Archival Report

Biological Psychiatry: CNNI

Atypical Mediofrontal Theta Oscillations Underlying Cognitive Control in Kindergarteners With Autism Spectrum Disorder

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ABSTRACT

BACKGROUND: Children with autism spectrum disorder (ASD) often exhibit deficits in cognitive control. Neuroimaging approaches have implicated disruptions to mediofrontal cortex structure and function. However, previous work is limited in testing whether young children with ASD exhibit disruptions to task-related theta oscillations thought to arise from the mediofrontal cortex.

METHODS: Children with ASD (n = 43) and age- and sex-matched typically developing peers (n = 24) at kindergarten entry performed a child-friendly Go/NoGo task while 64-channel electroencephalography was recorded. Time-frequency approaches were employed to assess the magnitude of mediofrontal theta oscillations immediately after error (vs. correct) responses (early theta) as well as later emerging theta oscillations (late theta). We tested whether error-related mediofrontal theta oscillations differed as a function of diagnosis (ASD/typical) and timing (early/late theta). In addition, links to social and academic outcomes were tested.

RESULTS: Overall, children showed increased theta power after error versus correct responses. Compared with typically developing children, children with ASD exhibited a selective reduction in error-related mediofrontal theta power during the late time window. There were no significant group differences for early theta power. Moreover, reduced error-related theta power during the late, but not early, time window significantly predicted poorer academic and social skills.

CONCLUSIONS: Kindergarteners with ASD demonstrated a selective reduction in error-related mediofrontal theta power during a relatively late time window, which is consistent with impairments in specific cognitive processes that recruit top-down control. Targeting these particular cognitive control processes via intervention prior to school entry may promote more successful functional outcomes for children with ASD.

https://doi.org/10.1016/j.bpsc.2021.03.016

The ability to self-monitor and flexibly adapt one's behavior in response to changes in the internal or external environment refers to neurocognitive processes known as cognitive control (i.e., executive functions) (1,2). In addition to social communication deficits, a core symptom domain of autism spectrum disorder (ASD) (3), a substantial body of work associates ASD with deficits in cognitive control (4–9). Work in typically developing (TD) children (10), adolescents (11), and adults (12) links cognitive control to a particular pattern of task-related brain oscillations within the theta band (approximately 4–7 Hz). However, the study of such brain oscillations and their link to cognitive control in children remains limited. Moreover, direct comparisons of task-related theta oscillations especially between younger TD children and younger children with ASD are limited. This reflects a crucial gap in the understanding of cognitive control among children with ASD, given that experimental studies have demonstrated that such oscillatory activity is causally linked to cognitive control (13,14). Clinically, deficits in cognitive control early in life can have cascading effects on later social and academic outcomes (7,15–19). Thus, an improved understanding of cognitive control neural dynamics in young children with ASD is critical for the development of targeted and effective interventions to maximize the outcomes of these individuals. This study leverages time-frequency (TF) analyses of electroencephalography (EEG) recorded during a cognitive control task to test whether the magnitude of task-related theta oscillations differs in kindergarteners with ASD, compared with TD control children.

Individuals with ASD display deficits in behavioral tasks requiring cognitive control (7,20), including inhibitory control tasks (21). At the neural level, the mediofrontal cortex (MFC)—to include the anterior cingulate cortex—is typically activated when healthy individuals perform cognitive control tasks (22). However, decreased blood oxygen level–dependent activity within the MFC (as measured via functional magnetic resonance imaging [fMRI]) has been observed while individuals with ASD perform inhibitory control tasks (23,24). Moreover, in TD individuals, the MFC is known to become more activated in response to events conveying a need to increase control, such as after error commission (25). However, individuals with ASD

ISSN: 2451-9022

also display reduced blood oxygen level–dependent activation of the MFC in response to errors, compared with correct responses (26). These findings are consistent with studies of brain structure differences between individuals with ASD and those in the TD group, which demonstrate differences in the morphometry of MFC subregions, including the anterior cingulate cortex (27).

While studies employing fMRI provide evidence for disrupted MFC function in ASD, it is also important to consider whether task-related mediofrontal theta oscillations are disrupted in individuals with ASD. Mediofrontal theta is increased during tasks requiring cognitive control, as well as in response to events signaling a need for control, including error commission (10,11,28). Similarly, mediofrontal theta dynamics observed during cognitive control tasks are thought to be generated, at least partially, within the MFC (29). Crucially, mediofrontal theta oscillations—which can be assessed noninvasively via EEG—do not simply provide an additional metric for assessing cognitive control. Instead, mediofrontal theta reflects a direct readout of a brain mechanism that has been causally implicated in cognitive control (13,14). Theta is thought to serve as an organizing rhythm that supports—through synchronization—a dynamic network of brain regions underlying cognitive control (12,30). Moreover, the enhanced temporal resolution of EEG provides the opportunity to measure the neural dynamics of cognitive control with greater specificity in time. Thus, examining mediofrontal theta in those with/without ASD can provide crucial information regarding the nature of how and when cognitive control dynamics are disrupted for this clinical population.

