Anxiety in adolescents with ASD modulates neural responses during a simulated social interaction

Developmental Electrophysiology Laboratory, Yale Child Study Center

Yale Child Study Center SINCE 1911

M. McNair[1], A. Naples[1], K. McNaughton[1], T. Day[1], T. Winkleman[1], M.J. Rolison[1], K. Ellison[1], E. Jarzabek[1], B. Lewis[1], J. Wolf[1], J. McPartland[1]

(1) McPartland Lab, Yale Child Study Center, New Haven, CT

Background

- Anxious symptomatology is highly prevalent (84.1%) among individuals with autism spectrum disorder (ASD) and up to 39.6% of individuals with ASD have at least one comorbid anxiety disorder[1,2].
- Electroencephalography (EEG) techniques have been used to study social perception, with the P100 and N170 event-related potentials (ERPs) serving as indicators of early visual processing and face-sensitive processing, respectively.
- Previous work has demonstrated atypical neural responses and looking patterns to social stimuli in both individuals with ASD[3] and anxiety[4].
- Most research has relied on passive observation of static and dynamic stimuli, and there is little research investigating the relationship of anxiety and brain response in interactive contexts.

Objective: To assess (1) brain response to faces that respond in a reciprocal manner between individuals with ASD and typically developing (TD) controls and (2) the potential effect of anxiety on brain activity.

Methods

Participant Demographics

Group	*n* (female)	Age (*SD*)[a]	IQ (*SD*)[a]
ASD	19 (4)	13.9 (1.90)	103 (20.7)
ASD-ANX[b]	20 (7)	14.1 (2.63)	102 (17.0)
TD	32 (18)	13.2 (2.59)	109 (12.2)

a) Groups were matched for age and IQ (p's>0.05).
b) Subgroup of children with ASD who received *T*-scores ≥65 on the *Child Behavior Checklist* (CBCL) Anxiety Problems Subscale[5].

Measures:

- CBCL: Parent-report questionnaire assessing problem behaviors in children ages 6-18 years old; variable used was Anxiety Problems Subscale *T*-score.
- *Social Anxiety Scale for Adolescents* (SAS-A)[6]: Self-report questionnaire assessing social anxiety; variable used was SAS Total Score.

Data Acquisition and Collection:

- EEG was recorded at 1000 Hz with a 128-channel Hydrocel Geodesic Sensor net.
- Participants viewed faces that would display reciprocal (eye to eye; E2E) (mouth to mouth; M2M) and nonreciprocal (E2M; M2E) facial movement in response to the participant's gaze (Figure 1).

Data Analysis:

- Data were filtered at 0.1 to 30Hz and segmented from -100 to 500ms relative to eyes or mouth opening.
- P100 (60-160ms) and N170 (150-300ms) peak amplitude and latency were extracted from electrodes over left and right occipitotemporal regions (Figure 2).

Statistical Analyses:

- Repeated measures ANOVAs (with group as a between-subject factor and gaze condition and hemisphere as within-subject factors) were used to determine interaction and main effects of group, hemisphere, and condition.
- Group differences on the CBCL and SAS-A were examined with one-way ANOVAs.
- Relationships between anxiety measures and neural responses were examined with Pearson's *r*.

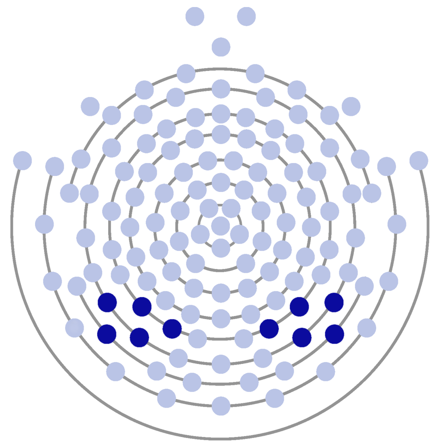

Figure 2. Selection of electrodes for analysis.

