Neural Dynamics of Executive Function in Cognitively-able Kindergarteners with Autism Spectrum Disorders (ASD) as Predictors of Concurrent Academic Achievement: Preliminary Study

So Hyun Kim, PhD[1]; George Buzzell, PhD[2]; Susan Faja, PhD[3]; Yeo Bi Choi, BA[1]; Natalie Hiromi Brito, PhD[4]; Lauren Shuffrey, PhD[5]; William Fifer, PhD[5,6,7]; Frederick Morrison, PhD[8,9]; Catherine Lord, PhD[10]; Nathan Fox, PhD[2]

[1]Center for Autism and the Developing Brain, Weill Cornell Medicine, White Plains, NY 10605

[2] Department of Human Development and Quantitative Methodology, University of Maryland, College Park, MA 20742

[3] Department of Pediatrics, Harvard Medical School, Boston, MA 02115

[4] Department of Applied Psychology, New York University Steinhardt, New York, NY 10003

[5]Department of Psychiatry, Columbia University Medical Center, New York, NY 10032

[6]Division of Developmental Neuroscience, New York State Psychiatric Institute, New York, NY 10032

[7] Department of Pediatrics, Columbia University Medical Center, New York, NY 10032

[8] Department of Psychology, University of Michigan, Ann Arbor, Michigan 48109

[9] School of Education, University of Michigan, Ann Arbor, Michigan 48109

[10]Department of Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine at UCLA, Los Angeles, CA 90095

Corresponding Author: So Hyun "Sophy" Kim, Department of Psychiatry, Weill Cornell Medicine, White Plains, NY 10601, sok2015@med.cornell.edu

Abstract

Although electrophysiological (EEG) measures of executive functions (EF) (e.g. error monitoring) and their link to academic achievement in typically developing children have been suggested, work investigating the link between error monitoring and academic skills in children with autism spectrum disorder (ASD) is limited. We employed traditional electrophysiological and advanced time-frequency methods, combined with principal components analyses, to extract neural activity related to error monitoring, and tested their relations to academic achievement in 35 cognitively-able kindergarteners with ASD. A child-friendly Go/No-go "Zoo Game" successfully elicited an error-related negativity (ERN) and error positivity (Pe) in children with ASD as young as 5 years. We also observed increased response-related theta power during error relative to correct trials. Both larger Pe and theta power were associated with academic achievement. However, only the effects of theta power on reading and math skills remained significant after controlling for behavioral performance on the Zoo Game and IQ. Results suggest that the use of time frequency EEG analyses may provide new opportunities to investigate neurobiological mechanisms of EF in young children with ASD. Results also provide further insights for the development of more targeted treatment programs designed to improve EF, which could have cascading effects on academic development.

Keywords: executive function, autism spectrum disorder, academic achievement

Recent estimates indicate that 512,000 students in the U.S. received educational services for autism spectrum disorder (ASD) under the Individuals with Disabilities Education Act in 2013 (Kena et al., 2015). With increasing early awareness and intervention efforts, greater numbers of children with ASD make significant cognitive and behavioral gains during the toddler and preschool years (e.g., Dawson et al., 2010) and are able to attend kindergarten with typically developing (TD) peers. Yet, we have limited knowledge about factors that contribute to academic outcomes in cognitively-able children with ASD, particularly at the neural level. Prior work has employed behavioral assessment of executive function (EF) encompassing inhibitory/interference control, working memory, and attention/set shifting (Fuster, 1997; Miyake et al., 2000) as one of the key predictors of academic outcomes including early literacy and math skills (Blair, 2002, 2016; Cameron et al., 2012; McClelland, Acock, & Morrison, 2006; McClelland et al., 2007; Ponitz, McClelland, Matthews, & Morrison, 2009; Willoughby, Kupersmidt, & Voegler-Lee, 2012). Furthermore, the effects of EF on academic achievement go above and beyond IQ and socioeconomic status (Blair & Razza, 2007; Morrison, Ponitz, & McClelland, 2010; Wiebe, Espy, & Charak, 2008). Evidence consistently suggests that inhibitory control, including the ability to control and sustain attention and participate in classroom activities, predicts academic achievement in children in preschool and kindergarten classrooms (Allan, Hume, Allan, Farrington, & Lonigan, 2014; Raver, Smith-Donald, Hayes, & Jones, 2005). Compared to TD children, teachers reported that children with ASD have significantly more difficulties with EF such as inattention and hyperactivity in the classroom (Happé, Booth, Charlton, & Hughes, 2006). It has also been shown that EF, including working memory and inhibitory control, was significantly more impaired in children with ASD than in TD peers (Konstantareas & Stewart, 2006), which may have cascading effects on their academic outcomes.

