Symptoms of Persistent Depression but not General Anxiety or Major Depression Predict Resting Alpha Power for Autistic Children: Results from the Autism Biomarkers Consortium for Clinical Trials (ABC-CT)

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Background

- Autistic individuals exhibit different patterns of resting-state EEG power spectra compared to neurotypical individuals.[1]
- These differences (i.e., elevations in resting gamma power and reductions in relative alpha power) are thought to represent possible biomarkers for autism spectrum disorder (ASD).[1]
- Distinct power spectra have also been observed in Major Depressive Disorder and Anxiety Disorder.[2,3]
- Anxiety and depression frequently co-occur in ASD; thus, understanding relationships among anxiety and depression and resting EEG in ASD could inform biomarker development.[4,5]

Objectives

1. Examine how resting-state EEG power varies as a function of parent-reported anxiety and depressive symptoms in autistic participants.
2. Investigate possible differential relationships between resting EEG power and parent-reported anxiety and depressive symptoms in autistic versus neurotypical children.

Methods

Participants

- Participants included 260 autistic children and 116 neurotypical children between the ages of 6 and 11 (N=376) (**Table 1**).

	Age (±SD)	Female (%)	Full-Scale IQ Score (±SD)
ASD (n=260)	9.1 (±1.6 years)	62 (24%)	99.57 (±18.7)
TD (n=116)	9.0 (±1.6 years)	36 (31%)	118.5 (±13.9)

Table 1. Participant demographics across diagnostic groups. Age (in years) and full-scale IQ scores reported as mean (standard deviation). Sex reported as number of female participants (percentage).

- Participants were recruited and seen as part of the Autism Biomarkers Consortium for Clinical Trials (ABC-CT) study.

Measures

- Parents completed the *Child and Adolescent Symptom Inventory-5* (CASI-5).
  - Subscales from the CASI-5 captured individual differences associated with symptoms of major depression (MD), persistent depression (PD), and general anxiety (GA).
    - Persistent depressive disorder is a more mild and chronic form of major depressive disorder.[6]
- Full-scale IQ (FSIQ) was assessed by the *Differential Ability Scales-II* (DAS-II).
- Eyes-open resting EEG data was collected with a 128 electrode EGI Hydrocel Geodesic Sensor Net.
- Participants watched non-social visual stimuli in three one-minute blocks (**Figure 1**).

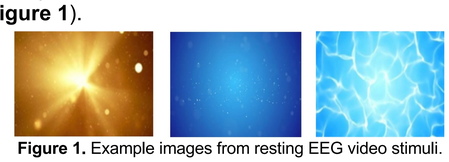

Figure 1. Example images from resting EEG video stimuli.

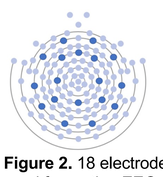

Figure 2. 18 electrodes used for resting EEG slope calculation from a 128 electrode net.

- Resting EEG slope was averaged across 18 electrodes (**Figure 2**).
  - Alpha power was defined as 9 to 12.99 Hz.
  - Gamma power was defined as 35 to 54.99 Hz.

Statistical Analysis

- CASI-5 psychiatric symptom scores and diagnostic group were used to predict log-scaled power spectral density EEG values in linear regression models. Age, sex, FSIQ, and number of valid EEG trials were included as nuisance variables in all models.
- 9 total linear regression models were run, including symptoms of persistent depression, major depression, and general anxiety as independent variables with resting-state alpha, theta, and gamma power as dependent variables.

Results

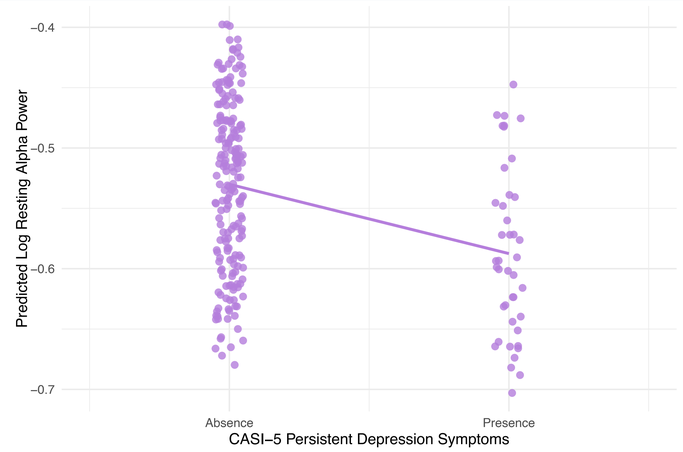

Figure 3. Plot depicting the relationship between parent-reported CASI-5 persistent depression symptoms and resting-state alpha power values for autistic participants. Values were adjusted for sex, age, FSIQ, and EEG data quality. The trendline represents the best-fit regression line.

