EEG and Pupillary Response in Children with Autism: Results from the ABC-CT Interim Analysis

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Background

- Dysregulated attention and arousal are co-occurring features of autism spectrum disorder (ASD). These symptoms are associated with both noradrenergic and cholinergic activity.
- Pupil diameter (PD) is a marker of noradrenergic and cholinergic (neuromodulatory) activity and indexes brain network dynamics.
- Prior work has established that individuals with ASD exhibit attenuated pupil response to light, suggesting altered neuromodulatory activity.
- However, there have been no studies in ASD linking the dynamics of the pupillary light reflex (PLR) to EEG features.
- Understanding the relationship between PD and EEG may help to parse heterogeneity among individuals with ASD by identifying more biologically homogeneous subgroups.

Method

Participant demographics

Group	n (n female)	age (sd)	IQ(sd)
TD	58 (21)	8.93 (1.72)	115.02 (13.96)
ASD	126 (23)	8.74 (1.64)	96.78(19.03)

***Diagnostic groups did not differ on age, [t(182)=.726, p=.89]. However, diagnostic groups significantly differed on full scale IQ, as measured by the Differential Ability Scales, Second Edition (DAS-II), [t(182)=2.69, p<.01] and sex [t(182)=6.53, p=.01].*

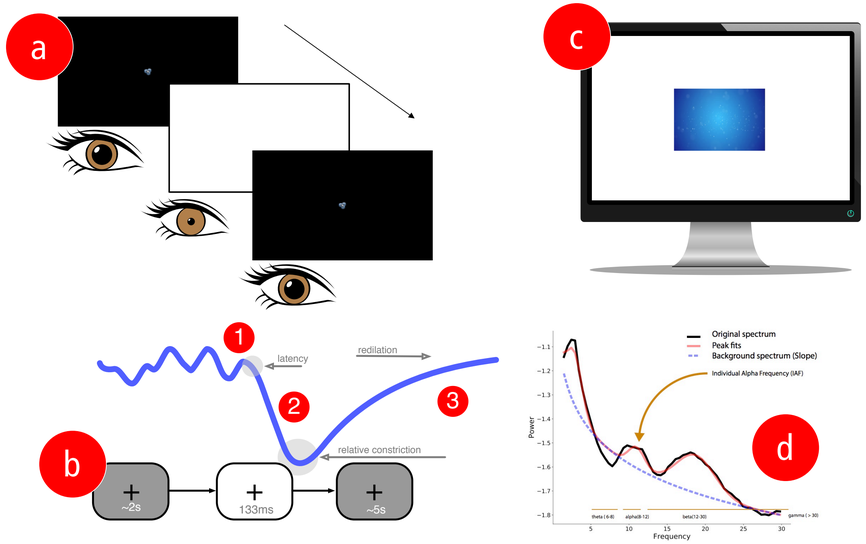
- EEG and eye-tracking (ET) data were collected from participants recruited from the New Haven, CT, Boston, MA, Los Angeles, CA, Durham, NC, and Seattle, WA metropolitan areas as a part of the Autism Biomarkers Consortium for Clinical Trials (ABC-CT).

EEG collection and processing:
- EEG was recorded at 1000 Hz with a 128-channel Hydrocel Sensor net.
- Resting data were collected while participants sat quietly watching an abstract video.
- Data were filtered from 0.1-100 Hz.
- Multitaper Fourier transforms were used to estimate band-specific power.
- EEG features were measured using customized MATLAB scripts.
- EEG power was averaged over 125 electrodes.

Pupil collection and processing :
- Pupil data were collected using an SR Eyelink-1000 + at 500 Hz.
- The PLR was calculated to a 133ms white flash followed by a black screen.
- PLR dynamics included constriction, latency to constrict, and redilation.

Behavioral Data:
- Diagnosis was confirmed via the Autism Diagnostic Observation Schedule, 2nd Edition (ADOS) and the Autism Diagnostic Interview (ADI).
- Social Responsiveness Scale, 2nd Edition (SRS).