Methods

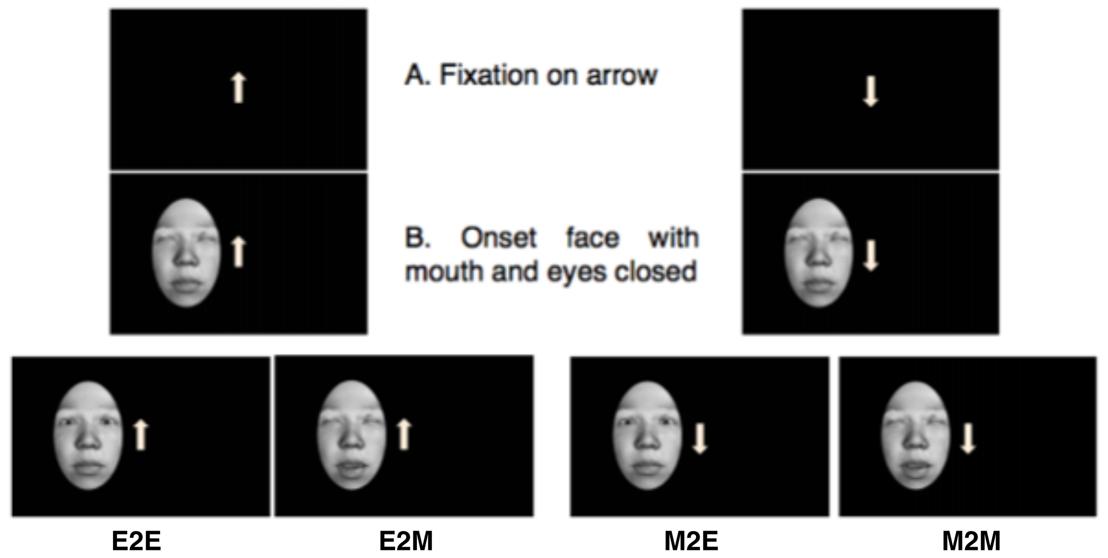

Figure 1. Participants were cued by an up or down arrow **(A)** to look at the eyes or mouth of a subsequent appearing face **(B).** In turn, the face responded by opening its eyes or mouth upon the participant's fixation to the cued region.

Results

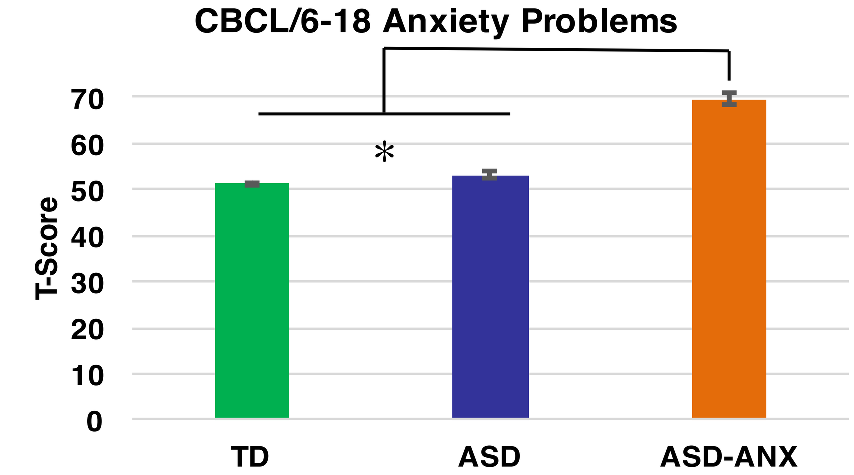

Figure 3. The ASD-ANX group displayed increased anxiety problems compared to both ASD and TD groups on the CBCL [$F(2,68)=145.599$, $p<0.01$]. Post-hoc tests revealed significant differences between ASD and ASD-ANX ($p<0.01$) and ASD-ANX and TD ($p<0.01$), but no difference between ASD and TD ($p>0.05$).