Existing behavioral work suggests that impairments in EF broadly may have significant effects on academic outcomes in cognitively-able children with ASD. The use of non-invasive neural measures, such as electroencephalography (EEG), allows the direct assessment of particular subdomains of EF such as “performance monitoring”, a subdomain of EF that refers to self-monitoring of behavior and the detection of negative or surprising events (e.g., such as when errors occur; Ullsperger, Fischer, Nigbur, & Endrass, 2014). When studied in relation to error detection, this particular performance monitoring process is often referred to as “error monitoring” (Taylor, Stern, & Gehring, 2007). Though EEG-based markers of error monitoring are well established (Cavanagh & Frank, 2014; Ullsperger et al., 2014), error monitoring is not easily assessed via behavioral metrics. When errors are made, analysis of event-related potentials (ERPs; Luck & Kappenman, 2011) in the EEG reveal more negative amplitudes over frontocentral scalp locations within ~100 ms of making an error, referred to as the “error-related negativity” (ERN; Falkenstein, Hohnsbein, Hoormann, & Blanke, 1991; Gehring, Goss, Coles, Meyer, & Donchin, 1993), along with later emerging positivity (200-500 ms after making an error) over centroparietal scalp regions, known as the “error positivity” (Pe; Overbeek, Nieuwenhuis, & Ridderinkhof, 2005). The ERN reflects a rapid, automatic and likely unconscious aspect of error monitoring (Frank, Woroch, & Curran, 2005; Larson, Clayson, & Clawson, 2014; Luck & Kappenman, 2011), with the Pe reflecting a slower and more deliberative form of error monitoring that relates to decisions about what to do after an error (Gehring et al., 1993; Hajcak, McDonald, & Simons, 2003; Overbeek et al., 2005; Schneider, 2010; Steinhauser & Yeung, 2010). ERN and Pe have been shown to at least partially involve anterior cingulate cortex (ACC) function although much more distributed activity is also present (Agam et al., 2011; Buzzell et al., 2017). The ACC has been implicated in cognitive control

functions such as detecting response conflict and attention control, and enabling the brain to adapt behavior to changing task demands and environmental circumstances (Botvinick, Cohen, & Carter, 2004; Posner & Raichle, 1994).

In contrast to the extensive literature in adult populations (for a review, see Gehring et al., 2012), less is known about the ERN and Pe in children, particularly in the preschool and kindergarten years as it relates to ASD. However, using child-friendly tasks, a few studies have detected the ERN at medio-frontal sites and Pe at the posterior sites in TD children as young as 3 years (Grammer, Carrasco, Gehring, & Morrison, 2014) and as well as in children with ASD as young as 4 years (Groen et al., 2008; Henderson et al., 2006; Kim, Grammer, Benrey, Morrison, & Lord, 2017). Prior work demonstrates that improved error monitoring, as indexed by an enhanced ERN is associated with improved academic achievement in adults (Hirsh & Inzlicht, 2010). Additionally, prior studies of TD children showed that academic skills were associated with Pe, but not with ERN (Kim et al., 2016). Finally, larger ERNs in cognitively-able school-age children with ASD have been found to be associated with fewer symptoms of social impairment (Henderson et al., 2006); however, it is unclear whether ERN and Pe are linked to academic achievement in young children with ASD. The current study directly tests this hypothesis.

Along with ERP components, a complementary approach to assessing neural activity related to error monitoring involves time-frequency decompositions of the EEG signal to quantify how power within particular frequency bands changes following errors (Cohen, 2014). Work in adults has shown that increased error-related theta power (e.g. ~4-8 Hz oscillations) over the medio-frontal cortex is related to error monitoring (Cavanagh & Frank, 2014). While studying error-related theta band dynamics is well established in adults (e.g., Cavanagh & Frank,

2014; Harper, Malone, & Bernat, 2014), much less work has been conducted in children or adolescents (but see DuPuis et al., 2015 or Buzzell et al., 2018 for recent examples). To our knowledge, work linking time-frequency measures to ASD, and particularly in relation to academic skills, is non-existent. Yet, analyzing time-frequency measures of error monitoring can provide additional, band-specific information, which might afford improved predictive power over approaches that only analyze ERPs. For example, it was recently shown that age-related changes in theta power following feedback in TD adolescents could be detected whereas no age-related changes were observed with ERPs (Bowers et al., 2018). Additionally, a practical reason for employing time-frequency metrics, particularly within developmental contexts, is that time-frequency measures are less susceptible to artifact and noise (Bernat, Williams, & Gehring, 2005).

Studies as a whole suggest that EF-related neural measures are linked to academic outcomes in TD children. However, links between academic achievement and specific cognitive processes, such as error monitoring (measured via electrophysiological methods), have not been studied in depth for cognitively-able children with ASD. More specifically, work that employs time-frequency measures to study error monitoring, particularly in children with ASD, has been limited. Therefore, the current study employed a series of neural measures, including the ERN and Pe ERPs, as well as time-frequency analyses of theta power, in an effort to better characterize the effects of error monitoring on academic skills in children with ASD.

Method

Participants

Participants included 35 cognitively-able 4-5-year-old children with ASD (Mean age=62.3 months, SD=4.4 months; 25 males) without general cognitive delays (full-scale IQ≥85; Mean IQ=104.7, SD=14.2) and without moderate to severe structural language delays (i.e., child must be using full, complex sentences). These children were assessed at kindergarten entry (Summer/Fall of 2017). A previous diagnosis of ASD was required as inclusion criteria; and the diagnosis of ASD was confirmed with the gold standard diagnostic measure, the Autism Diagnostic Observation Schedule-2 (ADOS-2; Lord et al., 2012; see measure below). The ADOS-2 was carried out by examiners who achieved research reliability and were under the supervision of a licensed clinical psychologist. All participants met the instrument classification of ASD. The sample included 16 (46%) White, 4 (11%) African American, 6 (17%) bi-racial, and 2 (6%) Asian children. The rest of the children were reported to be of other races (n=7, 20%). About 85% of caregivers had a bachelor's degree or above (n= 30). Out of 35 children, 10 (29%) children were enrolled in general education classrooms; 7 (20%) children in inclusion classrooms (children with ASD are taught together with TD children); and 18 (51%) children in special education classrooms recruited from schools in urban and suburban areas of New York. Twenty-eight (80.0%) children were right handed, 5 left (14.3%) and the rest were ambidextrous (n=2, 5.7%). No participants were taking medication at the time of testing.