A few studies investigated task-related frontal theta oscillations in individuals with ASD. For example, adults with ASD failed to exhibit the typical increase in mediofrontal theta when performing a working memory task (31). In older children and adolescents, those with ASD exhibited lower stimulus-locked frontal theta during an inhibitory control Go/NoGo task (32) and reduced synchrony within the theta band in response to feedback on a gambling task (33). Similarly, school-age children and adolescents with ASD exhibited reduced stimulus-locked theta when performing a cognitive flexibility task (34). Younger, school-aged children (ages 5–7 years) with ASD did not show increased theta during a counting task, whereas those in the TD group did (35). Work in younger children is still limited, although in a recent study with younger children with ASD assessed at kindergarten entry, we found that variability in task-related mediofrontal theta was predictive of academic outcomes (36). However, a key limitation of this work is that we did not include a TD group, preventing any direct comparisons between those with ASD and TD control children.

This study directly tests whether task-related mediofrontal theta oscillations are disrupted in young children with ASD compared with TD children. Based on previous work demonstrating that individuals with ASD exhibit impairments on inhibitory control tasks (21) and reduced fMRI–blood oxygen level–dependent activation of the MFC in response to errors on these tasks (26), we focused on mediofrontal theta after errors (vs. correct responses) on an inhibitory control Go/NoGo task. Emerging work in developmental populations also suggests a possible dissociation between the mediofrontal theta response that immediately follows errors (early theta) compared with a relatively later response (late theta) (37). Thus, when comparing ASD and TD groups, we extracted error/correct mediofrontal theta from both an earlier and a later window and tested for possible dissociations. Finally, while the role of mediofrontal theta in laboratory-based cognitive control tasks is relatively well established (12), only limited work has sought to examine how these oscillations relate to more functional outcomes. Therefore, we also explored possible relationships between early/late mediofrontal theta and academic and social outcomes. Based on a previous study in older children showing that a relatively later theta response was selectively disrupted in children with ASD (34), we hypothesized that mediofrontal theta would be reduced in children with ASD (compared with TD group), especially within the later time window. Based on previous work linking relatively later emerging error-related event-related potentials to motivation (38) and academic outcomes (36,39), we similarly predicted that theta from the later time window would also be predictive of concurrent academic and social outcomes. Because we were especially interested in functional outcomes critical for school success, the target sample of the study was children who were entering kindergarten (aged 4–5 years). The link between neurobiological correlates of cognitive control and functional outcomes at kindergarten entry also has clinical and educational implications such as intervention programming.

METHODS AND MATERIALS

Participants

Participants included 43 children with ASD (mean age = 63.16 months, SD = 4.30; 11 females) and 24 TD control children (mean age = 63.58 months, SD = 4.86; 10 females) assessed at kindergarten entry. The inclusion criteria were no cognitive delays (IQ $\geq$ 85) and the regular use of complex sentences. Children with ASD were included if they had a previous diagnosis of ASD, which was confirmed with the gold standard diagnostic measure, the Autism Diagnostic Observation Schedule-2, Module 3 (40). The Autism Diagnostic Observation Schedule-2, Module 3, was administered by examiners who achieved research reliability, under the supervision of a licensed clinical psychologist. All children with ASD received scores in the ASD classification (comparison scores on the diagnostic algorithm ranging 4–10) (41). TD children were invited to participate in the study if they did not have any previous psychiatric or medical diagnoses. No TD children showed clinically elevated scores on the Child Behavior Checklist (CBCL) (42) externalizing or internalizing behaviors subscales. Children with ASD did show significantly elevated scores on CBCL externalizing and internalizing domains ($p < .001$). Because the delivery of comprehensive assessments to identify externalizing and internalizing problems to establish formal diagnoses such as attention-deficit/hyperactivity disorder and generalized anxiety disorder were beyond the scope of this study, we controlled for these symptoms dimensionally using CBCL scores in all analyses. No children were taking any psychotropic medications.

As shown in Table 1, independent samples *t* tests revealed no significant differences between children with ASD and those in the TD group in nonverbal IQ (NVIQ) or age. The children in the ASD group were 53% White, 7% Black, 4%

Table 1. Sample Characteristics and Diagnostic Differences

Characteristics	ASD, n = 43	TD, n = 24	ASD vs. TD	
			Significance	Cohen's d
Sex, Female, n	11	10		
Age, mo	63.09 (4.27)	63.48 (4.79)	n.s.	0.08
NVIQ	106.14 (10.97)	110.96 (10.17)	n.s.	0.46
CBCL Standard Scores				
Internalizing behaviors	55.51 (11.70)	43.33 (10.09)	<.001	1.11
Externalizing behaviors	53.51 (13.01)	42.33 (9.56)	<.001	0.98
WJ Standard Scores				
Applied problems	99.93 (14.63)	108.00 (13.83)	.031	0.57
Math fluency	86.60 (13.38)	86.57 (8.80)	n.s.	0.00
Letter word identification	108.12 (14.57)	100.63 (11.42)	.034	0.57
Passage comprehension	110.88 (13.86)	107.24 (9.94)	n.s.	0.30
PIPPS Raw Scores				
Play disruption[a]	22.20 (5.74)	19.96 (4.92)	n.s.	0.42
Play disconnection[a]	16.95 (4.69)	11.91 (4.12)	<.001	1.14
Play interaction[b]	23.17 (4.88)	28.78 (4.01)	<.001	1.26

