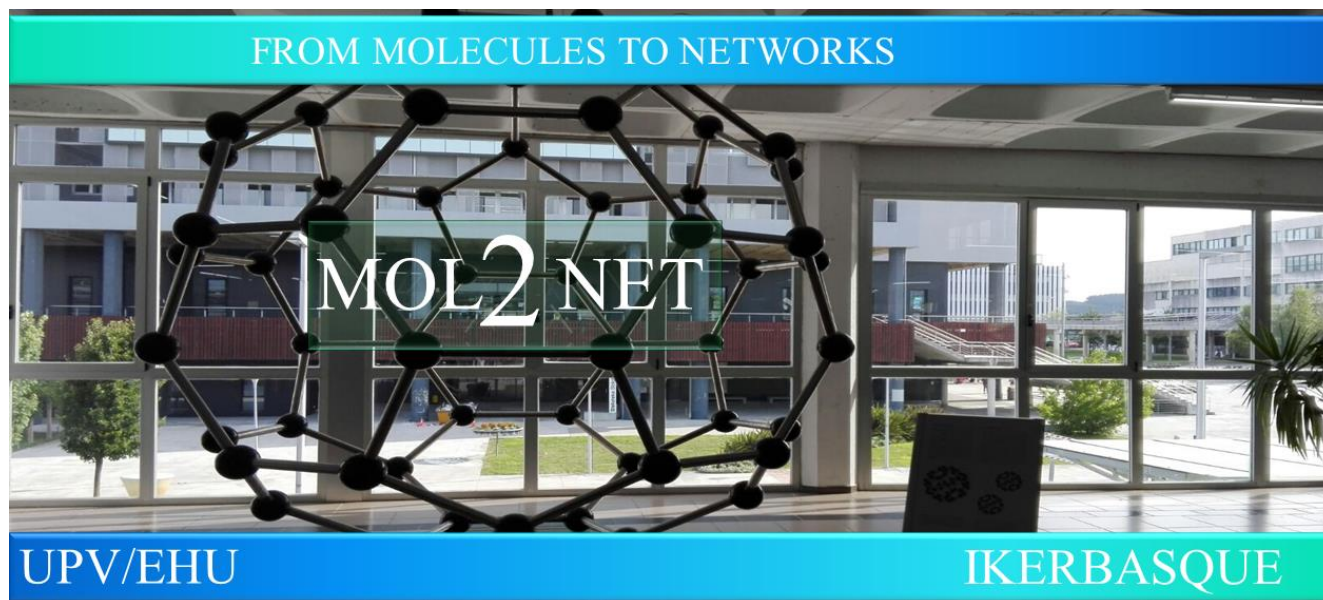




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Correlated NAAG metabolism imbalance with ‘attention switching/tolerance of change’: a biomarker in the actual triad of impairment in autism.

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Graphical Abstract

Abstract.

Background: The sensory impairment is a core diagnostic feature of autism spectrum disorder. However, the underlying mechanisms of symptoms across spectrum remain unknown. Deficits in eye contact are a hallmark of autism diagnostic [1], and figure most prominently determined by in clinical instruments knower [2].

Table 1. Pearson's bivariate correlations coefficient (r) of NAA/Cr, NAAG/Cr, and NAA / NAAG ratios with 'attention switching/Tolerance of change' in ASD vs. TD group. P < 0.05 considered significantly different.

Brain areas ratios	ASD		TD	
	r	p	r	p
ACC				
NAA/Cr	0,1714	0,4576	0,04361	0,7893
NAAG/Cr	0,4395	0,2759	- 0,08881	0,7436
NAA/NAAG	-0,0921	0,8283	-0,04227	0,914
PCC				
NAA/Cr	0.5396	0,0116	-0,1247	0,4434
NAAG/Cr	-0,7924	0,0109	-0,4265	0,0878
NAA/NAAG	0,7775	0,0137	0,02993	0,9346