Method



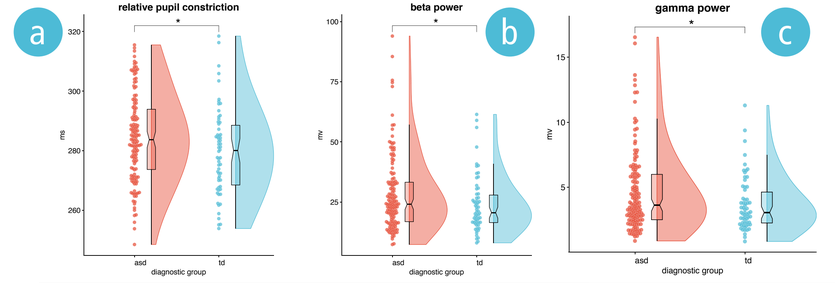
A. A black screen for ~ 2 seconds was followed by a white screen for 133ms and a black screen for ~5 seconds.

B. Schematic pupillary light response showing (1) latency to constrict, (2) relative constriction, and (3) redilation.

C. Resting EEG was recorded while participants watched a two minute abstract video on a computer screen.

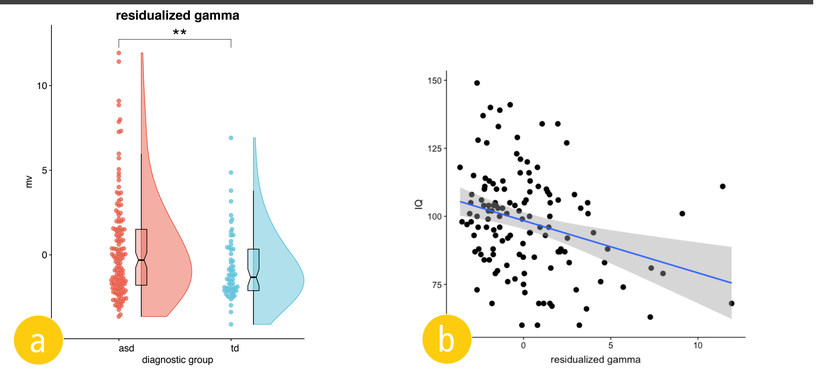
D. Resting EEG power spectra depicting slope and band-specific power ranges.

Results



- PLR comparisons revealed latency to constrict (t=2.1, *p*=.036) was faster in controls compared to individuals with ASD [a].
- EEG analyses revealed individuals with ASD exhibited greater beta (t=2.138, *p*=.032) and gamma (t=2.6, *p*=.001) power compared to controls [b,c].

Results



- Across groups, increased redilation time predicted reduced gamma power (B=-0.004, *p*=.01), indicating increased excitation with increasing arousal.
- Residual gamma activity was calculated, removing the effect of pupil redilation time, per person.
- Individuals with ASD, compared to controls, exhibited significantly greater residualized gamma, indicating increased excitation in the absence of arousal (t=2.9, *p*=.004) [a].
- Residualized gamma associated meaningfully with clinical variability among individuals with ASD, such that increased residual gamma correlated with lower IQ (r=-.29, *p*=<.001) and increased restricted and repetitive behaviors on the SRS (r=.19, *p*=.02).

Conclusions

- This is the largest dataset to examine relationships between EEG and PLR in individuals with ASD, revealing potential relationships between brainstem nuclei, cortical activity, and clinical symptomology.
- The differences between groups on PLR and EEG measures suggest increased excitation and arousal in ASD.
- The relationship between redilation time and EEG indicates that, on average, NE activity increases excitation. However, the differing patterns of residuals between groups suggests that individuals with ASD show less reduction in excitation in response to arousal.
- These findings suggest that the relationship between arousal and EEG activity may differ among individual with ASD and represent a promising neural circuit for further investigation.

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