Electrophysiological Tasks and Measures

EEG/ERP Task

ERP/EEG patterns related to error monitoring (ERN, Pe, theta power) were measured based on a child-friendly Go/No-go task ("Zoo Game"; Grammer et al., 2014; Lamm et al., 2014) in a testing room with minimal distractions. Children were told that they are playing a game to help a zookeeper catch all the loose animals in the zoo except for three friendly orangutans who are helping the zookeeper. Children were asked to press a button as quickly as possible when they see an animal (Go trials) but inhibit their responses when they see an orangutan (No-go trials). A child started the game with a practice block of 12 trials (9 animals; 3 orangutans) followed by 8 blocks of the task, each with 40 trials, with a total of 320 trials (240 Go and 80 No-go trials). Each image was preceded by a fixation cross displayed for a randomized interval ranging from 200-300 ms. The stimuli were presented for 750 ms, followed by a blank screen for 500 ms. Responses could be made while the stimulus was on the screen or at any point during the following 500 ms (**Figure 1**). This task successfully elicited specific ERP components of our interest (e.g., ERN, Pe) in 98 TD children as young as 3 years (Grammer et al., 2014). Each block consisted of novel sets of animal photographs, and each set is balanced with respect to color, animal type, and size. Children were given performance feedback of either "Try to catch them even faster next time!" or "Watch out for the orangutan friends!" after each block of the task. These prompts were given to the children based on the calculation of the error rates to ensure an adequate number of trials for stable ERP/EEG waveforms. Children were allowed to have "Wiggle Time" between blocks. From the Zoo Game, we extracted the number and percentage of error/correct trials and reaction times.

[insert **Figure 1**]

Electrophysiological recording, data reduction, and data processing

Stimuli were presented on a PC laptop using E-Prime 2.0 software. Displays were viewed in a testing room with minimal distractions. EEG was recorded using Net Station 5.4 on a Macintosh laptop. A 64-channel Geodesic sensor net (EGI) was soaked with potassium-chloride electrolyte solution, placed on the participant's head, and fitted according to the manufacturer's specifications. As recommended for this system, impedances were kept below 50 kΩ. The EEG signal was digitized and sampled at 500 Hz via a preamplifier system (EGI Geodesic NA 400 System). Data was processed offline using Matlab (The Mathwoks, Natick, MA), the EEGLAB toolbox (Delorme & Makeig, 2004) and custom Matlab scripts partly based on work by Bernat and colleagues (Bernat et al., 2005). EEG data was digitally filtered (0.3 Hz high-pass, 50 Hz low-pass) and globally bad channels were detected and removed using FASTER tools (Nolan, Whelan, & Reilly, 2010). Independent component analysis (ICA) was performed on a copy of the original dataset, after additional 1 Hz High-pass filtering, and segmented into arbitrary 1 second epochs to identify and remove epochs with excessive artifact prior to ICA decomposition. After performing an ICA decomposition on this copied dataset, ICA weights were coped back to the original dataset; components associated with ocular or other artifacts were identified and removed. Data were epoched to the response markers from -1000 to 2000 ms and baseline corrected using the -400 to -200 ms period preceding the response. Epochs with residual ocular artifact were identified and removed using a +/- 125 uV threshold based on the ocular channels. For all remaining channels, epochs for which a given channel exhibited voltage +/-125 uV, data for that epoch was removed and interpolated using a spherical spine interpolation, unless more than 10% of channels were bad within a given epoch, in which case the entire epoch was removed. Finally, any channels that were marked as bad throughout the entire recording were

interpolated (spherical spline interpolation) and an average reference was computed. Participants with less than 50% accuracy for Go trials were excluded from analysis (n=3 which was not included in our final sample of 35 children). Additionally, a bootstrapping procedure was employed in order to match the effective trial counts across conditions and participants, improving the robustness of results.

ERP/EEG measures of inhibitory control and response monitoring

Ern/Pe. For ERP analyses, data were down-sampled to 128 Hz. ERN was quantified as mean amplitude at a cluster of frontocentral electrodes (E7, E4, E52) during an approximately 100 ms window (14 samples; 109.38 ms) immediately following the response; Pe was quantified as mean amplitude at a cluster of centroparietal electrodes (E34, E33, E36, E38) during an approximately 200-500 ms post-response window (39 samples; 304.69 ms). These analysis locations and time windows are consistent with pilot work (Kim et al., 2017) and previous literature (Grammer et al., 2014); exact time windows reflect actual time resolution possible at the sampling rate. Mean amplitudes have been found to be robust to increased background noise and variations in the number of trials (Acton, 2013; Luck & Kappenman, 2011). Further, to account for individual differences in trial counts, we employed a bootstrapping approach, where the ERP/EEG data from a subset of trials is repeatedly selected (with replacement) and averaged 25 times, before being bootstrapped 100 times to yield robust estimates of condition-averaged ERPs (see Buzzell et al., 2018). The mean ERN and Pe amplitudes were computed on incorrect-response (No-go) trials, with the difference between amplitudes on error vs. correct trials (ΔERN

and ΔPe) calculated by subtracting correct-Go waveforms from error-No-go waveforms (error-No-go minus correct-Go).

