Event-related Potential Study of Visual Oddball Test in Children with Autism Spectrum Disorder, ADHD, comorbid Autism and ADHD, and Neurotypical Children

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Abstract

Background: Autism spectrum disorder (ASD) and attention deficit/hyperactivity disorder (ADHD) are two of the most commonly diagnosed childhood neurodevelopmental disorders. Although the comorbidity was excluded in DSM IV, DSM-5 does not preclude the concurrent diagnosis of ADHD and ASD (ASD+ADHD). In recent years the prevalence of both ASD and ADHD, as well as comorbid ASD+ADHD, has increased substantially.

Aims & Hypotheses: This study aimed to better understand the distinctions and similarities in manifestations of executive deficits among these conditions. For this purpose we used analysis of behavioral responses such as reaction time (RT)/accuracy and event-related potentials (ERP) during performance on a visual oddball task with illusory figures. Based on our prior data and other reports, we predicted that ASD diagnosis would factor more in such executive function as error monitoring, detection and correction, while those with an ADHD diagnosis would manifest changes in the latency of ERP responses.

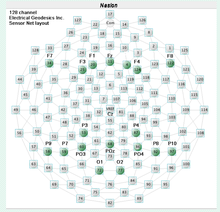
Methods: Participants were age-matched children (N=18 per group) with ASD, ADHD, comorbid ASD + ADHD diagnosis and neurotypical controls (CNT). EEG was collected using 128 channel EEG system. The task involved the recognition of a specific illusory shape, in this case a square or triangle, created by three or four inducer disks.

Results & Discussion: Analysis of data revealed that there were no between group differences in RT to target stimuli, but both ASD and ASD+ADHD groups committed more errors; more specifically, the ASD groups had higher omission error rates than neurotypical children. Post-error RT in ASD and ASD+ADHD groups manifested as a post-error response speeding rather than the corrective RT slowing typical of the controls. The ASD and ASD+ADHD group also demonstrated an attenuated error-related negativity (ERN) component as compared to ADHD and controls. The fronto-central N100 was enhanced and less differentiated in response to target and non-target figures in the ASD and ASD+ADHD groups as compared to CNT children. In addition, several frontal ERP components in response to non-target stimuli had prolonged latencies in the ADHD group as compared to both ASD and CNT groups.

Conclusion: This comparative ERP study confirmed the utility of using electrocortical responses to elucidate differences between ASD and ADHD and their impact in dual ASD+ADHD diagnosis. This information helps define the extent of overlap among these comorbidities both in terms of symptom expression as well as underlying neuropathology.

Methods: EEG Instrument

Equipment (EGI NetStation): EEG was sampled at 500 *Hz* with 0.1–100 *Hz* filtering. EEG data were segmented off-line into epochs spanning 200 ms pre- to 800 ms post-stimulus. Data were digitally screened for artifacts and contaminated trials were removed. Remaining data were sorted by condition and averaged to create the ERPs. Averaged ERP data were baseline corrected over the 200 ms pre-stimulus period, and re-referenced to an average reference representation.



Three stimuli oddball with novel distracter

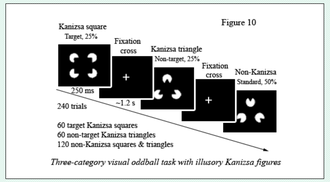


Figure 1. The stimuli employed in the test were Kanizsa square (target), Kanizsa triangle (non-target), non-Kanizsa square, and non-Kanizsa triangle (standards) (Kanizsa, 1976). The task represents a classic three-stimuli oddball with infrequent illusory Kanizsa target (square, 25%) and infrequent Kanizsa distracter (triangle, 25%) figures presented for 250 ms among frequent non-Kanizsa stimuli (so called standards, 50%) with inter-trial interval (ITI) varying in 1,100-1,300 ms range. Totally 240 trials were presented.

Subjects: Children with ASD, ASD+ADHD, ADHD and TD

Subjects (7-18 years old) were referred from the Weisskopf Child Evaluation Center and Autism Center at Uof, Louisville, KY.
The mean age of 18 participants enrolled in the ASD group was 13.2 ± (standard deviation) 3.5 years (range 8-18 years, 14 males, 4 females), the mean age of the ADHD group was 13.4 ± 2.9 years (N=18, range 8-18 years, 14 males, 4 females), the mean age of ASD+ADHD group was 12.5±3.1 (N=18, 7-17, 15 males, 3 females). The mean age of the control (CNT) group (N= 18) was 14.2 ± 3.9 years (9-18 years, 13 males, 5 females).

Reaction time: Accuracy, post-error RT slowing

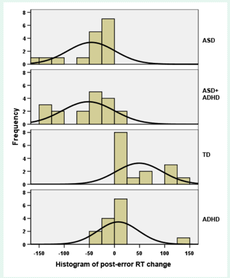


Figure 2. Histogram of distribution of individual post-error reaction time (RT) in children with autism, children with ASD+ADHD, typically developing (TD) controls and children with ADHD. Both ADHD and control groups demonstrate slower (positive) post-error RTs compared to correct response RTs. The ASD and ASD+ADHD groups show speeding of post-error RTs with a negative peak of distribution curve. The ADHD shows positive peak of the curve though still less expressed post-error RT slowing as compared to controls.

