Neural Response to Emotional Faces and Anxiety in Children with Autism Spectrum Disorder

K. Ellison, J. Wolf, A. Naples, K. McNaughton, T. Day, T. Winkelman, M. Rolison, E. Jarzabek, B. Lewis and J. McPartland

McPartland Lab, Yale Child Study Center, New Haven, CT

Background

- Research has revealed the importance of understanding comorbidities, such as anxiety disorders, in children and adolescents with Autism Spectrum Disorder (ASD; Magiati et al., 2017).
- Anxiety impacts how emotions are perceived and processed (Rossignol et al., 2004).
- Children with ASD have an atypical brain response to emotional faces (Dawson et al., 2004).
- Eye tracking indicates that children with ASD spend less time looking at core facial features (i.e., eyes and mouth) compared to typically developing (TD) children.
- The influence of anxiety on neural responses to social information in ASD is not yet understood.
- This study applied interactive neuroscience methods to study brain response measured by electroencephalogram (EEG) during a gaze-contingent eye-tracking (ET) paradigm that simulated face-to-face social interactions.
- We evaluated whether specific differences in facial expression processing and attention are associated with anxiety in children and adolescents with ASD.

Objectives:

- To examine the relationship between anxiety symptoms and face-related event-related potentials (ERPs) and eye gaze during viewing of emotional faces in children with ASD.

Methods

Participant Demographics:

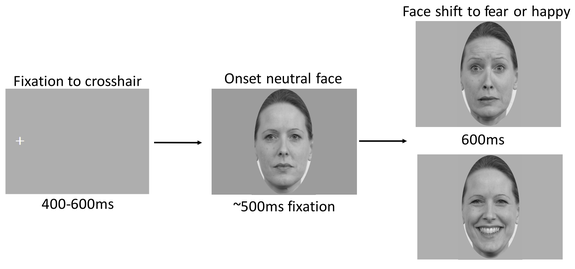
	N (Female)	Age (SD)[a]	Full Scale IQ (SD) [a]
ASD	24 (6)	14.4 (2.4)	109.2 (20.3)
TD	22 (9)	12.9 (3.0)	109.9 (11.6)

[a] The sample was matched for age and IQ.

Experimental Paradigm:

- Participants were presented with 80 distinct, photorealistic, animated faces matched for low-level visual features.
- Utilizing gaze-contingent ET, on-screen faces responded to a participant's direct fixation by exhibiting a happy or fearful expression (Figure 1).

Figure 1. Trial Structure. Trials began with a counterbalanced fixation crosshair at the left or right side of the screen for 400-600ms, followed by a centrally presented neutral face. After the participant looked to the neutral face for ~500ms, the face shifted to the fear or happy condition for 600ms. A 500ms blank screen separates each trial.



EEG and ET Data Acquisition and Collection:

- EEG recorded at 1000Hz with 128 channel Geodesic Sensor Net.
- ET data collected using an Eyelink-1000 remote camera.

ERP Processing:

- Data were filtered from 0.1-30Hz, re-referenced to the average reference, segmented from -100 to 500ms relative to shift in stimulus expression, baseline corrected, and artifact detected.
- ERP components were extracted from occipitotemporal electrodes (Figure 2). P100 and N170 latency and amplitude were extracted from 60-160ms and 150-300ms, respectively (See Figures 4 and 5).
- Difference scores were calculated as fear minus happy condition.

ET Processing:

- Eyelink DataViewer extracted dwell time in AOIs (Figure 3).
- Dwell time proportion was calculated and defined as the amount of time spent looking at a given AOI divided by the amount of time spent looking at the screen.

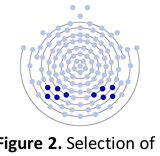


Figure 2. Selection of electrodes for analysis.

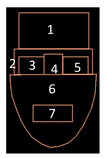


Figure 3. Areas of Interest (AOIs). 1=Upper Face; 2+3+4+5=Eyes; 3=Left Eye; 4=Between Eyes; 5=Right Eye; 6+7=Lower Face.