Frontal error-related theta power. Given our focus on theta (~4-8 Hz) oscillations, we down-sampled the EEG data to 32 Hz in order to improve computational efficiency with no loss of the signals of interest (i.e. Nyquist = 16 Hz). In order to extract error-related theta power, we employed Cohen's class reduced interference distributions (RIDs) to decompose time frequency (TF) representations of response-locked averaged power (Bernat et al., 2005), after first averaging/bootstrapping trials within each condition of interest to yield equal effective trial counts across conditions. The Cohen's class RID approach produces a time-frequency surface with proven superiority in both time and frequency resolution, as compared to other methods (Bernat et al., 2005). Additionally, in order to isolate error-related theta responses, we performed a principal components analysis (PCA) on the time-frequency surface, focusing on the period from -500 to 500 ms in the 3 hz to 12 Hz time-frequency surface, after first filtering out delta activity; all conditions of interest were entered into the same PCA. Analysis of the scree plot suggested that a 3-factor solution was the best fit to the data. Only one of these factors reflected a medio-frontal theta component near the response and so further analyses of theta power focused exclusively on this factor. For statistical analyses, factor weights were back projected onto the scalp surface and mean amplitude extracted from a cluster of medio-frontal electrodes (Electrodes 7, 4, 52). The difference between theta power on error vs. correct trials (Δtheta power) was calculated by subtracting correct-Go theta power from error-No-go theta power (error-No-go minus correct-Go).

Behavioral Measures

Academic achievement

Academic achievement in reading (Letter-Word Identification, Passage Comprehension) and math (Applied Math Problems, Math Fluency) was measured using the Woodcock-Johnson III NU tests of achievement (WJ; Woodcock, McGrew, Mather, & Schrank, 2001). Standard scores (Mean =100, SD=15) from the four domains were used.

Cognitive skills

Cognitive functioning (nonverbal and verbal IQ) was measured by the Differential Ability Scale (DAS; Elliott, 2007). Nonverbal IQ has been found to be more stable in children with ASD than verbal IQ (Bishop, Farmer, & Thurm, 2015). Therefore, NVIQ was used as an estimate of cognitive skills in our statistical models.

Statistical Analyses

For all behavioral analyses, response time (RT) analyses were restricted to correct trials and log-transformed prior to averaging. All analyses of RT data were performed on log Transformed data as RT data are known to be positively skewed (Luce, 1986); raw RT values are reported in the text for ease of interpretation. We also examined proportion of correct and error responses for Go and No-go trials, respectively. To confirm that ERN and theta power at the frontal sites were significantly larger for error vs. correct trials, t-tests were performed. The

relations between behavioral performance on the task and medio-frontal ΔERN and posterior ΔPe, as well as frontal Δtheta power were explored through Pearson *r* correlations. Additionally, we performed regression analyses to examine the effects of neural correlates of error monitoring (ΔERN, ΔPe, and Δtheta power) on academic skills while controlling for IQ and behavioral performance. All analyses were conducted using SPSS Version 24.

Results

Behavioral Assessments

As expected, our sample of cognitively-able children with ASD showed average reading and math skills (ranging from mean standard scores of 98-107) based on the Woodcock Johnson Test of Achievement (WJ), although math fact fluency varied widely with a standard score of 84 (**Table 1**) with 22 children not being able to achieve the basal on the subtest (but the standard scores ranged from 76 to 84 based on the child's age) but also a few children showing very high scores. For the Zoo Game, overall mean accuracy was 69% (SD=10%), with accuracy for correct trials at 75% (SD=11%) and accuracy for error trials at 52% (SD=18%). Mean reaction time for correct trials was at 624 ms (SD=413 ms).

Table 1. Behavioral Assessments (N=35)

	Mean	SD	Range
Woodcock Johnson Test of Achievement IV			
Letter Word Identification Standard Scores	107.1	15.9	76 – 123
Math Fact Fluency Standard Scores	84.3	12.1	77 – 152
Passage Comprehension Standard Scores	108.0	15.8	66 – 142
Applied Problem Standard Scores	97.7	13.1	69 – 120
Zoo Game			
Overall Accuracy (%)	69%	10%	50 – 85%
Accuracy for Correct Trials (% of responses for Go trials)	75%	11%	53 – 91%
Accuracy for Error Trials (% of no responses for No-Go trials)	52%	18%	15 – 88%
Reaction Time (Correct trials; ms)	624	413	413 – 811

Medio-Frontal ERN

Figure 2A shows a negative deflection around the time of error commission (relative to correct responses) at frontal electrode sites. Average amplitudes for the error and correct trials, as well as the difference between them, can be seen in **Table 2**. Mean amplitude for error trials at the frontal sites was significantly more negative than for correct trials ($t(34)= -4.55$, $p=0.001$; Table 3). These results confirm the presence of an ERN component.

Table 2 Mean (SD) ERN and Pe amplitudes and theta average power at the fronto-central and central-posterior sites.

