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


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Background

- Research has revealed the importance of understanding comorbidities, such as anxiety disorders, in children with Autism Spectrum Disorder (ASD; Magai 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 fully understood.

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:**

<table>
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<tr>
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<th>N (Female)</th>
<th>Age (SD)</th>
<th>Full Scale IQ (SD)</th>
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</thead>
<tbody>
<tr>
<td>ASD</td>
<td>24 (6)</td>
<td>14.4 (2.4)</td>
<td>109.2 (20.3)</td>
</tr>
<tr>
<td>TD</td>
<td>22 (9)</td>
<td>12.9 (3.0)</td>
<td>109.1 (11.6)</td>
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**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).

**ET Processing:**

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

**EEG and ET Data Acquisition and Collection:**

- EEG recorded at 100Hz with 128 channels, 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 1000-2000ms relative to shift in stimulation, 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 ADIs (Figure 3).
- Dwell time proportion was calculated and defined as the amount of time spent looking at a given ADI divided by the amount of time spent looking at the screen.

**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-efficient clinicians with expertise in ASD.
- The Differential Abilities Scale, Second Edition (DAS-II) was used to assess cognitive functioning. 
- Child-reported measures, the Multidimensional Intensity Spectrum Scale for Children (MASS) and Social Anxiety Scale for Adolescence/Children (SASS-A/SASS-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 ADIs.

Results

**P100 Peak Latency and Peak Amplitude:**

- In children with ASD, differential P100 latency to fear vs. happy in the left hemisphere was marginally significant compared to TD children (F(1,42)=3.18, p<.05).
- No other significant differences were found between the ASD and TD groups for any of the other ERP components regardless of hemisphere or condition.

**N170 Peak Latency and Peak Amplitude:**

- 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<.05).
- No other significant differences were found between the ASD and TD groups for any of the other ERP components regardless of hemisphere or condition.

**Group ERP Differences:**

- In children with ASD, differential P100 latency to fear vs. happy in the left hemisphere was associated with physical symptoms of anxiety and overall anxiety such that children with greater anxiety showed a faster response to fearful relative to happy faces (MASC-C Total Anxiety score: t(42) = 3.99, p<.05; MASC-C’s Physical Symptoms Total score: t(42) = 4.35, 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.

**Results**

**N170 Peak Latency and Peak Amplitude:**

- In children with ASD, differential P170 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’s Social Anxiety Scale Total 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’s Social Anxiety Scale Total score, r=42, p=.05; MASC-C’s Total Social Anxiety Total 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.**

**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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