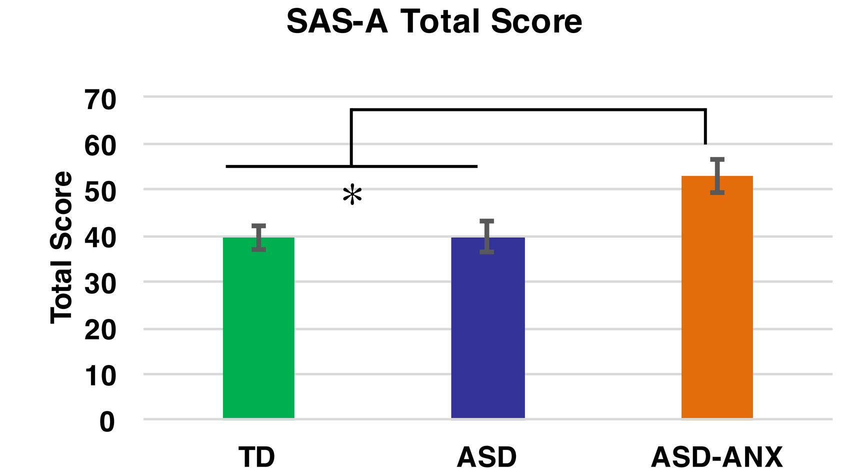

Figure 4. The ASD-ANX group displayed greater social anxiety than both ASD and TD groups on the SAS-A [$F(2,66)=5.247$, $p<0.01$]. Post-hoc tests revealed significant differences between ASD and ASD-ANX ($p<0.05$) and ASD-ANX and TD ($p<0.05$), but no difference between ASD and TD ($p>0.05$).

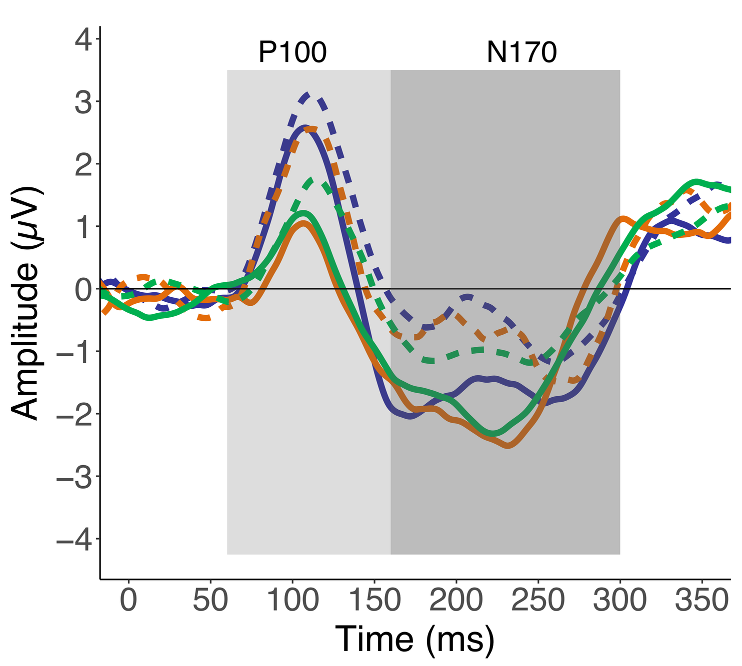

Figure 5. Neural response in the left hemisphere for adolescents with ASD, ASD-ANX, and TD in both conditions.

