The Relationship Between Resting EEG Frontal Theta Power, Eye-Blink Rates, and Restrictive and Repetitive Behaviors in Children with Autism Spectrum Disorder: Results from the ABC-CT

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Background

- Decreased central dopamine (DA) levels are thought to be indexed by reduced eye-blink rates (EBR).
- Poor performance on DA-mediated cognitive tasks (e.g., inhibitory control), is associated with lower frontal theta activity in autism spectrum disorder (ASD).
- Boys with ASD were found to have reduced EBRs and resting theta power compared to typically developing (TD) children, and decreased theta power was further associated with greater ASD symptomology.
- However, the relationship between DA levels, as indexed by theta power and EBRs, and restricted and repetitive behaviors (RRB) in ASD is poorly understood, despite the recognized influence of DA-related inhibitory control deficits on RRB severity.
- **OBJECTIVE:** To evaluate differences in (1) absolute resting frontal theta power and (2) EBRs between ASD and heathy controls; (3) to assess whether EEG or EBR-based indices of DA function explain variance in RRBs in ASD.

Methods

PARTICIPANT CHARACTERISTICS

Table 1. Participant demographics; presented as Mean (Standard Deviation)

	N (Female)	Age	Full Scale IQ[a]
ASD	260 (61)	8.57 (1.63)	97.01 (18.21)
TD	115 (36)	8.51 (1.60)	115.33 (12.31)

[a]Means significantly different between groups, p<.05

BEHAVIORAL AND COGNITIVE MEASURES

- ASD diagnoses were confirmed with the Autism Diagnostic Observation Schedule (ADOS-2), the Autism Diagnostic Interview-Revised (ADI-R), and clinician endorsement of DSM-5 criteria for ASD.
- Cognitive ability was assessed with the Differential Ability Scales-II (DAS-II).
- Autism symptomology, specifically RRBs, were assessed using the parent-report Social Responsiveness Scale (SRS-2), RRB subscale T-scores.

EEG ACQUISITION AND ANALYSIS

Figure 1. Midline frontal electrode, channel 11 (Fz), used in analyses of theta power.

- Eyes open resting electroencephalogram (EEG) was recorded at 1000 Hz with a 128-channel Hydrocel Geodesic sensor net.
- Absolute theta power was extracted from the midline frontal electrode (11, Fz; Figure 1).
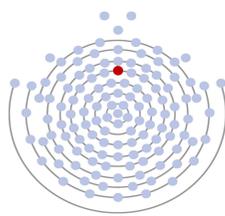
ET AND EBR ACQUISITION AND ANALYSIS

- Eye-tracking (ET) data was recorded at 500 Hz using the SR Eyelink 1000 plus.
- ET was collected during viewing of five paradigms assessing attention and social information: activity monitoring (AM), biological motion (BM), interactive social task (SI), static scenes (SS), and visual search (VS).
- Eye-blinks were defined as segments of missing data bounded by high-speed changes in estimated pupil size.
- EBR was calculated as the number of blinks per total time viewing each paradigm.

STATISTICAL ANALYSIS

- Independent samples t-tests were used to compare group means of EBRs, absolute theta power, and SRS-2 T-scores, and linear regression analyses were performed to examine the relationships between these variables.
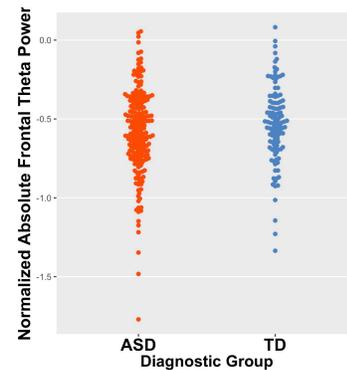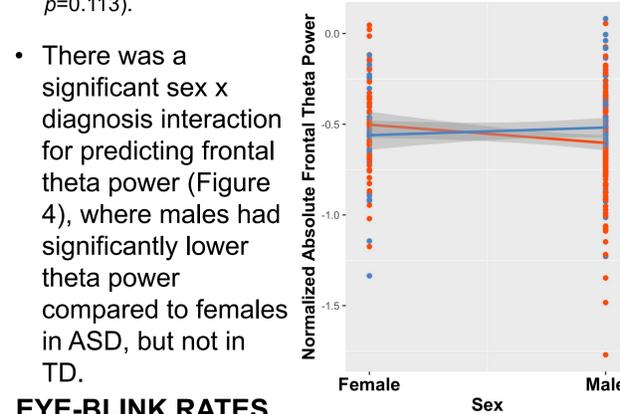
Results

FRONTAL THETA POWER

Figure 2. Distribution of frontal theta power in ASD and TD children (t(254) = -1.59, p=0.113).

- There were no significant differences in absolute frontal theta power between diagnostic groups (Figure 2).
- Across all participants, age predicted frontal theta power (F(1,325)= 15.93, p<.001), such that older participants had lower theta power. However, a significant age x diagnosis interaction (F(3,323)= 8.03, p=.0124) revealed this relationship was significant only in the TD group.

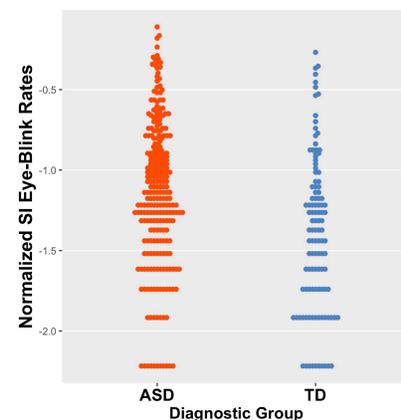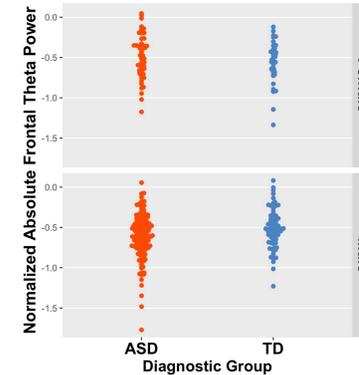**Figure 3.** (above) Group x sex differences in frontal theta power.