Values are presented as mean (SD), unless otherwise noted. Independent samples t tests were employed to examine diagnostic differences.
ASD, autism spectrum disorder; CBCL, Child Behavior Checklist; n.s., not significant; NVIQ, nonverbal IQ; PIPPS, Penn Interactive Peer Play Scale; TD, typically developing; WJ, Woodcock-Johnson.
[a]Higher scores denote higher levels of play disruption and disconnection.
[b]Higher scores denote more play interaction.

Asian, 22% biracial, and 14% of other or unknown race. Similarly, the children in the TD group were 43% White, 8% Black, 4% Asian, 34% biracial, and 11% of other or unknown race. A majority of caregivers (91% in TD and 85% in ASD) had a bachelor's degree or higher. Most children were reported being right-handed (84% for ASD, 80% for TD). All caregivers signed an institutional review board–approved informed consent form.

Behavioral Measures

Cognitive Skills. The Differential Ability Scales (43) was used to measure cognitive functioning for both groups. NVIQ was used as an estimate of cognitive ability in analyses, given that it is more stable than verbal IQ in children with ASD (44). One child in the ASD and another in the TD group had NVIQs ±3 SD from the mean and were considered outliers and excluded from analyses.

Social Skills. The Penn Interactive Peer Play Scale (45) was used to measure social skills. This parent report captures children's play behaviors with their peers at home and in the community. It comprises three subdomains: play disruption, which assesses aggressive play behaviors; play disconnection, which targets withdrawn play behaviors; and play interaction, which reflects play strengths. T scores were used in analyses (mean = 50, SD = 10). One TD child had a play disruption T score ±3 SD from the mean and was excluded from analyses. In addition, 1 TD child and 1 ASD child were missing scores for all domains.

Academic Achievement

Academic achievement was measured using Woodcock-Johnson III Normative Update tests of achievement (46). Math skills were captured by Applied Problems (math problem-solving skills) and Math Facts Fluency (basic arithmetic skills) domains. Reading ability was captured by Passage Comprehension (understanding of written text) and Letter-Word Identification domains. All subtests yield standard scores (mean = 100, SD = 15), which were used in statistical models. Outliers included 1 child with ASD for Math Facts Fluency and 1 child with ASD for Passage Comprehension who received scores ±3 SD from the mean in each subdomain.

Electrophysiological Tasks and Measures

EEG/Event-Related Potentials Task. EEG recordings were collected while children played a child-friendly Go/NoGo task (Zoo Game) (47,48) in a testing room with minimal distractions. The Zoo Game successfully elicits EEG activity associated with error monitoring in TD children as young as 3 years (47). Children are instructed that they are playing a game to help a zookeeper catch the loose animals that escaped their cages in the zoo. To catch an animal, children are told to click an identified button when a picture of a loose animal appears (Go trials), and they are not supposed to press the button when they see any of the three orangutans who are helping them (NoGo trials). Children start the game with a practice block. The actual task includes 8 blocks of 40 trials (320 trials total; 240 Go and 80 NoGo). The stimuli are presented for 750 ms and then a blank screen for 500 ms. All images are preceded by a fixation cross randomly jittered between 200 and 300 ms. Children can make their responses while the stimulus is on the screen or during the 500-ms blank screen that follows (1250-ms response deadline). Feedback on performance is provided to children after each block with prompts generated based on the calculation of error rates to ensure an acceptable number of trials for stable EEG waveforms. No trial-level

feedback was provided. Zoo Game behavioral accuracy was captured by the percentage of error/correct trials for Go and NoGo trials. Response time (RT) was also assessed for overall, correct-Go, and error-NoGo trials.

Electrophysiological Recording, Data Reduction, and Data Processing

EEG Recording. Stimuli from the Zoo Game were presented on a personal computer laptop using E-Prime 2.0 (Psychology Software Tools, Pittsburgh, PA). Net Station 5.4 (Electrical Geodesics Inc. [EGI], Eugene, OR) running on a Macintosh laptop was used to record EEG from a 64-channel Geodesic sensor net (EGI). Impedances for all electrodes were kept below 50 kΩ, following recommendations for this system. The EEG signal was digitized and sampled at 500 Hz via a preamplifier system (Geodesic NA 400 System [EGI]).

