Low Alpha Power Predicts Autism Severity in School-Aged Children with Below Average Head Circumference: Preliminary Results from the ABC-CT

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Autism Biomarkers Consortium for Clinical Trials

Background

- Electroencephalography (EEG) is commonly used to understand neurophysiological substrates underlying autism spectrum disorder (ASD)
- A growing body of research is using EEG to understand abnormalities of the resting brain in individuals with ASD
- Previous research has identified differences in alpha and gamma power between individuals with ASD and typical development (TD)
- Potential relationships among EEG and atypical head circumference, a common finding in ASD, is poorly understood

Objectives

1. Characterize EEG power in the low alpha (8-10 Hz), high alpha (10-12 Hz), and gamma (30-55 Hz) bands in children with ASD and TD with small, average, and large head circumferences
2. Examine relationships among EEG power, head circumference, and ASD symptomatology

Methods

Participants

- Clinical and EEG data were collected from 191 children participating in the Autism Biomarkers Consortium for Clinical Trials (ABC-CT; Table 1)
- Approximate head circumference was measured on the date of study participation prior to EEG acquisition

Cognitive & Behavioral Assessments

- ASD diagnoses were confirmed using the ADOS-2, ADI-R, and DSM-5
- Full-Scale IQ was measured using the DAS-II
- ASD symptom severity was measured using the ADOS-2 calibrated severity score (CSS)
- Social function was measured with the Social Responsiveness Scale (SRS-2

Table 1. Participant demographic data. ASD and TD groups were matched on age (p>0.05) but not on DAS-II, ADOS-2 CSS, or SRS-2 T-scores (p<0.05)

Group	N (Females)	Mean Age (SD)	DAS-II (SD)	ADOS-2 CSS (SD)	SRS-2 *T*-score (SD)
ASD	133 (26)	8.8 (1.6)	97.4 (18.8)	7.78 (1.9)	73.1 (11.1)
TD	58 (20)	8.5 (1.7)	115.8 (13.2)	1.5 (0.8)	42.0 (3.4)

Experimental Paradigm

- Resting eyes open
  - Videos of non-social, abstract moving images
- Each unique video (n=6) was played for 30 seconds in random order
  - Each video was clipped to 15 seconds and played forward and then in reverse
- 3 blocks total, with 60 trials in each block
  - 90 total seconds of EEG acquisition
- Only participants who had attended trial counts ≥ 18 trials in 2 blocks were included

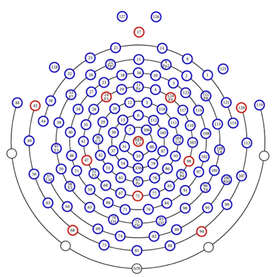


Figure 1.128-channel HydroCel Geodesic Sensor Net

Methods

Analytic Plan

- EEG collected using a 128-channel HydroCel Geodesic Sensor Net (Figure 1)
- Obtained EEG power in the low alpha, high alpha, and gamma bands
- Head circumference groups were based on a standardized growth chart accounting for age and sex (Roche et al. ,1987)
  - Small (< 1 SD), average (-1 SD to +1 SD), and large (> 1 SD) head circumferences

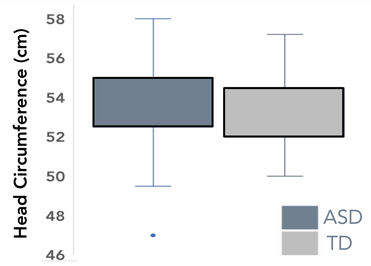


Figure 2. Head circumference distributions for children with ASD (mean=53.5 cm) and TD (mean=53.2 cm). ASD and TD groups did not differ in average head circumference (*p*>.05)

Table 2. Participant data for small, average, and large head circumference groups

Group	N (Female)	TD, ASD Distribution (%)	Head Size (SD)	Mean Age (SD)	DAS-II (SD)	ADOS-2 CSS (SD)	SRS-2 *T*-score (SD)
Small	21 (4)	12.1, 10.5	50.7 (1.1)	8.7 (1.5)	106.4 (19.4)	5.0 (3.2)	61.9 (17.5)
Average	117 (33)	58.6, 62.4	53.1 (1.1)	8.6 (1.6)	102.0 (19.0)	6.0 (3.3)	64.2 (16.8)
Large	53 (9)	29.3, 27.1	55.4 (1.0)	8.9 (1.8)	103.9 (19.8)	5.9 (3.5)	63.1 (18.1)