Reaction time and accuracy: There were no significant group differences in reaction time (RT) (492 ± 111 ms in ASD vs. 523 107 ms in ASD+ADD vs. 470 ± 89 ms in ADHD vs. 450 ± 97 ms in CNT, F3,71 =1.45, p=0.236, n.s.). Accuracy of response was different between groups, in particular total error percentage showed significant differences (F3,71=3.78, p=0.015). A post-hoc Tukey test yielded significant difference between ASD and CNT groups (17.9 ± 14.3 % in ASD vs. 2.4 ± 4.6 % in CNT, p=0.009). Omission error contributed significantly to group differences (F3,71=5.87, p=0.001). Post-hoc analysis showed both ASD and ASD + ADD vs. CNT difference (5.5 ± 4.9 % in ASD, 4.3 ± 5.3 % in ASD+ADD vs. 0.4 ± 0.9 % in typical children with p <0.01 in both comparisons).

ERP: Latency of parietal P3b

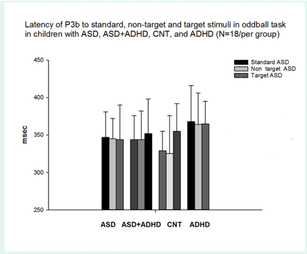


Figure 3. Latency of parietal P3b ERP component (mean with standard deviations) in response to standard, non-target Kanizsa and target Kanizsa figures in visual oddball task in 4 groups of children (ASD, ASD+ADHD, CNT, ADHD, N=18/per group). *Stimulus X Group* interaction was significant (F=2.39, p=0.029). Children with ADHD have delayed latencies to all type of stimuli, while ASD-only group is featured by similar latency to both task relevant and task-irrelevant stimuli. Note that control children (CNT group) showed shorter latency to both task-irrelevant items (standard and non-target Kanizsa).

Attention Deficit Symptoms

Attention symptoms on Achenbach ASEBA. Main group differences were found in Attention Deficit Hyperactivity Problem (DSM-oriented scale) T-scores (57.4 ± 6.1 in ASD vs. 69.9 ± 8.3 in ASD+ADHD, F1,34=23.24, p<0.001) and in general Attention Problems T-scores (76.3 ± 9.1 in ASD+ADHD vs. 59.1 ± 6.5 in ASD, F1,34=31.04, p<0.001). **ABC scores**. Group differences were present only in the Stereotypic Behavior scores (F2,53=6.74, p=0.001). ASD+ADHD group showed higher scores (7.67 ± 5.39) as compared to the ASD (3.55 ± 2.39, p=0.002) and ADHD (2.69 ± 4.64, p=0.005) groups.

ERP to targets, non-targets and standards at frontal and parietal ROI

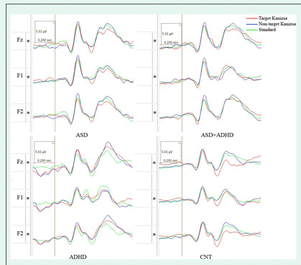


Figure 4. Frontal (Fz, F1, F2) ERPs to target Kanizsa, non-target Kanizsa and standard stimuli in ASD, ASD+ADHD, ADHD and CNT groups (N=18/per group).

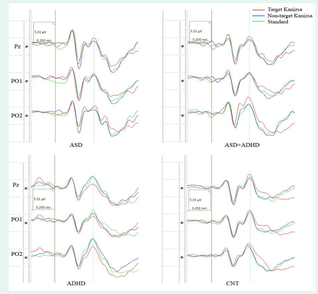


Figure 5. Parietal and parieto-occipital (Pz, P01, P02) ERP to target and non-target Kanizsa and standard stimuli in ASD, ASD+ADHD, ADHD and CNT groups. P3b component is marked by a blue line.

Summary

The current ERP study supports the proposed suggestion that some between group differences could be manifested in the frontal ERP indices of executive functions during performance on task. Our study suggests that investigation of quantitative EEG and ERP biomarkers of executive function abnormalities and other behavioral performance deficits present in ASD and ADHD is a feasible research strategy that may contribute to the better understanding of nosology of these two disorders and their co-occurrence.

The study supports the use of objective neurophysiological biomarkers such as ERP and behavioral (e.g., reaction time and accuracy) measures to delineate pathophysiological mechanisms in such complex and often overlapping disorders. These findings have significant implications for both shared and discrete symptom presentations for the two conditions.

Moreover, they can help delineate the boundaries and overlap between ADHD and ASD, especially if children with ADHD-alone and ASD- alone are compared with those with dual ASD+ADHD diagnosis, and further compared to neurotypical children used as a normative contrast group.