EEG Preprocessing. EEG data were processed using MATLAB 2017b (The MathWorks, Inc., Natick, MA), EEGLAB (49), FASTER (50), ADJUST (51), and custom MATLAB scripts partly based on work by Bernat *et al.* (52). Preprocessing methods reflect a precursor to the Maryland Analysis of Developmental EEG pipeline (53). Briefly, EEG data were digitally filtered and bad channels removed. A copy of the dataset was further cleaned via automated methods before running independent component analysis. Independent component analysis weights were copied back to the original dataset and used to remove ocular and other artifacts (54,55). Data were epoched to response markers from −1000 to 2000 ms and baseline corrected using the −400 to −200 ms pre-response period. A final rejection of residual ocular artifacts using a ±125 μV threshold was conducted, missing channels were interpolated, and an average reference was computed. See the Supplement for complete details.

TF Decomposition. Given our focus on theta (approximately 4–7 Hz) oscillations, the EEG data were downsampled to 32 Hz to improve computational efficiency with no loss of the signals of interest (i.e., Nyquist = 16 Hz). Cohen's class–reduced interference distributions were used to decompose TF representations of response-locked power for each trial before averaging across all trials (52). TF surfaces were baseline corrected relative to the –400 to –200 (pre-response) period using a subtractive baseline correction to isolate response-related changes in power. Data were not converted to a dB scale, and units reflect response-related changes in (baseline-corrected) raw power. As part of a standard preprocessing pipeline of TF data that allows meeting additional assumptions necessary for synchrony-based analyses, a subsampling approach was implemented (10). However, given that the subsampling procedure was conducted only as a preprocessing step for analyses of synchrony (not reported here) and do not serve to improve the reported power-based analyses, details of the subsampling procedure are described elsewhere (10).

Extraction of Response-Related Frontal Theta Power. Given previous work in adults (28), adolescents (11), and children (36) linking error-related changes in theta power over frontal scalp sites to error monitoring and cognitive control, we extracted response-related theta power (4–7 Hz) from a cluster of three mediofrontal electrodes (E4/FCz, E7, E54). In line with previous work, we extracted frontal theta power during a predefined region of interest (ROI) based on the first ~200 ms after the response (exact window timing based on sampling resolution; first six samples = 0–192 ms). Consistent with emerging work suggesting a dissociation between early and late theta power after responses, we additionally extracted response-related theta power from a second ~200-ms window immediately after our first ROI (exact window timing based on sampling resolution; next six samples = 192–384 ms). Thus, for each participant, response-related theta power within the 4–7 Hz band was extracted from a frontocentral cluster of electrodes during an early (first ~200 ms) and late (next ~200 ms) window, separately for error and correct trials.

Determining how many clean EEG trials each participant should have to be included in error-related analyses involves balancing reliability of the EEG signal on the one hand and risk of creating a biased sample on the other. Creating a biased sample through participant exclusion is particularly problematic within the context of comparisons between clinical and nonclinical groups. Moreover, simulation studies have yet to identify the optimal number of trials necessary for calculating reliable error-related theta signals. However, at least one simulation study of the associated error-related negativity (ERN), a time domain EEG signal to which theta is known to contribute substantially (56), suggests that four to six trials may be sufficient for computation of a reliable ERN (57). Therefore, we conducted analyses of the TF data utilizing an inclusion criterion of four trials (and a minimum Go accuracy of 50%) to maximize participant inclusion and guard against sample biases. Nonetheless, see the Supplement for additional analyses that use increasingly strict trial cutoffs (4, 6, 8, 10 trials) as well as an analysis that controlled for trial counts, which resulted in consistent findings. We also report the number of clean trials as a function of condition and group (see the Supplement).

Statistical Analyses

Independent *t* tests were conducted to examine differences in social and academic skills between the ASD and TD groups. Generalized linear mixed models (GLMMs) were used to examine diagnostic differences (ASD vs. TD) in accuracy and reaction time on the Zoo Game. A GLMM was also used to examine diagnostic difference in ERN (see the Supplement). RT data are known to be positively skewed (58); therefore, analyses were performed with log-transformed RT. At the neural level, a GLMM with a three-way interaction term (accuracy [correct vs. error] by timing [early vs. late theta] by diagnosis [ASD vs. TD]) was used to examine whether children exhibited error-related theta (significant increases in theta power for error vs. correct trials) and whether these effects differed as a function of diagnosis or timing (early vs. late theta ROIs). A GLMM was also used to examine diagnostic difference in ERN (see the Supplement). Post hoc analyses explored the nature of any significant interactions. Finally, regression analyses explored whether error-related differences in early or late theta power predicted academic and social skills across both groups with subsequent false discovery rate analyses

employed to control for multiple comparisons within academic and social domains. Age, sex, internalizing, and externalizing domain T scores on CBCL along with NVIQ scores were controlled for in all GLMMs and regressions. All analyses were conducted using SPSS version 24 (IBM Corp., Armonk, NY).

RESULTS

Diagnostic Differences in Social and Academic Skills

Based on parent report, children with ASD showed significantly more impairments in Play Interaction ($t_{63} = -4.78$, $p < .001$, $d = 1.26$) and Disconnection ($t_{63} = 5.27$, $p < .001$, $d = 1.14$) compared with TD children, with large effect sizes. In areas of academic achievement, the ASD group scored significantly lower than the TD group in math with a medium effect size (Applied Problems: $t_{65} = 2.21$, $p = .031$, $d = 0.57$). Children with ASD scored significantly higher than the TD sample for Letter Word Identification with a medium effect size ($t_{65} = -2.17$, $p = .034$, $d = 0.57$). See Table 1.