Fronto-central electrode sites	Mean (SD)
ERN	-1.08 (2.45)
CRN	1.09 (2.18)
ΔERN	-2.17 (2.83)
PC-Weighted Error Theta Power	0.05 (0.04)
PC-Weighted Correct Theta Power	0.03 (0.03)
PC-Weighted Δ Theta Power	0.02 (0.03)
Central-posterior electrode sites	Mean (SD)
Pe	-0.62 (8.43)
Pe Correct	-10.17 (7.81)
Δ Pe	9.56 (10.18)

ERN, error-related negativity; CRN, correct-related negativity; PC, Principal Component; Pe, error positivity.

Posterior Pe

Examination of **Figure 2B** revealed the presence of the Pe at central-posterior electrode sites. Mean amplitude for error trials at the posterior sites was significantly more positive than for correct trials ($t(34)= -4.55$, $p=0.001$; Table 3). These results indicate the presence of the Pe component.

[insert **Figure 2**]

Time Frequency PC-Weighted Theta Power

Figure 3 demonstrates increased theta power (4-8 Hz) on error trials compared to correct trials at the medio-frontal electrode sites. Based on the mean and SD of theta average power, two outlier cases (+/- 2.5 SDs) were excluded from all analyses to minimize the effects of those scores on the correlation and regression analyses. A t-test showed that theta average power was significantly larger for error trials (compared to correct trials) at the medio-frontal sites (t(1,33=-2.351, p=0.03).

[insert **Figure 3**]

Associations between ERP/EEG Measures and Behavioral Performance on the Zoo Game

As expected, more negative frontal ΔERN and larger posterior Δ Pe and frontal Δ theta average power were all significantly correlated with higher overall accuracy. Larger frontal Δ theta average power was also significant correlated with higher go accuracy. Larger posterior Δ Pe was significantly correlated with longer reactions times overall and go trials in particular. See **Table 3.**

Table 3. Correlations between ERP/EEG measures and behavioral performance on the Zoo Game

	Frontal ΔERN (n=35)	Posterior Δ Pe (n=35)	Frontal Δ Theta Average Power (n=33)
Overall accuracy	-0.35*	0.61**	0.52**
Go accuracy	-0.21	0.22	0.44*
No-go accuracy	-0.34*	0.67**	0.27
Overall Reaction Time	-0.26	0.53**	0.01
Go Reaction Time	-0.31	0.56**	0.02
Nonverbal IQ	-0.35*	0.15	0.03

WJ Woodcock Johnson Test of Achievement

ERP/EEG Measures as Predictors of Academic Skills

Regression analyses showed that after controlling for overall accuracy on the Zoo Game and NVIQ, larger theta average power significantly predicted better reading (WJ Passage Comprehension; *B*=184.53, p=0.039; R^2=0.27, F(3,29)=3.50, p=0.03) and math (WJ Math Facts Fluency *B*=151.53, p=0.011; R^2=0.30, F(3,29)=4.20, p=0.01). Although larger ΔPe was significantly correlated with math (WJ Math Facts Fluency, r=0.41, p=0.01, R Square =0.27), the effect of ΔPe on the math achievement was not significant when overall accuracy on the Zoo Game and NVIQ were controlled for (*B*=0.416, p=0.09; R^2=0.19, F(3,31)=2.49, p=0.08). ΔERN was not significantly associated with academic achievement.

Discussion

Studies based on behavioral assessments of EF have shown that a broad range of EF skills play a key role in the development of academic ability in TD children as well as in children

with ASD (Allan et al., 2014; Blair, 2002, 2016; Cameron et al., 2012; Fuster, 1997; Happé et al., 2006; McClelland et al., 2006, 2007; Miyake et al., 2000; Morrison et al., 2010; Passolunghi & Costa, 2016; Ponitz et al., 2009; Raver et al., 2005; Wiebe et al., 2008; Willoughby et al., 2012). Using more traditional (ERP) and advanced (time-frequency) electrophysiological methods, we extracted neural activity related to error monitoring—a specific construct falling under EF—in cognitively-able kindergarteners with ASD. Using the child friendly Go/No-go Zoo Game, we were able to observe the ERN and increased theta power for error trials at medio-frontal sites and Pe at posterior sites in these children. Moreover, we found that a larger Pe and increased theta power were both associated with concurrent academic skills in these young children with ASD at school entry.

Our findings on the presence of an ERN and Pe in children with ASD as young as 5 years during a child-friendly Go/No-go task are consistent with past studies based on typically developing children as young as 2-3 years (Abundis-Gutiérrez, Checa, Castellanos, & Rosario Rueda, 2014; Barry & De Blasio, 2015; Ciesielski, Harris, & Cofer, 2004; Grammer et al., 2014) and in older school-aged children with ASD (Henderson et al., 2006; Kemner, Verbaten, Cuperus, Camfferman, & Van Engeland, 1994; Santesso et al., 2011; Sokhadze et al., 2012; South, Larson, Krauskopf, & Clawson, 2010; Vlamings, Jonkman, Hoeksma, van Engeland, & Kemner, 2008). To our knowledge, our study is one of the first to observe ERN in young children with ASD under 8 years and its connection to behavioral performance (accuracy rate) on the ERP task, besides our prior work with a smaller sample (Kim et al., 2017).

