

**Program Number:** 800.11      **Day / Time:** Tuesday, Oct. 26, 3:00 PM – 4:00 PM

## *in vivo* <sup>31</sup>P spectroscopy evidence of different regional neurodevelopmental alterations in children with ADHD

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The neurodevelopmental disorder, attention-deficit/hyperactive disorder (ADHD), is one of the most prevalent childhood behavioral disorders and studies have implicated the basal ganglia (BG) and prefrontal (PF) regions, which are associated with the neural networks of attention. The purpose of this study is to assess possible molecular/biochemical alterations in ADHD children using a multi-voxel *in vivo* <sup>31</sup>P spectroscopy method. We hypothesize membrane phospholipid (MPL) metabolite deficits in the PF and BG regions of ADHD children.

Freely mobile MPL precursors [PME(s-<sup>γ</sup>C)] and breakdown products [PDE(s-<sup>γ</sup>C)], phosphocreatine (PCr), adenosine triphosphate (ATP), and inorganic orthophosphate (Pi) were quantified in the PF and BG regions of 10 ADHD and 14 healthy children using *in vivo* <sup>31</sup>P spectroscopy. None of the ADHD subjects have a first-degree relative diagnosed with a major psychiatric disorder.

Compared to controls, PME(s-<sup>γ</sup>C) levels of ADHD children were significantly reduced in the PF (p=0.017), which was more pronounced on the right side (p=0.0031), and in the BG (p=0.0034) with a greater effect on the left side (p<0.0001). The PME(s-<sup>γ</sup>C)/PDE(s-<sup>γ</sup>C) ratios were significantly lower in the right PF of ADHD children compared to controls (p=0.025). Additionally, the group-by-age interaction for PCr levels was significant in the BG (p=0.014) suggesting higher PCr levels in the older ADHD children.

These alterations are consistent with structural MRI data, which in general show overall smaller brain volume and more pronounced differences on the right side. When compared to metabolite levels of normal developing brains, these results suggest an alteration in the pruning of overproduced cells in the PF, and an underdevelopment of neuronal processes and synapses in the BG.

**Citation:** J.A.Stanley, H.Kipp, E.Greisenegger, K.Panchalingam, J.W.Pettegrew, M.S.Keshavan, O.G.Bukstein. *in vivo* <sup>31</sup>P spectroscopy evidence of different regional neurodevelopmental alterations in children with ADHD. Program No. 800.11. *2004 Abstract Viewer/Itinerary Planner*. Washington, DC: Society for Neuroscience

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