Connectivity of the posterior cingulate cortex in ADHD children patients.

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Target audience: Medical doctors and researchers in the field of image processing, neurosciences and neurological disorders.

Purpose/Introduction: ADHD is the most common neurological disorder in children and adolescents with prevalence circa 7% (**1**). The Posterior Cingulate Cortex (CC) which comprises Broadman Areas (BA) 23 and 31 is a key node of the default mode network of resting states and together with its neighbor structure, the retrosplenial cortex (BA 29), has been shown to be affected by ADHD (**2**). Several studies exist on the resting states of this disorder (**2**) but little to no amount of work to our knowledge exists studying the specific ROI to ROI connectivity for resting states networks in ADHD patients. Connectivity studies establish the strength of functional relations between different brain regions. This analysis might be of more interest than resting state networks on their own as they can highlight abnormal relations even when both regions appear "active" in a network. In this project we compared ADHD (AD) children patients with healthy (H) ones. We assessed the differences in connectivity in their resting states with a special focus in the role of the posterior cingulate and retrosplenial cortex.

Methods: Experiment: 30 volunteers all of them children (9.4±2 years) of both sexes (27 males and 3 females) were used in this study. This group was subsequently divided into two cohorts of 15 subjects each, one with AD (all from the combined subgroup of ADHD) and the other with H patients (matched in age). All the AD volunteers had received medication for the last two months ((methylphenidate 1 mg/kg/day) and atomoxetine (1.2 mg/kg/day)). Protocol: Volunteers laid in the scanner for 7.25 min. in silence and with closed eyes. MRI Hardware: Experiments were performed in a 1.5 T Philips Intera-Achieva scanner using an 8 channel SENSE head-coil. Resting State: 150 brain volumes comprising 35 coronal slices covering the whole of the brain (including cerebellum) were acquired with a Fast-Echo-EPI sequence. TR=2.9 s., TE=50 ms., 64x64 matrix with a 3.6 x 3.6 mm *in-plane* resolution and 4 mm slice thickness (no gap between slices). Resting State analysis was performed using CONN fMRI software (http://www.nitrc.org/projects/conn). fMRI and structural data were segmented and CFS, white and grey matter masks were obtained for every individual. After slice time correction, realignment, motion correction and smoothing; data was masked and filtered (keeping frequencies between 0.01 and 0.1 Hz). Time courses from 94 Areas (47 Broadman areas (BA) divided in left and right) were extracted from each individual in our groups. Second level analysis was then performed comparing results from two groups with a statistical threshold of $p<0.05$ with FWE corrections for multiple comparisons. ROI to ROI correlations or connectivity data is presented here for the dorsal CC (BA 31), the ventral CC (BA 23) and the retrospenial CC (BA 29).

Results: Connectivity results are presented in Figure 1. These are results from the ADHD-Control comparison (red indicates stronger correlation for AD patients than H and blue the opposite). Volunteers with ADHD presented larger amounts of cerebral correlations from CC (97%) than healthy controls (3%). In image 1a connectivity of the left ventral CC to cingulate gyrus, supramarginal gyrus, right posterior superior temporal lobe and a negative correlation to the medial prefrontal cortex (MPFC) are presented. Figure 1b connections from left dorsal CC to the right anterior superior temporal gyrus and to the cingulate gyrus are presented. For 1a and 1b data from the corresponding right structures showed the same connectivity and are not presented here. Finally the retrosplenial cortex showed large number of connectivity and differences between the left and right structures (1c and 1d respectively). Common connections were found to the somatosensory association cortex, cingulate gyrus, primary auditory cortex, dorsal prefrontal cortex, supramarginal cortex and right posterior sup cingulate cortex. Nevertheless in 1c connections to the premotor, motor and insular cortex were not present. For the right retrospenial cortex (1d) connections to primary and secondary visual cortex were found.

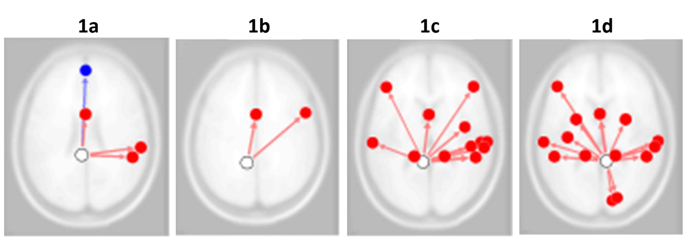

Figure 1: Connectivity for posterior CC when comparing AD-H. Red indicates stronger correlation for AD patients than H and blue the opposite. 1a Are left ventral CC connections, 1b left dorsal CC connections and 1c and 1d retrosplenial connections (left and right respectively).

Discussion and Conclusions: The larger number of connections in posterior CC and retrosplenial structures in ADHD patients indicated a larger role or involvement of these regions in the disorder when compared to H controls. A strong connection existed between the ventral CC (episodic memory retrieval) and the MPFC for healthy subjects (1a). The MPFC is a region related between others to memory consolidation. In contrast the retrosplenial cortex and the ventral CC presented strong connections to the cingulate gyrus (1a and 1b) in the AD group. The cingulate gyrus is related to emotion formation and processing, memory and learning. We hypothesize that the differences in information processing and regional connectivity between MPFC and cingulate gyrus could be the source of the difficulty that ADHD patients have following orders and organizing activities. These conclusions are just one of the connections we present here but there are plenty more connections that can be studied and the neurological implications considered. This study is limited by the many factors that have to be considered when creating a population for studies of ADHD. Several variables might affect the outcome and some of those are: Age, sex, IQ, kind of medication, time under medication, secondary syndromes induced by ADHD (i.e. sluggish learner), etc.

References: (**1**) Polanczyk, G., De Lima, M. S., Horta, B. L., Biederman, J. & Rohde, L. A. 2007. The worldwide prevalence of ADHD: a systematic review and metaregression analysis. *Am J Psychiatry,* 164, 942-8. Med Image Comput Comput Assist Interv. 2005;8(Pt 2):468-75. (**2**) Eur J Radiol. 2013 Sep;82(9):1552-7. doi: 10.1016/j.ejrad.2013.04.009. Epub 2013 May 14.Altered regional homogeneity patterns in adults with attention-deficit hyperactivity disorder. Wang X, Jiao Y, Tang T, Wang H, Lu Z. (**3**) Discriminative analysis of brain function at resting-state for attention-deficit/hyperactivity disorder. Zhu CZ, Zang YF, Liang M, Tian LX, He Y, Li XB, Sui MQ, Wang YF, Jiang TZ. Med Image Comput Comput Assist Interv. 2005;8(Pt 2):468-75.