Hemispheric and developmental differences in the neural processing of mutual eye contact in individuals with autism spectrum disorder

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Background

- Autism spectrum disorder (ASD) is defined by difficulties in social interaction.
- Electroencephalography (EEG) can be used to study social perception, with the N170 event-related potential (ERP) marking face-sensitive processing.
- Previous work from our group identified an ERP index of mutual eye contact in adults with typical development (TD) during a simulated face-to-face interaction, enhanced relative to other facial movements.

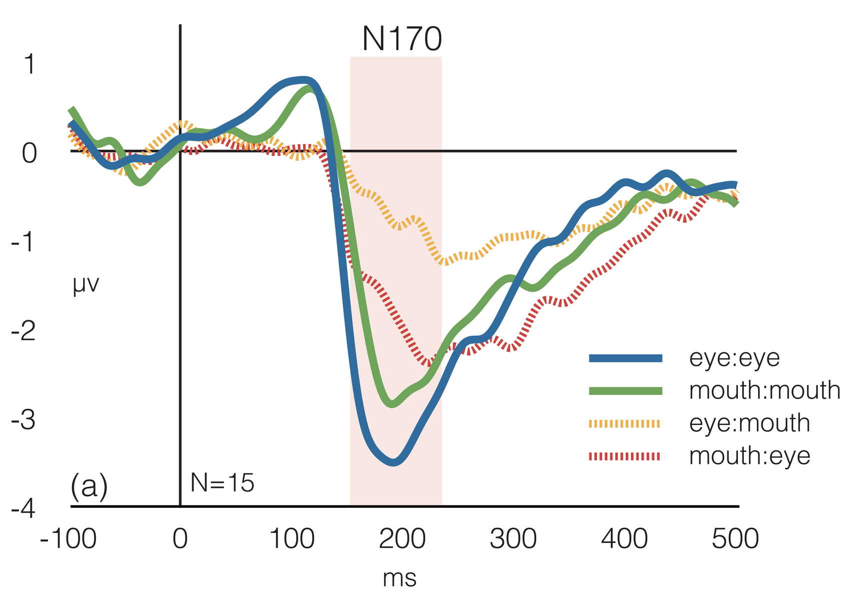

Figure 1. N170 response to mutual eye contact (eye:eye) differs from response to reciprocal mouth movement or non-reciprocal face movement (mouth:mouth, eye:mouth, mouth:eye) (Naples et al., 2017).

- The objective of this study was to identify **differences in neural processing of mutual eye contact in individuals with ASD and TD** and to examine how these processing patterns **change over development** in a cross sectional sample.

Method

Participants

Diagnosis	*n*	*n* male	Mean Age (Range)	Mean IQ (Range)
ASD	52	41	17.8 (10-35)	107 (76-137)
TD	70	42	18.4 (9-37)	111 (72-140)

- Diagnostic groups did not significantly differ in age, IQ, or handedness (*p*s>0.05).

EEG and ET Data Acquisition and Collection:

- EEG was recorded at 1000 Hz with a 128-channel Hydrocel Geodesic Sensor net.
- ET data was collected using an Eyelink-1000 remote camera system.

ERP Analysis

- N170 (150-300ms) ERPs were extracted from electrodes over left and right occipitotemporal regions (electrodes 58, 64, 59, 66, 65, and electrodes 96, 95, 91, 84, 90 respectively, see Fig. 2). Data were filtered at 0.1 to 30Hz and segmented from -100 to 500ms relative to eyes or mouth opening.
- Peak amplitude and latency were analyzed for response to gaze-contingent eye and mouth movement in repeated measures ANOVAs (with diagnostic group as a between-subject factor and face condition and hemisphere as within-subject factors).
- Pearson correlations between age and N170 peak amplitude (averaged across hemispheres) were also examined.

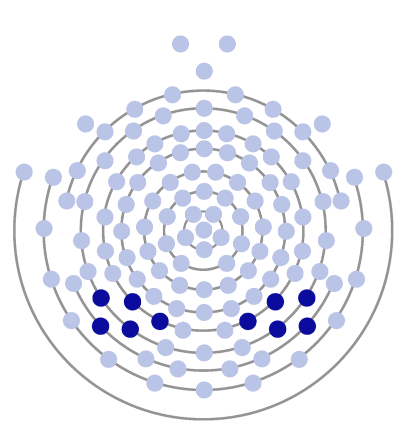

Figure 2. Selection of electrodes for analysis.

