Resting-state alterations in EEG-fMRI coupling in adults with attention-deficit/hyperactivity disorder

Lars Michels[1,2], Steffen Bollmann[2], Diego Manuel Baur[2], Anthony Schläpfer[3], Maya Schneebeli[3], Carmen Ghisleni[2], Peter Klaver[2,4], Daniel Brandeis[3,5], and Ruth O'Gorman[2]

[1]Institute of Neuroradiology, University Hospital Zurich, Zurich, Zurich, Switzerland, [2]Center for MR-Research, University Children's Hospital, Zurich, Zurich, Switzerland, [3]Department of Child and Adolescent Psychiatry University of Zürich, University of Zurich, Zurich, Switzerland, [4]Institute of Psychology, University of Zurich, Zurich, Switzerland, [5]Department of Child & Adolescent Psychiatry and Psychotherapy, Central Institute of Mental Health Ma, Medical Faculty Mannheim / Heidelberg University, Mannheim, Mannheim, Germany

Target audience – Researchers interested in EEG, functional MRI, and attention-deficit/hyperactivity disorder.

Introduction – Attention-deficit/hyperactivity disorder (ADHD) is a developmental psychiatric disorder with high prevalence, affecting approximately 3-5% of the adult population[1]. The precise neurobiological mechanisms underlying the disorder remain unclear. The aim of this study was to localize and better characterize resting EEG-fMRI coupling differences between ADHD and control adults using simultaneous EEG-fMRI. We hypothesized that ADHD patients show a different EEG-fMRI signal coupling in frequency bands and brain regions previously associated with ADHD, particularly for theta, alpha, and beta bands in regions of the default mode network (DMN) and cognitive control network (CCN)[2,3,4].

Methods – We examined 17 adults with ADHD (9 females, age 37.6 (SD=11.1)) and 26 control adults (16 females, age 33.5 (SD=9.9)). Groups were matched for age and handedness. For fMRI, 35 axial slices covering the whole brain were acquired with a multi-slice EPI sequence (slice thickness: 3 mm; gap: 0.3 mm; slices: 35; TR: 1.93 s; TE: 32 ms; flip angle: 74°; matrix: 64 x 64; FOV: 240 mm). Each resting state fMRI session consisted of two alternating eyes-closed (EC) and eyes-open (EO) blocks of 2.5 min duration. The 60 channel EEG was recorded using MR-compatible BrainAmp Plus amplifiers (Brain Products, Germany) using 5 kHz sampling rate, 0.5 μV amplitude resolution, and DC to 250 Hz hardware bandpass filters. Offline processing of the EEG data was done using Brain Vision Analyzer software. To construct the regressors for the general linear model, we convolved each EEG frequency-band (delta (1-3 Hz), theta (4-8 Hz), alpha1/2 (8-10 and 10-13 Hz), and beta1/2 (14-19 and 20-30 Hz)) dependent global spectral power time series with the hemodynamic response function, resulting in 4 regressors (EC1, EO1, EC2, EO2). EO/EC transition phases and motion parameters were modeled as confound regressors. Correction for physiological noise was applied similar to the CompCor approach[5]. EEG-fMRI results were corrected based on the cluster extent correction for multiple comparisons at $p < 0.05$ (voxel type I error of $p = 0.005$, $t > 2.7$, $k > 241$ voxels).

Results – Pronounced differences in EEG-fMRI BOLD coupling between controls and ADHD were found in theta, alpha1, and beta1. Decreased theta EEG-fMRI signal correlations in ADHD were seen in the parietal operculum (EO), whereas increases were seen in the precuneus (EO/EC) and posterior cingulate cortex (EO, part of the DMN). Increased alpha1-fMRI signal coupling in ADHD was observed in the thalamus, caudate nucleus (both EC), precentral-, superior temporal-, and angular gyrus (EO). During EO, beta1 showed a coupling increase in ADHD in the precentral-, postcentral-, angular gyrus, and lateral occipital cortex (LOC). Decreases were observed in the supplementary motor area (SMA, part of the CCN), middle/superior frontal-, and occipital/fusiform gyrus. During EC, coupling decreases in ADHD were observed in the LOC.

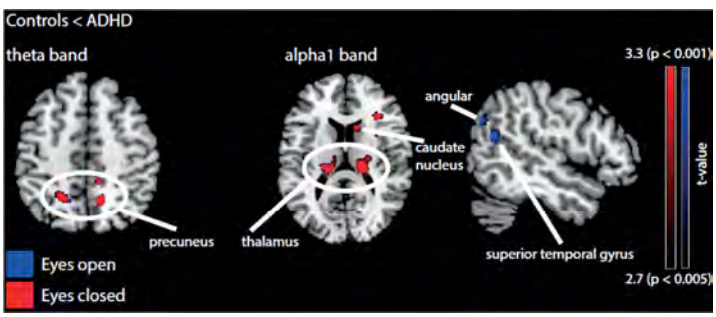

Fig. 1: Positive EEG-fMRI signal correlations in the theta (left panel) and alpha (right panel) band. Adults with ADHD show stronger coupling in parietal-, thalamic-, and frontal areas.

Discussion – Our findings indicate that several regions of the DMN and CCN show resting EEG-fMRI coupling alterations in adults with ADHD. These results fit with those from studies that reported functional and structural abnormalities in these regions and frequency bands[2,3,4]. The mixed pattern with increased and decreased group coupling differences suggests the presence of non-uniform physiological resting-state alterations in ADHD. Specifically, we conclude that regions involved in visual memory processing (precuneus and caudate nucleus) and sensory regulation (thalamus and angular gyrus) are functionally abnormal in adults suffering from ADHD.

Conclusion – Future work should clarify whether ADHD-specific EEG-fMRI signal coupling alterations are already a functional hallmark in children with ADHD.

References

[1]Faraone et al., J Atten Disord, 2005; 9(2): 384-91, [2]Castellanos et al., Biol. Psychiatry 2008; 63: 332–337, [3]Posner et al., Neuropsychol. Rev 2014; 24: 3–15, [4]Sripada et al., Human Brain Mapping 2014; doi:10.1002/hbm.22504, [5]Behzadi et al., NeuroImage, 2007; 37(1):90-101.