Response to Helen Pincham review of Lenartowicz et al. (2014) "[EEG] correlates …"

We thank Pincham for her thoughtful and appreciative discussion. Some comments: First, we agree that extending our analysis to a larger sample size is necessary to test the robustness of our classification model exemplar. Our intention here was to test and demonstrate that source-resolved EEG measures can extract information from the data that is useful for subject classification. A more useful goal may be to develop EEG indices of ADHD heterogeneity and to understand how they may inform treatment response and clinical outcome. Such an approach could also be important for teasing apart the relationship between the observed neural signatures and co-morbidities such as ADHD and ODD.

In our sample, there was in fact no significant difference in P2 amplitude between the 37 study subjects with ADHD alone (mean=.17) and the 10 subjects diagnosed with co-morbid ADHD and ODD (mean=.14; p=.86); there was however a significance difference between ADHD plus ODD and controls (mean=.62; p=.05). We also cannot find differences in P3 between these subgroups ($p>.68$, at electrodes Pz, P3 and P4), suggesting that the alpha and P2 measure differences primarily index a deficit in vigilance rather than in ODD 'disinhibition.' Consistent with this conclusion, the increase in the source-resolved central occipital alpha band activity during stimulus encoding, and to a lesser extent the magnitude of the frontal midline source P2 peak were correlated with inattentive symptoms not hyperactive symptoms. It could be interesting to further test, for example, whether children with ODD and/or primarily hyperactive symptoms show the reverse effect (a group difference in P3 but not alpha or P2 measures), supporting a double dissociation.

Pincham also questions whether the larger midline frontal theta activity during memory maintenance in ADHD participants need indicate neural compensation for ineffective encoding processes, because their overall behavioral performance was lower than that of controls. Note, however, that we here analyzed only the behaviorally successful trials. Since many studies have associated frontal midline theta activity and similarly localized anterior cingulate activation in BOLD studies with effortful concentration, attempts to resolve conflicting evidence, etc., our results suggest that this EEG feature, and the larger increase in ADHD subjects in central occipital alpha power during memory maintenance, may have indexed ADHD subjects' effort to compensate their inefficiency in attending the just-presented encoding stimuli during these trials in which they did achieve behavioral success. The first author is now attempting to further explore this question by combining EEG with fMRI recordings – both by fusing the two modalities collected independently in the same individual and by concurrent data collection – to test how spectral measures may correlate with BOLD signal levels in and/or interactions between occipital, parietal, prefrontal, and/or medial frontal cortices.

Our paper highlighted the importance of source-resolved EEG signal processing and modeling for capturing spatially and temporally precise information about brain dynamics, allowing better understanding of cortical mechanisms characterizing or underlying psychiatric disorders. This can in turn, we believe, accelerate identification of refined endophenotypes and biomarkers of disease risk, causal genetic variants, and treatment response.

Agatha Lenartowicz*, Scott Makeig‡, Sandra Loo*
*UCLA Department of Psychiatry
‡UCSD Institute for Neural Computation