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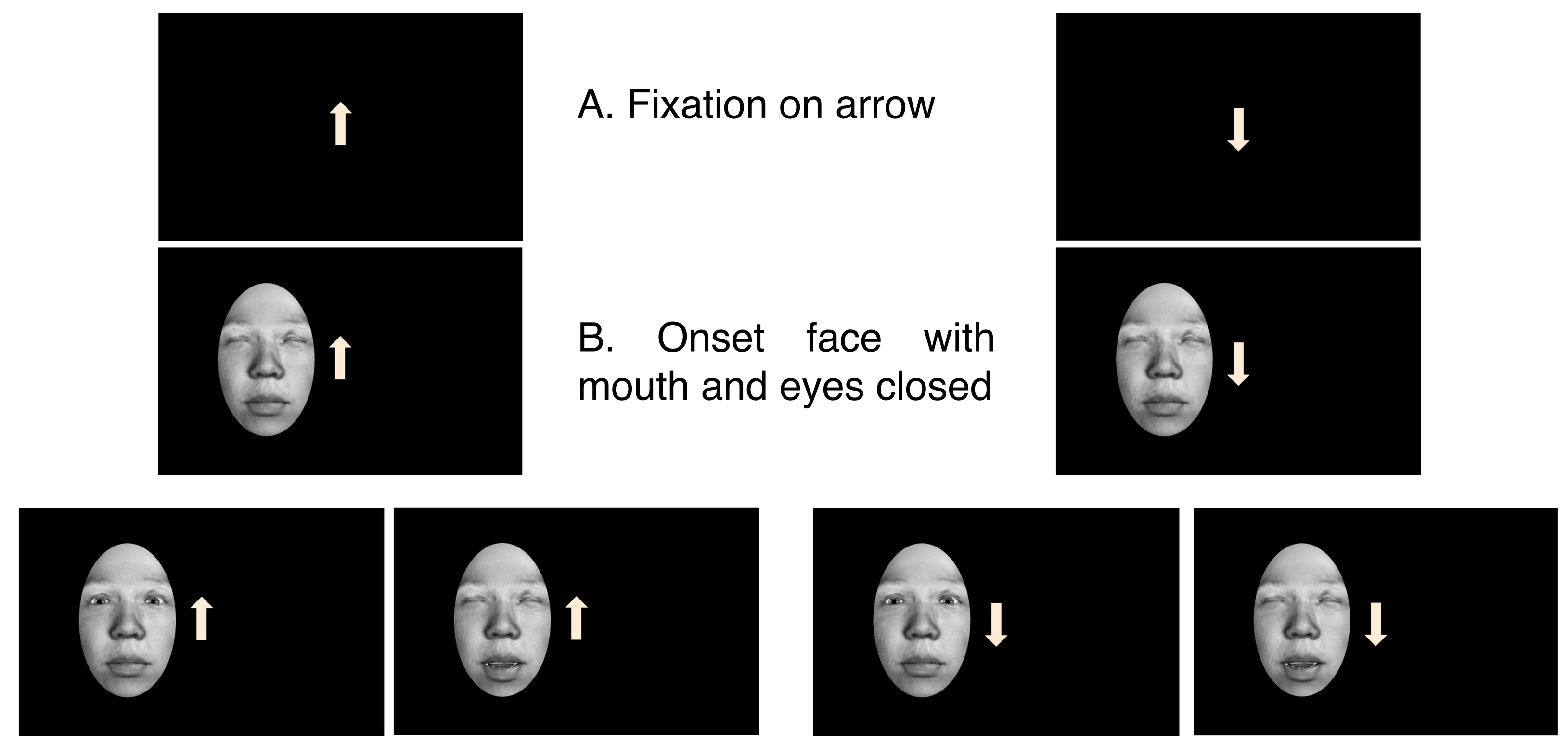
Paradigm

- Participants were cued by an up or down arrow (A) to look at the eyes or mouth, respectively, of a subsequently appearing face (B).
- In response to participant gaze to the region cued by the arrow, the mouth or eyes of the face opened, resulting in 4 conditions: fixate on eyes, eyes open (eye:eye), fixate on eyes, mouth opens (eye:mouth), fixate on mouth, eyes open (mouth:eye), fixate on mouth, mouth opens (mouth:mouth).