This study is also the first to successfully employ time-frequency measures to study error monitoring in young children with ASD and to detect significantly increased medio-frontal theta power following error (compared to correct) responses. These data are consistent with prior work

in adults and adolescents suggesting that increased theta power over medio-frontal cortex (MFC) underlies error and conflict monitoring (Bowers, Buzzell, Bernat, Fox, & Barker, 2018; Buzzell et al., 2018; Cavanagh & Frank, 2014). It is also worth noting that increased theta power during error trials in the cognitively-able kindergarteners with ASD was significantly correlated with higher levels of task performance (accuracy rates) on the Go/No-go task. However, it remains unclear if increased accuracy rates (and a lower frequency of errors) are what drive increased theta power. In adults, medio-frontal theta power has been shown to arise, at least in part, from ACC, a cortical region that is not only sensitive to errors and conflict, but also demonstrating a sensitivity to infrequent events (Brown & Braver, 2005; Wessel & Aron, 2017). Thus, the correlation between accuracy rates and theta power in this sample of young children with ASD is consistent with a broader literature on theta power and medio-frontal cortex more generally. The current results provide the first evidence of increased error-related theta power and the expected associations with error frequency, in a sample of children with ASD as young as 5 years.

We found that increased theta power was related to academic achievement in reading and math skills in cognitively-able kindergarteners with ASD. More importantly, the effects of theta power on the academic achievement in these young children with ASD were still significant even after controlling for the level of accuracy on the Go/No-go Zoo Game and IQ. These results suggest that the direct neural measures based on the time frequency approach may predict additional variance in academic achievement for children with ASD, beyond behavioral performance on the Go/No-go task and IQ data alone. Previous studies with TD children have shown the link between academic achievement and other ERP components, such as the error positivity (Pe; Kim et al., 2016) and P3 (Hillman et al., 2012) which are thought to reflect slower, and more deliberative aspects of error monitoring such as motivation and stimulus processing,

respectively. However, the ERN observed in one of these studies based on TD children was not associated with academic skills (Kim et al., 2016). Similarly, in the current study of young children with ASD, the ERN did not significantly relate to academic achievement. However, a larger Pe was significantly correlated with math achievement, although this association was not robust, as the effect of Pe on achievement scores was no longer significant when overall accuracy on the Zoo Game and IQ were controlled for. Collectively, our current results are consistent with prior work, finding that the Pe relates to academic achievement even in children with ASD, whereas the ERN does not. Nevertheless, more robust associations between error monitoring and academic achievement were revealed by time-frequency analyses of EEG data, with error-related theta power appearing to reflect a strong predictor of academic skills.

These results have both practical and clinical implications. First, in our study, use of the child-friendly Go/No-go Zoo Game adapted from a well-validated task developed by Fox, McDermott and colleagues, as well as Grammer and colleagues (Grammer et al., 2014; Lamm et al., 2014; Troller-Renfree, Zeanah, Nelson, & Fox, 2018), enabled us to maximize the child's ability to be engaged during the EEG/ERP session allowing us to more effectively examine error-related ERPs and time-frequency data in our sample. Second, researchers should note that because time-frequency analyses allow for extraction of power within specific ranges (e.g. ~4-8 Hz for theta), combined with a PCA approach, effects of high or low frequency artifacts are reduced and the signal-to-noise ratio is maximized (Bernat et al., 2005). This approach appears to enhance our ability to observe EF-related neural dynamics that may be missed by traditional ERP approaches that can be highly sensitive to artifacts and noise (Luck & Kappenman, 2011). Thus, the use of time frequency analyses, particularly when paired with a PCA approach, may provide new opportunities to investigate neurobiological mechanisms of EF related cognitive

processes more effectively and accurately, especially in young children and those with special needs. Finally, our results highlight the importance of developing more effective and targeted treatment programs for young children with ASD that are aimed to improve error and conflict monitoring even prior to their school entry, which could have cascading effects on their academic development.

Limitations and future direction

Although large for a preliminary study, the results of our study are drawn from a small sample of children with ASD. Also, our sample was focused on cognitively-able children with ASD with average to above average cognitive skills without notable structural language delays. Moreover, math skills in this sample of children showed a wide range of variability with more than the half of the sample not achieving basal scores and a few children showing exceptional computational skills. Thus, replications with larger, independent, and more representative samples with other developmentally appropriate measures will be important before we can generalize these results to other children with ASD. Furthermore, findings for the EF-related EEG/ERP measures are still limited in young children even in typically developing samples, especially based on time-frequency analyses. Therefore, a direct comparison between children with ASD and TD children matched on factors such as IQ, performance level on ERP/EEG tasks, and gender will provide further insights into the examinations of atypical neural activities related to error monitoring, or more broadly, EF and their functions. Finally, our focus was to examine the link between the EEG/ERP measures of error monitoring and concurrent academic achievement. However, it will be important to investigate their predictive capability for future

academic development as well as other important domains such as social and adaptive functioning in children with ASD. For these reasons, a replication study with a larger sample of children with ASD as well as matched TD controls based on a longitudinal design will be important.

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Figure Legends

Figure 1. The Go/No-Go Zoo Game (Grammer et al., 2014)

Figure 2. Error-related negativity (ERN) and Error Positivity (Pe). Figure 2A depicts the response-locked ERN at a cluster of frontocentral electrodes, where the ERN is typically maximal. Note that the ERN is more negative (larger) on error trials (red) than correct trials (blue). Dotted line is for ΔERN. Figure 2B depicts the response-locked Pe at a cluster of centroparietal electrodes, where the Pe is typically maximal. Note that the Pe is more positive (larger) on error trials

Figure 3. Error-related time-frequency theta power. Figure 3A depicts response-locked theta power after subtraction of correct from error trials and weighting by a principal component that captures error-related theta power. Figure 3B and 3C depict response-locked theta power during error and correct trials respectively. Note that theta power is increased on error trials. Left plots: time-frequency surface plotted for a cluster of frontocentral electrodes. Right plots: corresponding topographic plot of the principal component capturing theta power.

