Adolescents with ASD Show Attenuated Neural Response to Reciprocal Eye Contact

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Background

Difficulty with interpersonal interactions is a unifying symptom of autism spectrum disorders (ASDs). Yet most social neuroscience research in ASD has focused on passive perception of static images. Brain mechanisms subserving *interactive* social behavior are poorly understood.

Event related potential (ERP) studies in typical development (TD) have examined brain response to dynamic faces, revealing two components sensitive to facial movement: an occipital N170 and a central P300. Neural responses to facial movements that occur contingent to one's own actions in the context of social interaction, such as responsive eye gaze, remain unexplored.

We investigated the relationship between **visual attention** to faces and **neural response** to shared gaze in TD and in ASD by using a **gaze-contingent** experiment. We predicted:

- modulation of face-sensitive ERP components by reciprocal gaze in TD children and adults
- reduced neural sensitivity to reciprocal gaze and atypical patterns of looking to faces (i.e., the absence of a characteristic bias to look towards the left eye) in ASD

Method

Experimental Design

- **Experiment 1 (Eye Contact).** Four conditions in which participants looked to:
  - closed eyes and the eyes opened (eyes:eyes, reciprocal eye-contact)
  - closed eyes and the mouth opened (eyes:mouth)
  - closed mouth and the eyes opened (mouth:eyes)
  - closed mouth and the mouth opened (mouth:mouth)
- **Experiment 2 (Gaze Shift).** We examined two conditions:
  - reciprocal direct gaze in response to participant fixation
  - averted gaze in response to participant fixation

Study Design

- Study 1 included 20 TD adults who participated in Experiment 1.
- Study 2 included a sample of 6 children with ASD and 5 TD children who participated in Experiment 1 and Experiment 2.

Data Acquisition

- ERPs were recorded using a 128 electrode Hydrocel Geodesic Sensor Net
- Eye-tracking (ET) was concurrently recorded from:
  - a three camera remote eye-tracking system (SmartEye Pro v 5.8; Study 1)
  - SR-Research Eyelink 1000 (Study 2)

Data Extraction

ERPs were time-locked to face movement. The minimum amplitude of the **N170** was measured at occipito-temporal sites between 130 and 210 ms, and mean amplitude of the **P300** was measured at central electrodes between 250 and 350 ms.

Behavioral Questionnaires

Self-report questionnaires measuring the broader autism phenotype were collected from adult participants:

- Autism Quotient (AQ)
- Broader Autism Phenotype Questionnaire (BAPQ).

Participants				
	Adults		Children	
	N	Age	N	Age
ASD	-	-	6	13.3(1.8)
TD	20	22.7(3.2)	5	14.9(2.3)

Data Analysis

Effects of condition were analyzed using separate univariate repeated measures analysis of variance for each dependent variable. Significant effects were explored with post-hoc t-tests. To investigate the relationship between sensitivity to eye-contact and social behavior, we calculated the difference in component amplitude between reciprocal gaze (eye:eye) and mouth movement (mouth:mouth) and correlated this difference with behavioral measures.

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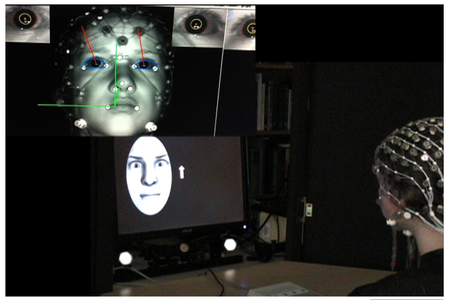
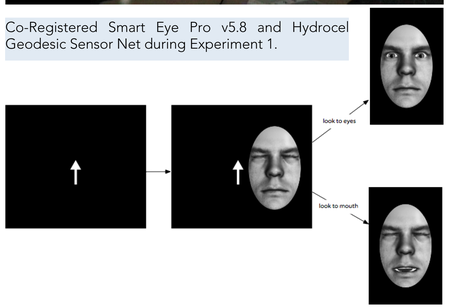
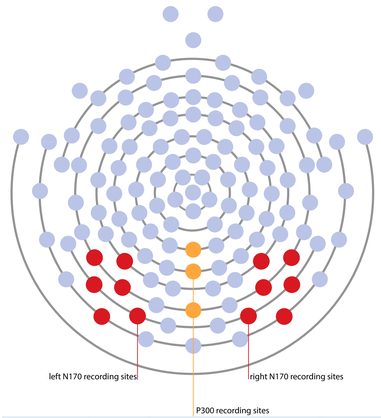


Co-Registered Smart Eye Pro v5.8 and Hydrocel Geodesic Sensor Net during Experiment 1.



Trial structure, Experiment 1: Fixation arrows preceding face presentation cued participants to look either to the mouth or eyes of the face. Contingent upon participant fixation, the face responded by either opening its eyes or mouth.

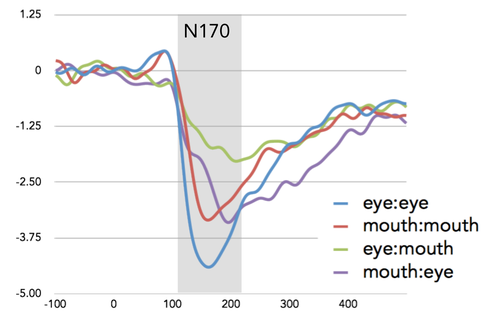
Trial structure, Experiment 2: Peripherally presented fixation crosshairs preceded a centrally presented face exhibiting either direct or averted gaze. Contingent on participant fixation to the eyes, the face responded by changing gaze, establishing eye-contact or averting gaze.