Diagnostic Differences in Zoo Game Performance

Diagnosis emerged as a significant main effect; children with ASD performed worse than the TD group for Zoo Game accuracy ($F_{125} = 17.76$, $p < .001$), while controlling for age, sex, internalizing and externalizing behaviors, and NVIQ. There was also a main effect of trial type, with accuracy being lower on NoGo trials than on Go trials for all children ($F_{125} = 95.76$, $p < .001$). However, there was no significant interaction effect for diagnosis and trial type accuracy. In regard to RT, there was a main effect of trial type, with all children showing slower RT for correct responses on Go trials compared with error responses during NoGo trials ($F_{124} = 83.14$, $p < .001$). No significant diagnostic differences were observed in RT. Results using raw RT were similar. See Table 2 for details on accuracy and RT by diagnostic group.

The Presence of Error-Related Theta Power and Diagnostic Comparisons on Early Versus Late Theta

A GLMM revealed a significant main effect of accuracy ($F_{241} = 9.81$, $p = .002$), while controlling for age, sex, internalizing and externalizing behaviors, and NVIQ, confirming higher mediofrontal theta power for error versus correct trials overall (Figure 1). A significant main effect of diagnosis ($F_{241} = 14.63$, $p < .001$) emerged, with the ASD group having overall lower mediofrontal theta power. Crucially, there was also a significant three-way interaction between accuracy, timing of theta, and diagnostic group ($F_{2,241} = 3.56$, $p = .030$). To explore the nature of this interaction, a pair of post hoc, two-way (accuracy [correct vs. error trials] by diagnosis [ASD vs. TD]) GLMMs were used to explore specific diagnostic differences in theta between error and correct trials for each theta timing ROI. A significant two-way interaction of accuracy $\times$ diagnosis was revealed for the late theta ROI ($F_{119} = 4.82$, $p = .030$); TD children exhibited a larger error (vs. correct) increase in late theta power relative to children with ASD (Figure 2). In contrast, no interaction between accuracy and diagnosis emerged for the early theta ROI ($F_{119} = 2.00$, $p = .160$). When analyses were repeated with ERN, TD children also showed significantly greater ERN compared with children with ASD (see the Supplement).

Theta Power Predicting Social Skills and Academic Achievement

Regression analyses showed that late theta power significantly predicted math skills on the Woodcock-Johnson Applied Problems subdomain ($p = .01$) and social skills on the Penn Interactive Peer Play Scale Play Interaction subdomain ($p = .045$), while controlling for age, sex, internalizing and externalizing behaviors, and NVIQ. The Woodcock-Johnson Applied Problems subdomain remained significant after false discovery rate corrections. See Table 3 for detailed results of the significant regression results; see Table S1 for additional

Table 2. Behavioral Performance on the Zoo Game by Diagnostic Group

	ASD			TD		
Performance	Mean (SD)	Minimum	Maximum	Mean (SD)	Minimum	Maximum
Zoo Game Accuracy, %						
Overall[a]	0.70 (0.09)	0.49	0.88	0.82 (0.06)	0.69	0.93
Go	0.77 (0.11)	0.53	0.93	0.88 (0.06)	0.77	0.97
NoGo	0.51 (0.19)	0.13	0.88	0.63 (0.16)	0.14	0.91
Zoo Game RT, Log						
Overall[b]	6.24 (0.19)	5.72	6.58	6.34 (0.14)	6.04	6.59
Go	6.27 (0.19)	5.80	6.62	6.37 (0.14)	6.03	6.61
NoGo	6.08 (0.21)	5.36	6.40	6.10 (0.18)	5.78	6.53
Zoo Game RT, ms						
Overall	610.51 (79.57)	388.27	791.65	629.22 (67.49)	515.67	766.72
Go	622.33 (82.18)	413.49	811.58	641.94 (68.04)	524.09	774.36
NoGo	535.59 (82.38)	288.56	703.61	519.68 (82.08)	406.21	706.43

ASD, autism spectrum disorder; GLMM, generalized linear mixed model; NVIQ, nonverbal IQ; RT, response time; TD, typically developing.

[a]GLMMs showed significant differences between ASD and TD on Zoo Game accuracy while controlling for age, sex, internalizing and externalizing behaviors, and NVIQ ($p < .001$).

[b]GLMMs showed that both groups had significantly higher RT for correct responses for Go trials compared with error responses while controlling for age, sex, internalizing and externalizing behaviors, and NVIQ ($p < .001$).