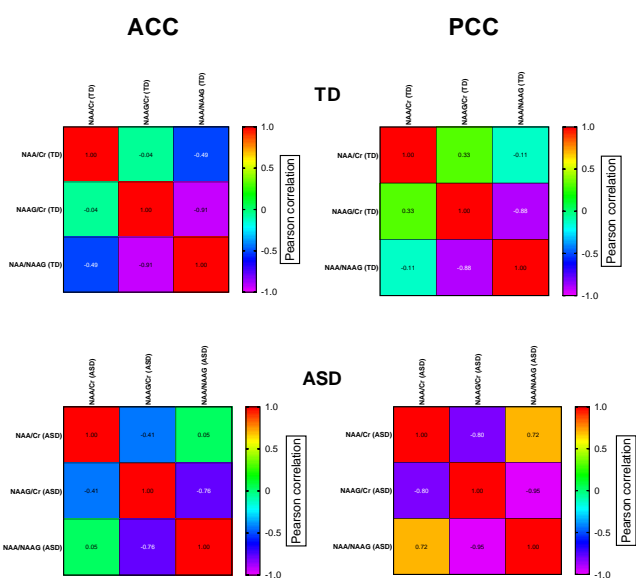


Figure 1. Heatmap of the Pearson correlation coefficient matrix between 'attention switch-ing/tolerance of change' and, NAA/Cr, NAAG/Cr, and NAA/NAAG ratio in ACC, and PCC. ASD and TD groups were compared.

The original triad of autism impairments in the late 1970s [3] described the behavioral manifestation (impaired communication, impaired social skills, and a restricted and repetitive way to existing), while the actual triad of impairment in autism is visual as opposed to linguistic processing, impaired abstraction, and lack of theory of mind, and it is central to all diagnoses that together makes up the autism spectrum disorders (ASD) [4]. In this sense, deficits of in "attention switching/tolerance to change" are one of autism impairments that is linked to the limbic system, according to early neuropathology studies [5]. More recently, ASD has been associated with metabolic and functional abnormalities of the posterior cingulated cortex (PCC), specifically, abnormal functional responses and reductions in functional connectivity [6, 7].

Aim: To study of neuropeptide NAAG metabolism in the cingulated cortices correlated with the AQ domain 'attention switching /tolerance of change' associated with the actual triad of impairment in ASD.

Methods: To examine the NAAG metabolism imbalance correlates of attentional impairment symptoms that are associated with autism spectrum disorder, we analyzed spectroscopy MRI data obtained from 65 people with either autism spectrum disorder (n = 21 autism spectrum disorder, mean age = 21.0) and 44 neurotypical controls (mean age = 23.3, range: 18–35 years) using a cases-control study design. Autism quotients (AQ) scores were assessed. Statistic one-way ANOVA and Pearson correlation coefficient was applied.

Results: The results shown there is a significant positive correlation between NAA/Cr ratio and 'attention switching /tolerance of change' in the node PCC (r = 0.5396; p = 0.0116), and opposite direction to negative (This means that when one variable increases, the other variable decreases) correlation in TD (see Table 1, Figure 1).

Despite, although positive correlation is moderate ($0.40 < r < 0.60$) in magnitude, its direction show there is significant, i.e., the changes in the variable influence the changes in the other variable in ASD. Besides, there is a higher significant negative correlation with NAAG/Cr ($r = -0.7924$, $p = 0.0109$), and higher significant positive correlation with NAA/NAAG ($r = 0.7775$, $p = 0.0137$) in ASD, compared to TD. In contrast in ACC, a moderate positive correlation with NAAG/Cr ($r = 0.4395$, $p = 0.2759$) highlight in ASD. According to, other authors that reported that attention is closely related to the reward value of stimuli, activating the ACC to mediate attention [8], which supports our results.

Conclusion: *The neuropeptide N-Acetyl aspartyl glutamate (NAAG) is non correlated to the 'Socio-communicative' skills ASD impairment [9], however was correlated to 'Attention switching / tolerance of change' in ASD suggesting the neuropeptide imbalance as biomarker of diagnostic to the real triad of autism.*

Keywords: *Autism spectrum disorders; Cingulated cortices; Autism Quotient (AQ) domain; 'attention switching /tolerance of change'; 1H-MRS*

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