Methods

Clinical Measures:

- The *Autism Diagnostic Observation Schedule, Second Edition (ADOS-2)*, a diagnostic assessment, and the *Autism Diagnostic Interview – Revised (ADI-R)* were administered by research-reliable clinicians with expertise in ASD.
- The *Differential Abilities Scale, Second Edition (DAS-II)* was used to assess cognitive functioning.
- Child-reported measures, the *Multidimensional Anxiety Scale for Children, Child Report (MASC-C)* and *Social Anxiety Scale for Adolescence/Children (SAS-A/SASC-R),* captured anxiety symptomology in both populations.

Statistical Analyses:

- Correlations were conducted between standard scores on measures of self-reported anxiety and P100 and N170 difference scores and dwell time within AOIs.

Results

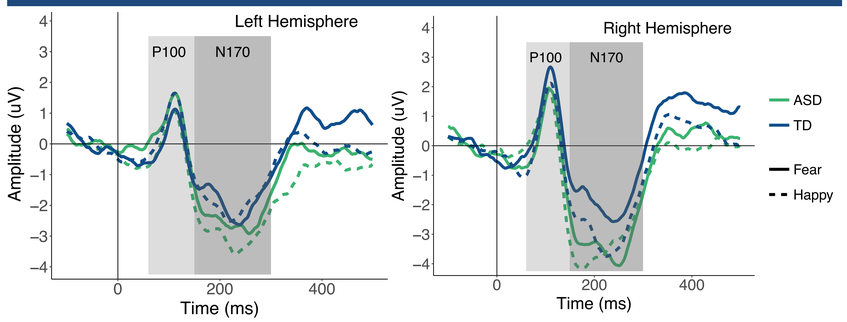


Figure 4. Left hemisphere ERP components, condition by DX

Figure 5. Right hemisphere ERP components, condition by DX

Group ERP Differences:

- A larger response to fearful faces in the right hemisphere for children with ASD was marginally significant compared to TD children $F(1,42)=3.18$, $p=.08$).
- No other significant differences were found between the ASD and TD groups for any of the other ERP components regardless of hemisphere or condition.

P100 Peak Latency and Peak Amplitude:

- In children with ASD, differential P100 latency to fear vs. happy in the left hemisphere was associated with physical symptoms of anxiety and overall total anxiety such that children with greater anxiety showed a faster response to fearful relative to happy faces (*MASC-C* Tense/Restless T- score, $r=-.61$, $p<.001$; *MASC-C* Somatic/Automatic T-score, $r=-.39$, $p=.06$; *MASC-C* Physical Symptoms Total T-score, $r=-.60$, $p<.001$, see Figure 6; *MASC-C* Total Anxiety T-score, $r=-.41$, $p=.05$; see Figure 7).
- In TD children, differential P100 amplitude to fear vs. happy in the right hemisphere was negatively associated with overall social anxiety such that TD children with greater social anxiety showed a smaller response to fearful relative to happy faces (*MASC-C* Social Anxiety Total T-Score, $r=-.43$, $p=.05$).
- No significant associations were found between either anxiety measure and P100 peak amplitude in the ASD group or P100 peak latency in the TD group, regardless of hemisphere.

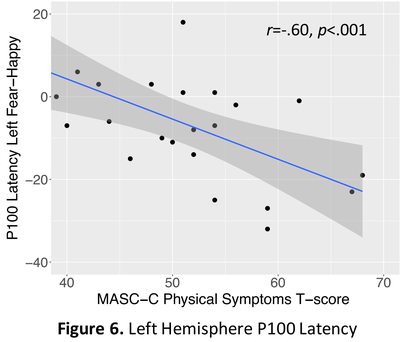


Figure 6. Left Hemisphere P100 Latency to Fear Minus Happy and MASC-C Physical Symptoms T-Score for ASD group

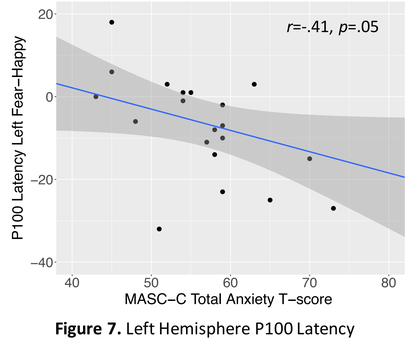


Figure 7. Left Hemisphere P100 Latency to Fear Minus Happy and MASC-C Total Anxiety T-Score for ASD group