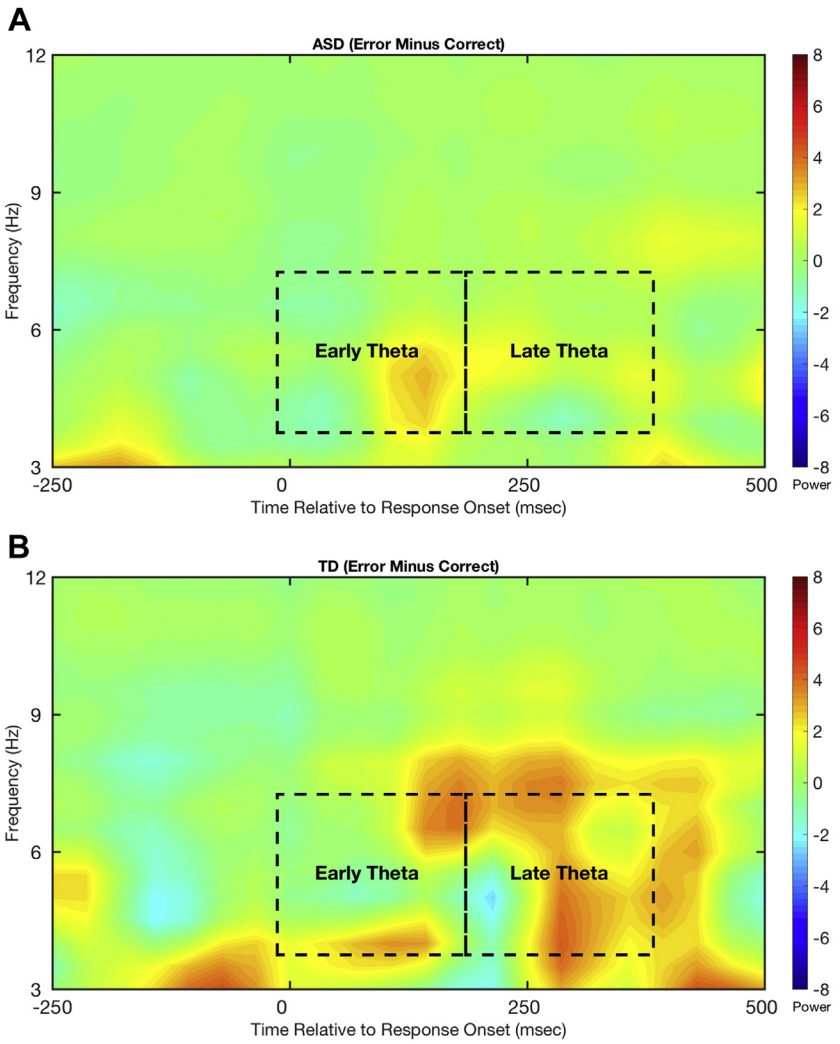

Figure 1. Time-frequency plots of response-locked error-related (error minus correct) power at a mediofrontal electrode location (E4/FCz). Zero ms corresponds to the time of response commission. Units of power reflect baseline-corrected raw power. The theta band (4–7 Hz) regions of interest for early and late theta are indicated with dashed boxes. Error-related time-frequency surfaces are plotted separately as a function of diagnostic group: **(A)** children with autism spectrum disorder (ASD); **(B)** typically developing (TD) children.

nonsignificant results. Early theta did not significantly predict any of the social or academic domain measures (all $p > .05$).

DISCUSSION

While previous work has studied task-related mediofrontal theta oscillations in ASD, to our knowledge, this study is one of the first to demonstrate that mediofrontal theta oscillations underlying cognitive control are disrupted in kindergarteners with ASD compared with those in the TD group. While individuals with ASD did not exhibit significant differences in theta immediately after error responses (early theta), they displayed a reduced magnitude in later emerging mediofrontal theta (late theta). Moreover, these differences in late, but not early, theta predicted academic and social outcomes. These data are consistent with previous work reporting impairments in cognitive control in ASD at the behavioral level (7,20). The current data are also in line with results from neuroimaging studies that identify functional (23,24,26) and structural (26,27,59) abnormalities associated with the MFC and cognitive control networks in ASD. Similarly, these results complement previous work in older children, adolescents, and adults that also found disruptions to mediofrontal theta in individuals with ASD (32–35). Crucially, EEG provides the opportunity to directly assess oscillatory activity not captured by behavioral or neuroimaging (f/MRI) approaches. Given that mediofrontal theta oscillations are causally linked to cognitive control (13,14) and EEG affords the opportunity to identify transient brain activity more precisely, our findings may provide direct insight into understanding how and when cognitive control is disrupted in young children with ASD. Of equal importance, the current report grounds the assessment of mediofrontal theta oscillations in terms of how they relate to more traditional functional outcomes (social and academic domains).

Utilizing a child-friendly Go/NoGo task (Zoo Game) (47), we extracted error/correct mediofrontal theta power measures in kindergarteners with ASD and typical peers to examine behavioral and neural differences in cognitive control.