Results

- Two-way ANOVA revealed a statistically significant interaction between the effects of head circumference and diagnosis on low alpha power [F(2,183)=3.17, *p*=.044]
  - Simple main effects analysis indicated no differences in low alpha power based on head circumference group or diagnosis alone (*p*>.05)
- There are no significant interactions between head circumference and diagnosis on high alpha power or gamma power (*p*>.05)

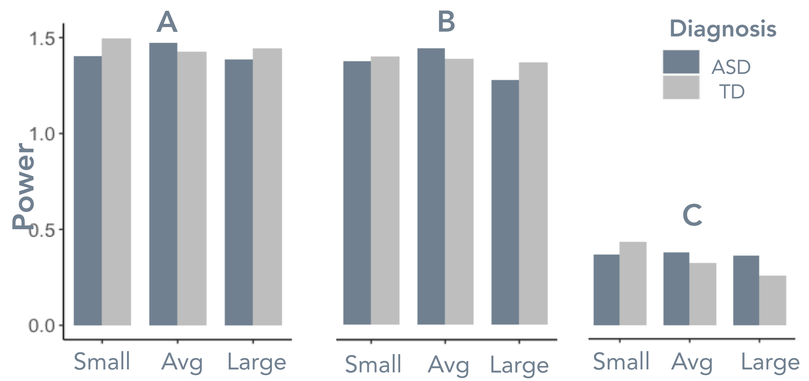
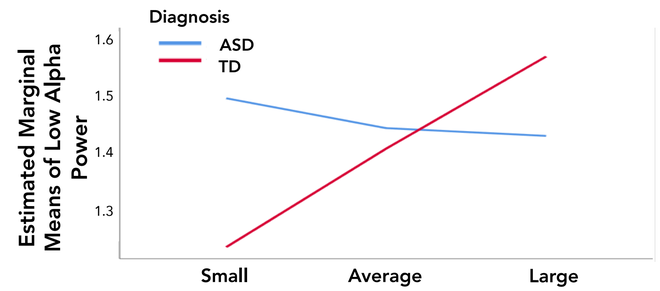


Figure 3. Differences in low alpha (A), high alpha (B), and gamma (C) power between ASD and TD participants with small, average, and large head circumferences. No significant differences between diagnosis or head circumference emerged for low alpha, high alpha, or gamma power

Results

Figure 4. Visualization of the significant interaction between head circumference and diagnosis for low alpha power (*p*=.044)



- Linear regressions were used to evaluate the relationship between low alpha power, head circumference, and social function across groups
- Within a linear regression model, low alpha power explained 26.2% of the variance in SRS T-scores across participants in the small head circumference group [R^2=.262, F(1,13)=5.98, p=.029]
- Low alpha power did not predict SRS T-scores in participants with average or large head circumferences (*p*>.05)
- Neither high alpha nor gamma power predicted SRS T-scores in any of the head circumference groups (*p*>.05)

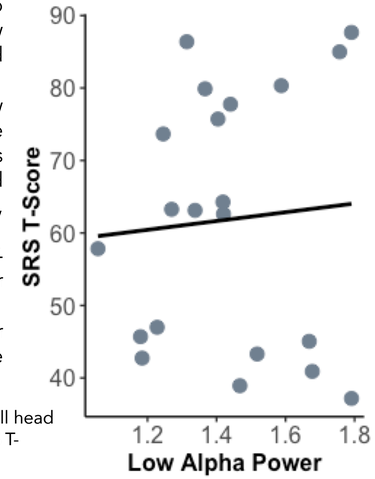


Figure 5. In ASD and TD participants with small head circumference, low alpha power predicted SRS T-scores (β=.561, *p*=.029)

Conclusions

- Preliminary results indicate an interaction between diagnosis and head circumference on low alpha power at rest
- In both ASD and TD, low alpha power predicted social function in children with below average head circumferences
- Head circumference should be considered when evaluating relationships among EEG spectral power, specifically low alpha power, and the clinical phenotype

References Roche, A. F., Mukherjee, D., Guo, S., & Moore, W. M. (1987). Head circumference reference data: birth to 18 years. Pediatrics, 79(5), 706-712.

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