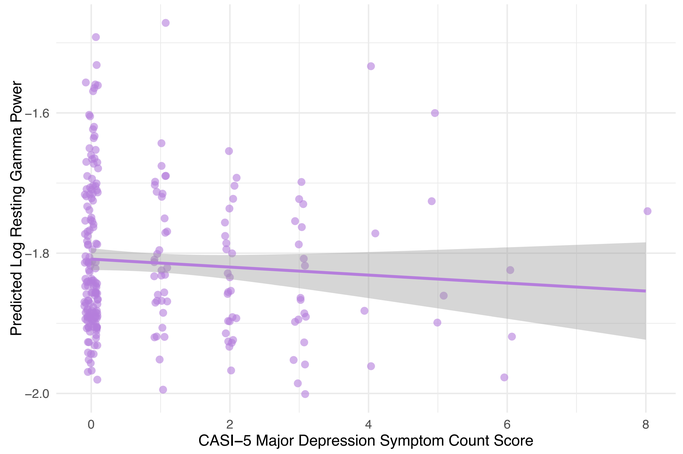

Figure 4. Plot depicting the relationship between parent-reported CASI-5 major depression symptoms and resting-state gamma power values for autistic participants. Values were adjusted for sex, age, FSIQ, and EEG data quality. The trendline represents the best-fit regression line.

Alpha Power

- Omnibus regression models revealed a significant main effect of CASI-5 PD score on resting-state alpha power (β=-0.34, *p*=.011). It also revealed a significant interaction between CASI-5 PD scores and diagnostic group on measures of resting alpha power, indicating that the association between PD symptoms and alpha power differed for autistic and neurotypical children (β=0.28, *p*=.022).
  - Follow-up models within each diagnostic group revealed a main effect of PD symptom report on alpha power for autistic participants (β=-0.07, *p*=.049), such that PD symptoms were negatively associated with resting alpha power (**Figure 3**).
- MD (*p*=.447) and GA (*p*=.458) symptom scores did not exhibit significant relationships with resting alpha power.

Gamma Power

- Omnibus regression models found a significant main effect of CASI-5 MD scores on resting-state gamma power (β=-0.12, *p*=.024). A significant interaction between MD scores and diagnostic group revealed that the relationship between MD scores and resting gamma power differed as a function of diagnostic status (β=0.12, *p*=.023).
  - Follow-up models within the ASD group demonstrated that there was no significant effect of MD scores on gamma power for autistic children (*p*=.512) (**Figure 4**).

Results

Gamma Power

- Omnibus regression models revealed a significant main effect of CASI-5 PD scores on resting-state gamma power (β=-0.39, *p*=.011) in addition to a significant interaction between PD symptoms and diagnostic group on resting gamma power, indicating that the relationship between PD symptom report and resting gamma power differed between diagnostic groups (β=0.38, *p*=.007).
  - Follow-up models within the ASD group revealed that there was no significant effect of PD symptoms on gamma power for autistic children (*p*=.696).
- GA scores exhibited no significant interactions with gamma power (*p*=.199).

Other Analyses

- Follow-up analyses within the neurotypical group revealed significant main effects of PD symptom report with both alpha power (β=0.20, *p*=.048) and gamma power (β=-0.43, *p*=.019), in addition to a positive relationship between MD symptom scores and gamma power (β=0.11, *p*=.021).
- All comparable analyses investigating theta band activity produced null results.

Conclusions

- The experience of depression symptoms was reflected in quantitative differences in the magnitude of resting-state EEG activity, confirming trends reported in prior work.[2,3]
- This study shows that the relationship between these psychiatric symptoms and resting-state EEG activity varied across autistic and neurotypical children.
- Parent-reported persistent depression symptomology was negatively associated with resting alpha power in autistic children.
- Contrary to previous literature, general anxiety and major depression symptoms were unrelated to resting state alpha or theta power in our sample of autistic children.[2,3]
- Results highlight the importance of considering co-occurring conditions when evaluating EEG biomarkers for autism.

Limitations and Future Directions

- Neurotypical participants were initially excluded based on elevated clinical symptomatology of any psychiatric disorder, rendering their little variability in their scores.
  - These analyses were limited by the low number of neurotypical children whose parents reported depression and anxiety symptoms, thus models pertaining to our neurotypical cohort should be interpreted with caution.
- Future research could explore these relationships among measures that can provide more insight into the severity of comorbid psychological disorders for children with autism.

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