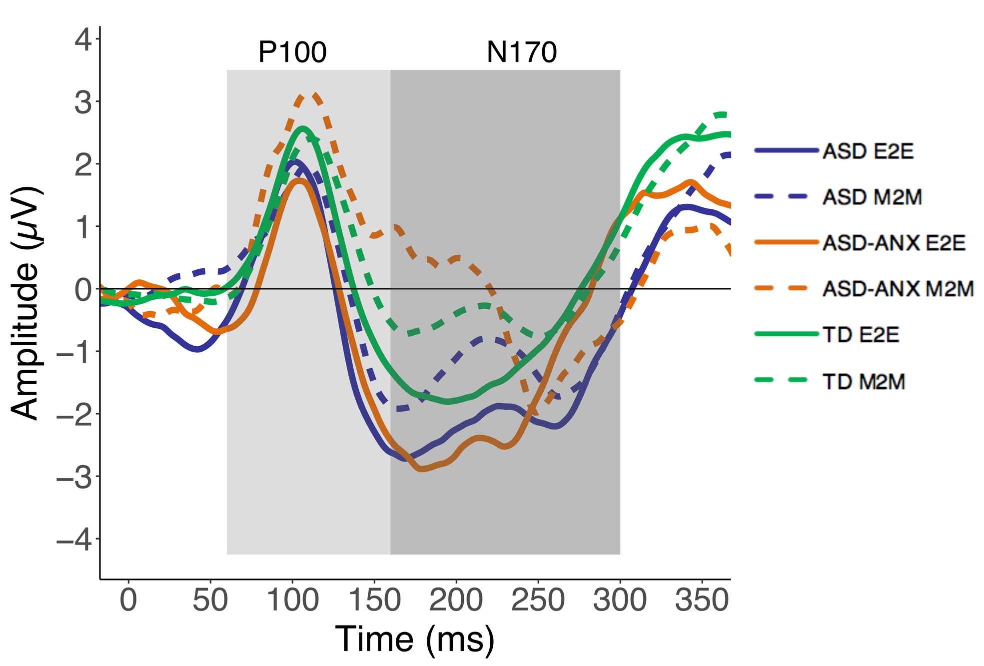

Figure 6. Neural responses in the right hemisphere for adolescents with ASD, ASD-ANX, and TD in both conditions.

P100 Peak Amplitude

- There was a significant interaction between hemisphere and diagnosis, [$F(2, 68)=4.133$, $p<0.05$].
- Pairwise comparisons revealed that the ASD group exhibited larger P100s in the left hemisphere ($M=0.902\pm0.374$, $p<0.05$) compared to the ASD-ANX and TD groups, while the TD group ($M=0.874\pm0.387$, $p<0.05$) exhibited larger P100s in the right hemisphere compared to the ASD-ANX and ASD groups (Figures 5 and 6).

P100 Latency

- There was a significant main effect of condition, [$F(1, 68)=6.120$, $p<0.05$], such that E2E elicited faster P100 responses than M2M (Figures 5 and 6).

Results

N170 Peak Amplitude

- There was a significant main effect of condition, [$F(1, 68)=12.930$, $p<0.01$], such that E2E elicited more negative (i.e., greater amplitude) N170 responses than to M2M (Figures 5 and 6).

N170 Latency

- There was a significant main effect of condition, [$F(1, 68)=26.214$, $p<0.01$], such that E2E elicited faster N170 responses than to M2M (Figures 5 and 6).