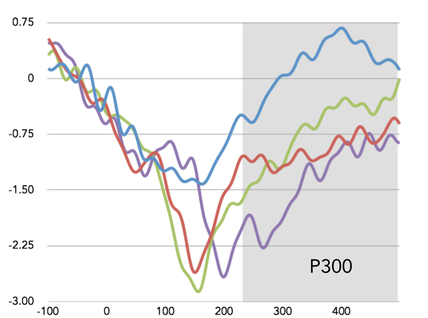
Recording sites for N170 (red) and P300 (yellow)

Results

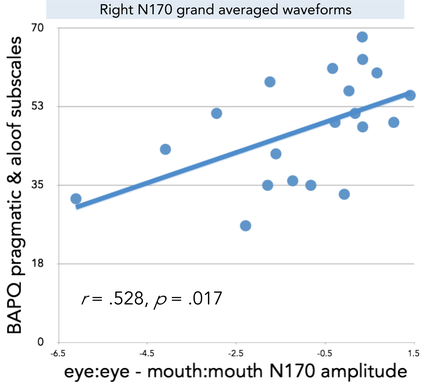
Adults: Experiment 1

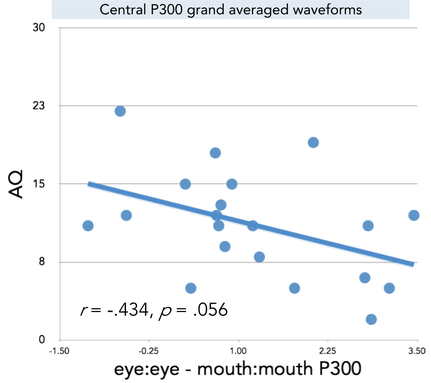


Right N170 grand averaged waveforms



Central P300 grand averaged waveforms

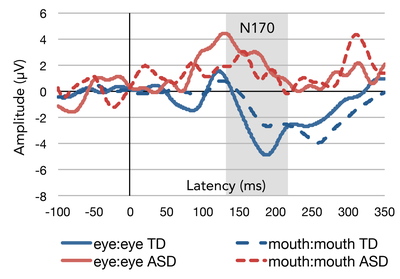




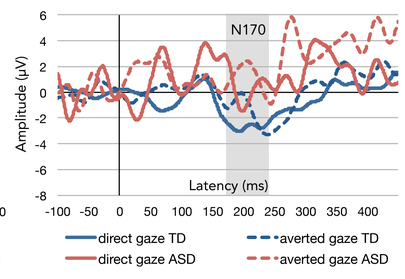
Relationships among BAPQ, AQ, and sensitivity to reciprocal gaze

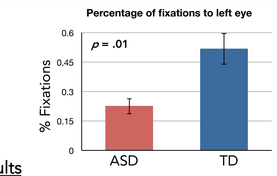
Results

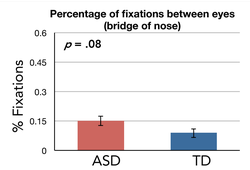
Children: Experiment 1



Children: Experiment 2







Adults

Analyses of N170 and P300 amplitude in adults in Experiment 1 revealed:

(a) A main effect of condition on N170 amplitude [$F(3,17)=13.99, p<.001$]

- Post-hoc tests revealed that the eye:eye condition differed significantly from all other conditions (all $ps<.013$).

(b) A main effect of condition on P300 amplitude [$F(3,17)=7.23, p=.002$]

- Post-hoc analyses revealed that the eye:eye condition was significantly greater than mouth:mouth ($p=.003$) and mouth:eye ($p=.004$).

ERP-Behavioral correlations

Greater sensitivity to reciprocal eye-contact at the right N170 predicted lower scores on the aloof and pragmatic subscales of the BAPQ ($r=.528, p=.017$). Greater sensitivity to eye-contact at the P300 predicted lower scores on the AQ ($r=-.434, p=.056$).

Children

In Experiment 1, TD children exhibited enhanced N170 amplitude to reciprocal eye-contact in both hemispheres. In the left hemisphere, children with ASD did not differentiate eye contact from mouth movement at the N170 and showed attenuated overall N170 amplitude relative to TD children.

In Experiment 2, TD children showed enhanced N170 to direct gaze relative to averted gaze, while children with ASD did not display modulation of ERP amplitude by gaze.

Eye-tracking results

Compared to children with ASD, TD children displayed a characteristic bias in fixation pattern, orienting more to the left eye ($p=.016$). Children with ASD spent more time fixating between the eyes ($p=.08$) and looked significantly less to the eye region of the face ($p=.01$).

Conclusions

This study co-registered EEG and eye-tracking in a gaze contingent paradigm to reveal a novel electrophysiological marker of shared gaze. This index of shared gaze was present bilaterally in TD adults and children and reflected in enhanced N170 amplitude to eye contact. In contrast, children with ASD displayed no modulation of brain activity in response to eye contact in the left hemisphere. Measures of visual fixation indicated atypical looking patterns in ASD, with reduced left hemiface bias and a tendency to fixate to the bridge of the nose rather than to the eyes. In addition to marking clinical levels of social dysfunction in ASD, this index of shared gaze predicted levels of social behavior and autistic traits in typical adults.

These methods and this novel marker of social perception offer promising clinical applications, such as measuring response to treatment and detecting atypical social development in infants. Work in progress assesses the plasticity of this index of gaze sensitivity.

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