Results

N170 Peak Latency and Peak Amplitude:

- In children with ASD, differential N170 amplitude to fear vs. happy in the left hemisphere was positively associated with symptoms related to social anxiety, such that children with greater social anxiety had a smaller response to fearful relative to happy faces (*SAS-A/SASC-R* Fear of Negative Evaluation, $r=.43$, $p=.04$).
- Differential N170 amplitude to fear vs. happy in the ASD group was marginally associated in the same direction with symptoms related to social anxiety *MASC-C* Humiliation/Rejection T-Score, $r=.38$, $p=.07$).
- In TD children, differential N170 amplitude to fear vs. happy in the right hemisphere was associated with symptoms of social anxiety, such that TD children with greater social anxiety had a greater response to fearful relative to happy faces (*MASC-C* Humiliation/Rejection T-score, $r=-.47$, $p=.03$; *MASC-C* Performance Fears T-score, $r=-.42$, $p=.05$; *MASC-C* Social Anxiety Total T-score, $r=-.48$, $p=.02$).
- No significant associations were found between either anxiety measure and N170 peak latency in either the ASD or TD group, regardless of condition or hemisphere.

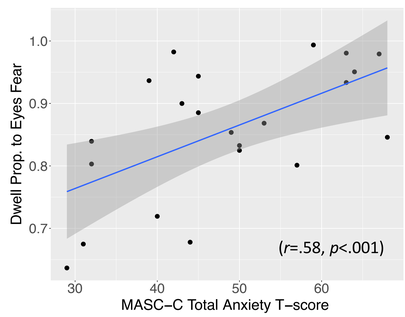


Figure 8. Dwell Proportion to the Eyes in Fear Condition and MASC-C Anxiety Total T-Score in TD group

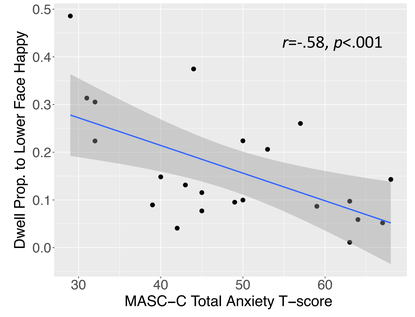


Figure 9. Dwell Proportion to the Lower Face in Happy Condition and MASC-C Anxiety Total T-Score in TD group

Eye Tracking Analyses:

- No significant associations were found between the dwell proportion to any AOI and levels of anxiety for the ASD group, for either expression.
- In TD children, significant positive associations were found between overall level of anxiety (*MASC-C* Total Anxiety Score) and the dwell time proportion to eyes in both the fear ($r=.58$, $p<.001$; see Figure 8), and happy ($r=.58$, $p<.001$) conditions.
- In TD children, significant negative associations were found between overall level of anxiety (*MASC-C* Total Anxiety Score) and the dwell time proportion to the Lower face in both the fear ($r=-.61$, $p<.001$) and happy ($r=-.58$, $p<.001$; see Figure 9) conditions.

Conclusions

- Anxiety influences brain response to emotional faces in ASD, providing information potentially useful for stratification in a heterogeneous population.
- Quicker neural response to fear was associated with increased overall anxiety and self-reported physical symptoms in individuals with ASD.
- In the TD group, more anxiety was associated with longer looking at the eyes and less looking at the lower part of the face. This relationship was not evident in ASD.
- Higher levels of anxiety in TD children may lead to increased attention to the eyes to glean more social information. The absence of this behavior in ASD is consistent with observed difficulties interpreting emotional facial expressions in ASD.
- Understanding the role of anxiety in relation to social-communicative biomarkers may inform development of targeted, biologically-based treatments.
- Limitations of this study include: small sample size and sole use of child self-report to assess levels of anxiety.

References:

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mcp.lab@yale.edu