Results

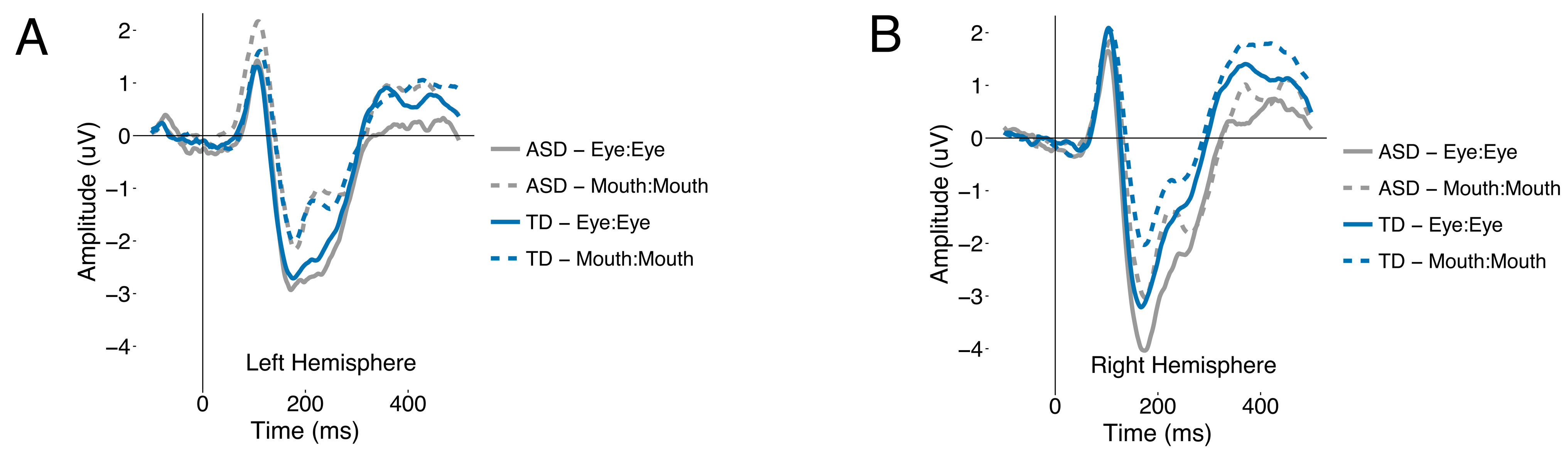


Figure 3. Grand average waveforms of left hemisphere (A) and right hemisphere (B) brain response to gaze-contingent eye and mouth movement for individuals with TD and ASD.