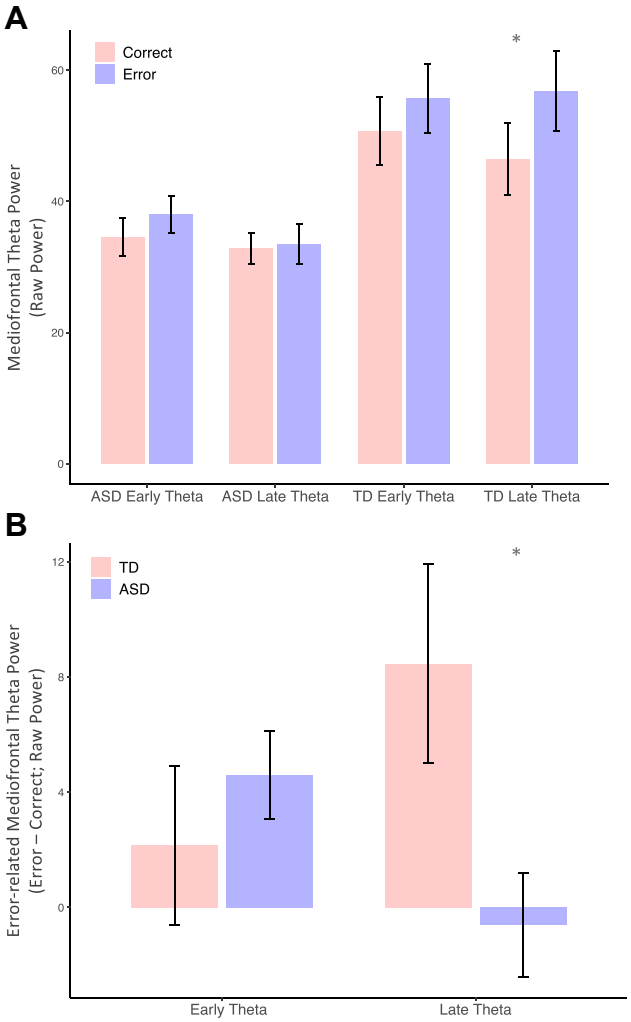

Figure 2. **(A)** Diagnostic differences in early and late mediofrontal theta power by response type. **(B)** Comparison of early and late window accuracy differences in mediofrontal theta power between diagnostic groups. *$p < .05$. ASD, autism spectrum disorder; TD, typically developing.

Behaviorally, children with ASD showed reduced overall accuracy on the Zoo Game, even after accounting for age, sex, internalizing and externalizing behaviors, and NVIQ. These results replicate studies indicating behavioral deficits in tasks targeting general cognitive control in this clinical population (7,20,21). However, task-related behavioral measures did not reveal differences in more specific executive function domains, such as changes in overall attention (i.e., Go accuracy) or inhibitory control (i.e., NoGo accuracy). Thus, relying solely on behavioral measures may limit a more detailed examination and nuanced understanding of how and why individuals with ASD exhibit deficits in cognitive control. In contrast, employing analyses of mediofrontal theta in this study allowed a more comprehensive assessment of cognitive control dynamics within ASD.

To further investigate the neural underpinnings of impairments in cognitive control in ASD, we compared response-related mediofrontal theta oscillations between children with ASD and those in the TD group based on their magnitude and timing. Drawing on work suggesting possible dissociations between mediofrontal theta oscillations that arise relatively earlier or later in the post-error period (37), we separately analyzed an early theta (approximately 0–200 ms) and late theta (approximately 200–400 ms) time window. Notably, children with ASD (compared with TD children) exhibited a selective reduction in mediofrontal theta power during the late, but not early, time window. Similarly, a recent study examining event-related theta power in older children with ASD also found selective reductions in theta within a later postevent time window when performing a cognitive flexibility task that relies on higher-order cognitive processes such as inhibition and attention shifting (34). Cognitive control is generally thought to involve a cascade of processing whereby the need for control is first detected and later followed by the recruitment and allocation of top-down control to bias behavior favorably (1). Thus, error-related theta power within the early time window may be associated with the detection of errors and need for control, whereas the late theta time window may more closely map onto higher-level neural processes associated with the recruitment of top-down control. The current data suggest that this second stage of cognitive control may be particularly impaired in young children with ASD compared with the TD group.

Consistent with the notion that late theta may more closely relate to higher-level aspects of cognitive control, we found that increased error-related theta power during the late time window, but not early theta, was a significant predictor of academic (math) and social skills in children with ASD and those in the TD group. Various behavioral studies have shown that impairments in cognitive control may negatively affect academic and social functioning (7,15–19). Moreover, our previous work found that variability in mediofrontal theta predicted math abilities in children with ASD (36). This study further extends these results by revealing a more specific pattern of neural dynamics that may play a key role in social and academic development in young children.