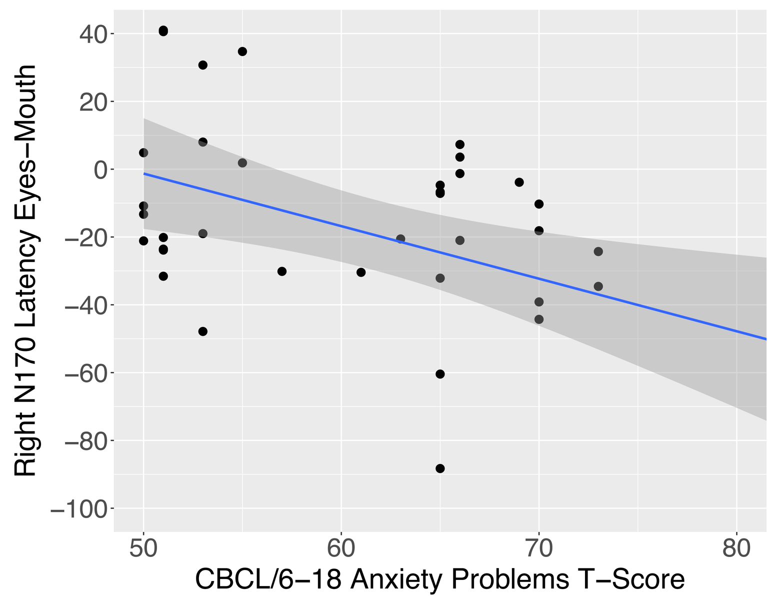

Figure 7. In the ASD group, N170 latency to reciprocal eye-contact in the right hemisphere related to increased CBCL Anxiety Problems, [$r(39)=-0.429$, $p<0.01$].

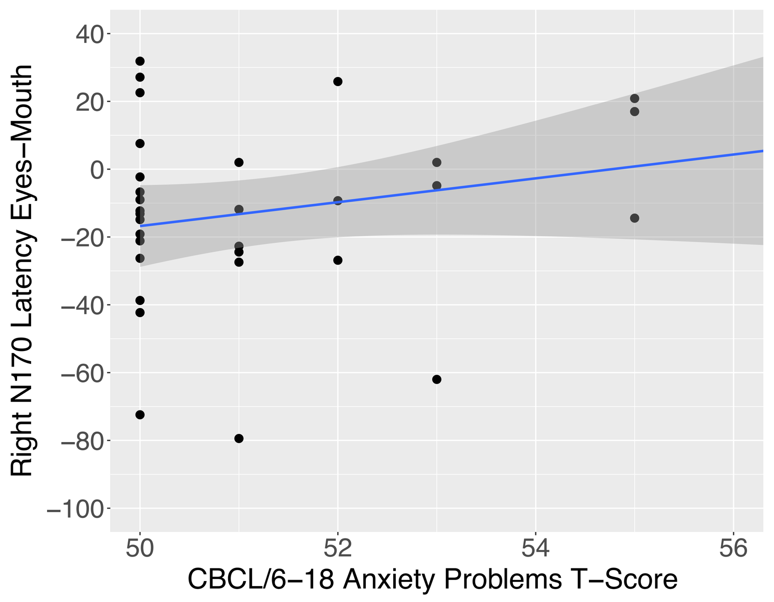

Figure 8. In the TD group, there was no association between N170 latency to reciprocal eye-contact in the right hemisphere and CBCL Anxiety Problems, [$r(32)=0.243$, $p>0.05$].

Discussion

- Based on both self- and parent-report, adolescents in the ASD-ANX group experienced significantly greater anxious symptomology compared to their peers with ASD and TD.
- Both the ASD-ANX and TD groups exhibited smaller P100s in the right hemisphere compared to individuals with ASD and lower anxiety, while TD individuals showed larger P100s in the right hemisphere compared to the ASD-ANX and ASD groups. This suggests that increased anxiety in ASD may result in more normative early visual processing of social stimuli.
- Individuals with ASD exhibited shorter N170 latencies to reciprocal eye-contact as parent-reported anxious symptomatology increased, suggesting a hypervigilance to eye-contact with increasing anxiety symptoms.
- Given the prevalence of co-morbid anxiety in ASD and the differential neural response to social interactions observed in these individuals, anxiety could serve not only as a treatment target for alleviating ASD symptomology but also as a specific subtype of ASD.
- A limitation of this study is its small sample size. Analysis of concurrent eye-tracking data would enhance these findings by overlaying exact gaze location to ERP responses and serves as a direction for future investigation.

References

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mcp.lab@yale.edu
mcp-lab.org