- There was a significant sex x diagnosis interaction for predicting frontal theta power (Figure 4), where males had significantly lower theta power compared to females in ASD, but not in TD.

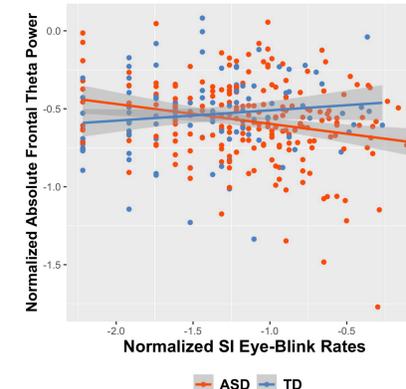**Figure 4.** (left) Sex x diagnosis interaction for predicting frontal theta power (F(3,323)=3.05, p=.029).

- Males with ASD had significantly lower theta power compared to TD males (t(174)=-2.53, p=.012), while this relationship was not significant in females (Figure 3).

EYE-BLINK RATES

- Children with ASD had significantly higher EBRs during the SI paradigm compared to TD (Figure 5), but no group difference in EBR was found during the other four paradigms.

Figure 5. Distribution of EBRs during the SI paradigm in ASD and TD children (t(197)=4.93, p<.001).

- Across all participants, there was a significant association between theta power and EBRs during SI (F(1,313)= 4.76.18, p=.030), VS (F(1,316)=8.21, p=.004), and SS (F(1,314)=4.55, p=.033), such that increased EBRs were associated with reduced theta power.
- For the SI paradigm only, there was a significant EBR x diagnosis interaction for predicting frontal theta power (Figure 6), such that higher EBRs were associated with lower theta power in ASD, but not in TD.

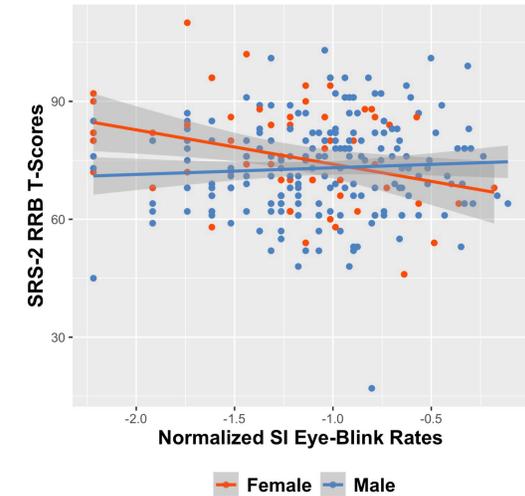**Figure 6.** (right) SI EBR x diagnosis interaction for predicting frontal theta power (F(3,311)=5.207, p= 0.002).

- Across all participants, males had significantly higher EBRs compared to females during the SI (t(168)=3.76, p<.001), BM (t(156)=2.97, p=.003), and VS (t(169)=2.34, p=.020) paradigms.

Results

RESTRICTIVE AND REPETITIVE BEHAVIORS IN ASD

Figure 7. SI EBRs x sex interaction for predicting SRS-2 RRB T-scores in ASD (F(3,253)=3.57, p=.008).

- There was no significant relationship between theta power and SRS-2 RRB t-scores (F(1,209)=.328, p=.567); there were no significant relationships between EBRs during any paradigm and RRBs.
- There was a significant interaction between sex and SI EBRs for predicting RRB T-scores, where lower EBR was associated with higher RRB T-scores in females with ASD, but there was no significant relationship in males (Figure 7).
- An SI EBR x frontal theta interaction for predicting RRB T-scores in ASD trended towards significance (F(3,199)=1.76, p=.050).

Conclusions

- Consistent with previous literature, boys with ASD were found to have reduced absolute resting frontal theta power compared to TD children.
- This difference in theta power was not observed in females, suggesting there may be sex specific differences in frontal neural activity within ASD.
- Contrary to previous findings, EBRs were found to be elevated in ASD during the viewing of a social interaction, which may be indicative of increased DA activity during this specific stimulus.
- However, future studies should also examine levels of attention during such paradigms by looking at visual scanning patterns alongside EBRs, as attention may also impact DA levels.
- EBRs were only predictive of RRB T-scores in females with ASD, again suggesting the need for further exploration of sex differences in both neural activity and behavior.

References

1. Jongkees, B. J., & Colzato, L. S. (2016). Spontaneous eye blink rate as predictor of dopamine-related cognitive function—A review. Neuroscience & Biobehavioral Reviews, 71, 58-82.
2. Yeung, M. K., Han, Y. M., Sze, S. L., & Chan, A. S. (2016). Abnormal frontal theta oscillations underlie the cognitive flexibility deficits in children with high-functioning autism spectrum disorders. Neuropsychology, 30(3), 281.
3. Schmitt, L. M., White, S. P., Cook, E. H., Sweeney, J. A., & Mosconi, M. W. (2018). Cognitive mechanisms of inhibitory control deficits in autism spectrum disorder. Journal of Child Psychology and Psychiatry, 59(5), 586-595.
4. Hornung, T., Chan, W. H., Müller, R. A., Townsend, J., & Keehn, B. (2019). Dopaminergic hypo-activity and reduced theta-band power in autism spectrum disorder: A resting-state EEG study. International Journal of Psychophysiology, 146, 101-106.

Funding Sources