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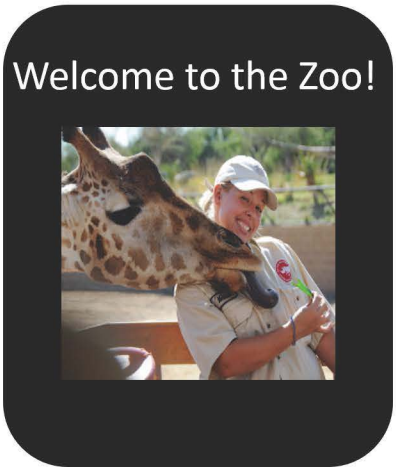
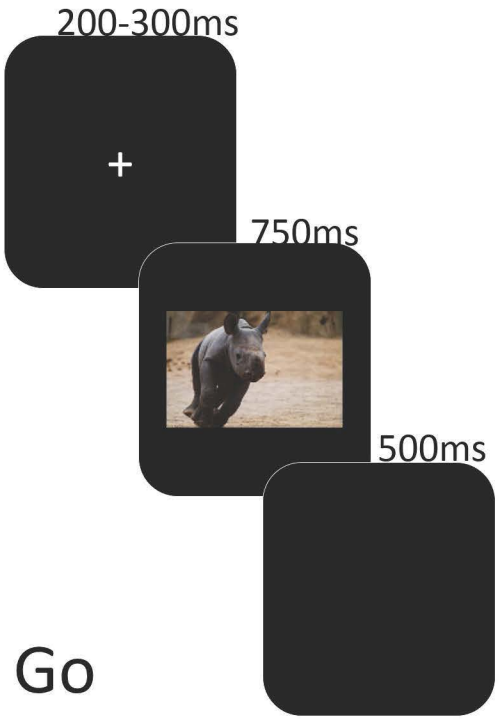
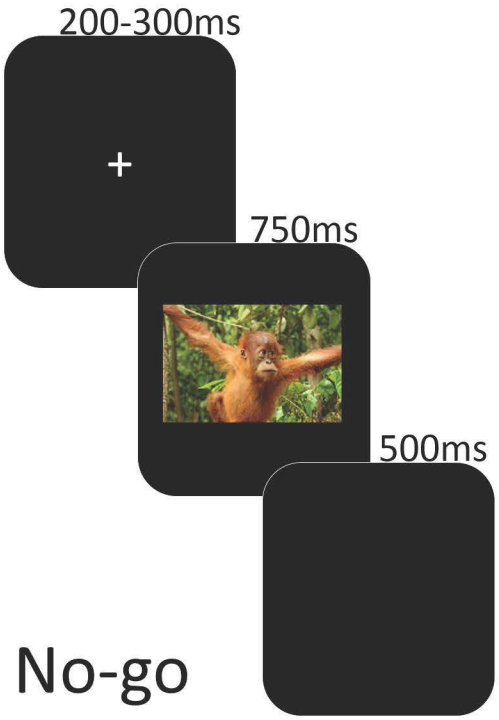
Conflict of interest

C.L. receives royalties from the sale of the ADOS-2. All royalties related to the research were donated to a non-profit organization. No other authors have conflicts of interest with regard to this study.

KOALA KOVE
MONKEY MOUNTAIN
ZOO ENTRANCE
PANDA PALACE
KANGAROO KINGDOM
ZOO EXIT


Welcome to the Zoo!