Limitations and Future Directions

Given the heterogeneity of behavioral presentation in children with ASD and developmental effects on cognitive control, this study included a focused sample of verbal, kindergarten-aged children with ASD without cognitive delays (IQ $\geq$ 85). This provided us with the opportunity to examine neural correlates of cognitive control, critical for school success in children with ASD, which will have cascading effects on later outcomes such as mental health and independence (36,60). In addition, the TD group had no previous psychiatric diagnoses or clinically elevated CBCL externalizing or internalizing scores; however, children with ASD did show elevated scores. While we statistically controlled for externalizing and internalizing behaviors, future work should explore children with ASD and TD children matched for levels of externalizing and internalizing problems and also include children with diagnoses of attention-deficit/hyperactivity disorder or generalized anxiety disorder as comparison groups to examine the interrelationships among these co-occurring symptoms and cognitive

Table 3. Regression Analyses of Late Theta Power as a Predictor of Academic and Social Skills

Outcome Variable	Predictors in Model	*B*	SE	*t (df)*	Significance	95% CI		R^2
						Lower Bound	Upper Bound	
WJ Applied Problems[a]	Covariates only			(61)				.24
	Age	0.03	0.38	0.08	n.s.	−0.73	0.80	
	Sex	−2.02	3.61	−0.56	n.s.	−9.24	5.21	
	Internalizing behaviors	−0.08	0.24	−0.34	n.s.	−0.57	0.40	
	Externalizing behaviors	0.16	0.23	0.71	n.s.	−0.30	0.63	
	NVIQ	0.65	0.16	4.03	<.001	0.33	0.97	
	Predictor and covariates			(58)				.33
	Age	−0.04	0.37	−0.11	n.s.	−0.78	0.70	
	Sex	−1.45	3.49	−0.42	n.s.	−8.43	5.54	
	Internalizing behaviors	0.53	0.16	3.27	n.s.	0.21	0.86	
	Externalizing behaviors	−0.17	0.24	−0.71	n.s.	−0.65	0.31	
	NVIQ	0.27	0.23	1.20	.002	−0.18	0.73	
	Late theta difference	0.33	0.12	2.68	.010	0.08	0.57	
PIPPS Play Interaction	Covariates only			(59)				.34
	Age	0.35	0.33	1.05	n.s.	−0.32	1.01	
	Sex	6.93	3.13	2.21	.031	0.66	13.21	
	Internalizing behaviors	−0.04	0.21	−0.19	n.s.	−0.47	0.39	
	Externalizing behaviors	−0.51	0.20	−2.55	.013	−0.91	−0.11	
	NVIQ	−0.12	0.15	−0.77	n.s.	−0.42	0.19	
	Predictor and covariates			(56)				.38
	Age	0.30	0.33	0.896	n.s.	−0.37	0.96	
	Sex	7.12	3.13	2.274	.027	0.85	13.40	
	Internalizing behaviors	−0.06	0.22	−0.271	n.s.	−0.53	0.10	
	Externalizing behaviors	−0.45	0.20	−2.197	.032	−0.50	0.38	
	NVIQ	−0.21	0.16	−1.342	n.s.	0.86	−0.04	
	Late theta difference	0.25	0.12	2.053	.045	0.01	0.48	

CI, confidence interval; n.s., not significant; NVIQ, nonverbal IQ; PIPPS, Penn Interactive Peer Play Scale; WJ, Woodcock-Johnson.
[a]Late theta difference remained significant after false discovery rate corrections for multiple comparisons ($p < .05$).

control. Therefore, generalization of the results is limited until they are replicated with a larger sample of individuals with ASD and other disorders across a wider range of ages and abilities. Additional studies should also investigate theta dynamics across various cognitive tasks targeting other cognitive processes such as working memory or attentional/set-shifting, which may also have cascading effects on social and academic outcomes in children with ASD. Finally, future work could explore synchronization in theta power across various clusters of electrodes beyond the frontocentral region, which may provide additional insight into the neural dynamics underlying cognitive control more generally.

Conclusions

Previous work finds that individuals with ASD have deficits in cognitive control at the behavioral level and neurally exhibit structural and functional abnormalities within the MFC. However, previous studies have not directly investigated whether task-related mediofrontal theta oscillations, thought to arise from the MFC, are disrupted in young children with ASD. We identified selective reductions in error-related theta oscillations emerging in a relatively late post-error time window. Moreover, such reductions in late theta were found to predict academic and social outcomes. These results indicate that accounting for the neural dynamics of cognitive control in individuals with ASD may provide specific information about deficits not observable behaviorally. Moreover, the results, if replicated, suggest a novel neurocognitive target for interventions designed to support social and academic outcomes in cognitively able children with ASD.

ACKNOWLEDGMENTS AND DISCLOSURES

This project was funded by the Kellen Junior Faculty Award (principal investigator, SHK).

We thank Catherine Lord, Nathan Fox, Frederick Morrison, Jennifer Grammer, William Fifer, Natalie Brito, Lauren Shuffrey, Susan Faja, Nurit Benrey, Claire Klein, and Denisse Janvier for help with study conceptualization and data collection. We also thank the children and the families who participated in the study.

The authors report no biomedical financial interests or potential conflicts of interest.

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Received Dec 14, 2020; revised Mar 28, 2021; accepted Mar 29, 2021.

Supplementary material cited in this article is available online at https://doi.org/10.1016/j.bpsc.2021.03.016.

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