200-300ms
+
750ms
500ms
Go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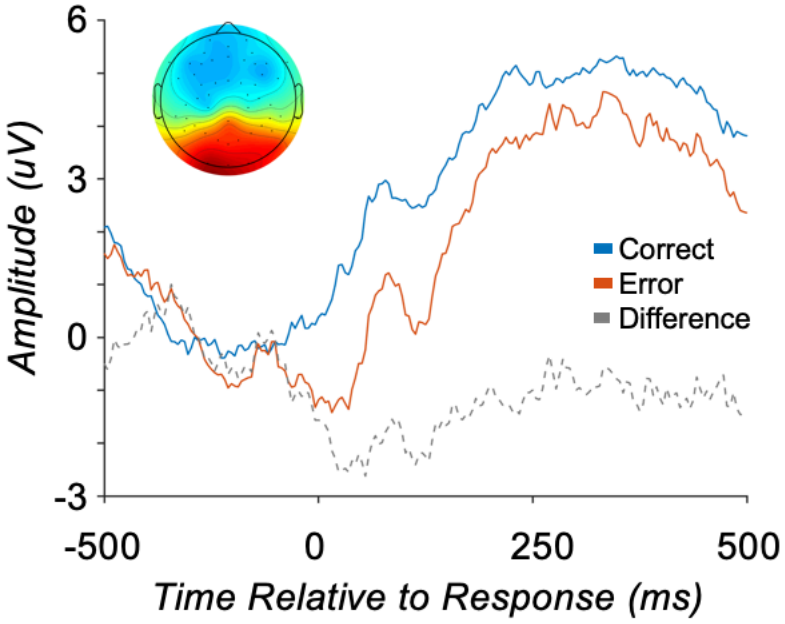
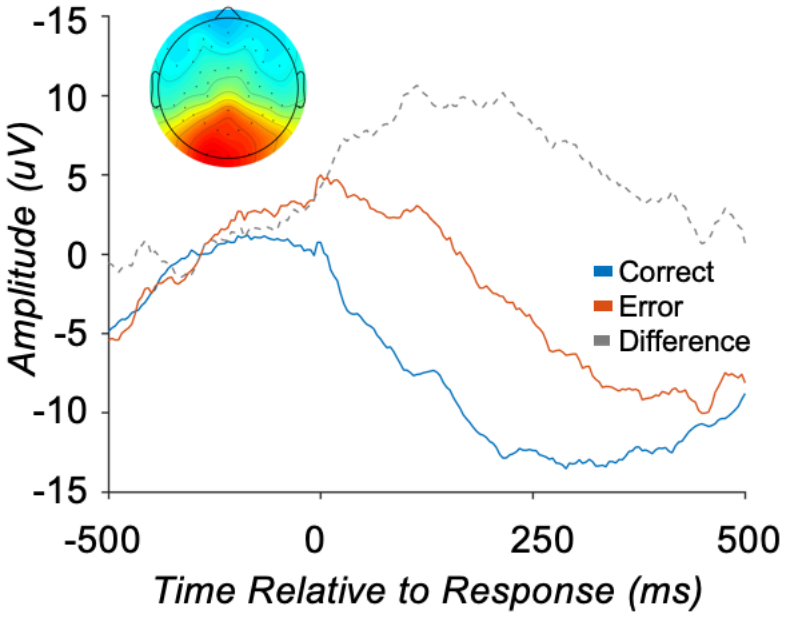
No-go

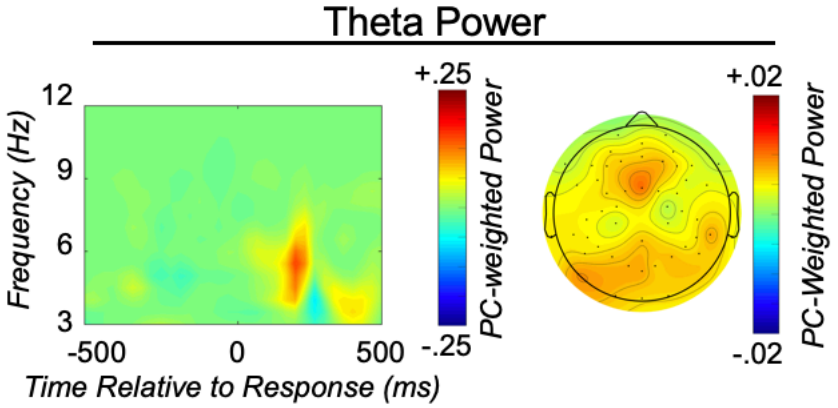
A. ERN (Medio-Frontal Cluster)



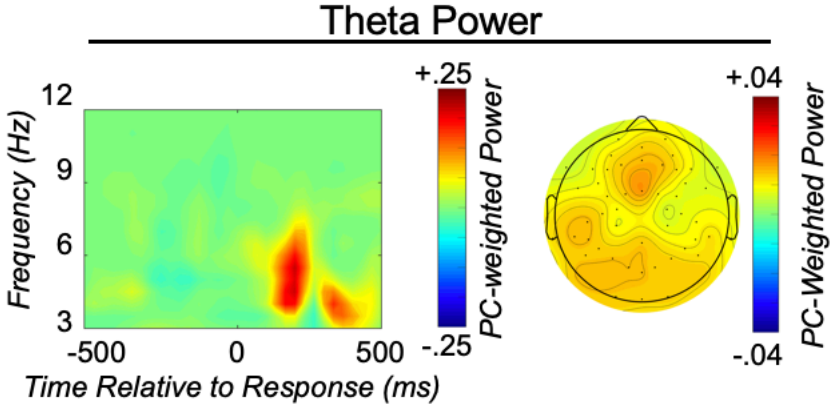
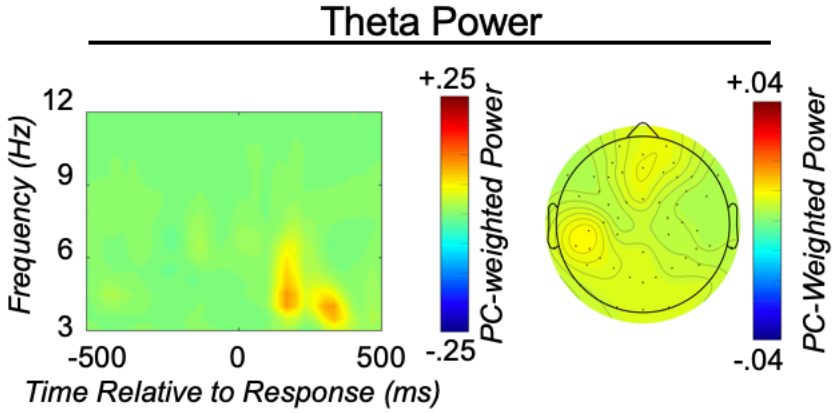
B. Pe (Centro-Parietal Cluster)



A. Error Minus Correct Difference



B. Error-Incongruent



C. Correct-Incongruent