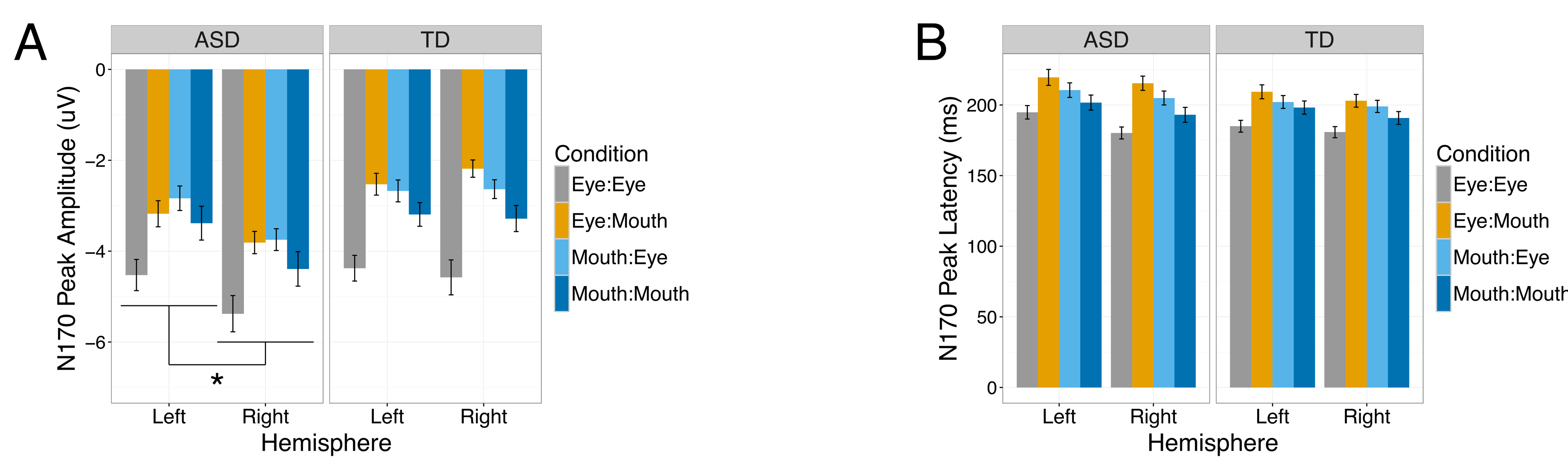


Figure 4. Differences in N170 peak amplitude (A) and latency (B) in response to faces displaying gaze-contingent mouth and eye movements for individuals with ASD and TD. (*) = indicates right hemisphere amplitude significantly more negative than left hemisphere amplitude (*p*<0.01).

- <u>N170 Amplitude:</u> There was a significant main effect of condition (*F*(3, 360)=43.6, *p*<0.01), such that responses were more negative to mutual eye contact (eye:eye) than other conditions. There was a significant main effect of hemisphere (*F*(1, 120)=9.0, *p*<0.01), a significant main effect of diagnosis (*F*(1, 120)=6.3, *p*<0.05), and a significant interaction of hemisphere and diagnosis (*F*(1, 120)=10.0, *p*<0.01). Individuals with ASD demonstrated more right-lateralized processing of dynamic faces (right hemisphere N170s significantly more negative than left hemisphere N170s, *p*<0.01) while individuals with TD did not display significant lateralization patterns.
- <u>N170 Latency</u>: There was a significant main effect of condition (*F*(3, 360)=29.1, *p*<0.01) such that there were faster N170s to mutual eye contact than other conditions. There was a significant main effect of hemisphere (*F*(1, 120)=8.1, *p*<0.01), such that there were faster responses in the right hemisphere.

Results

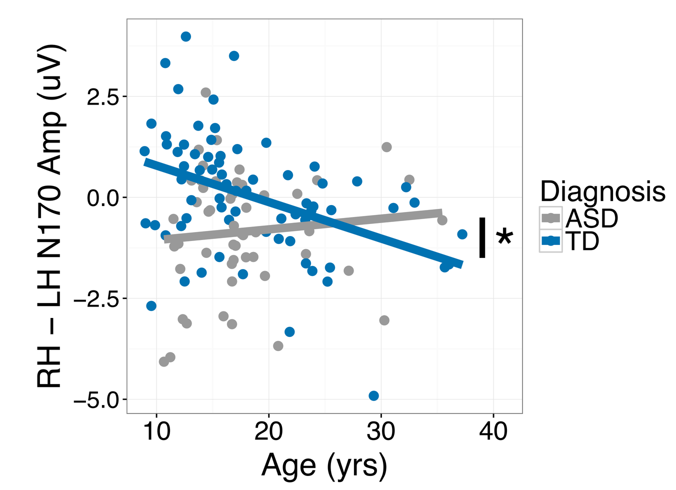


Figure 5. Change in lateralization of N170 amplitude to dynamic faces over development. (*) indicates correlations significantly different (*p*<0.05). RH=right hemisphere, LH=left hemisphere.

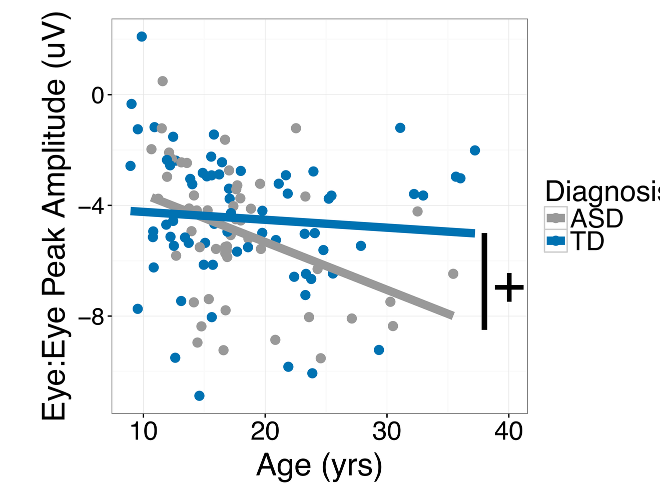


Figure 6. Change in N170 amplitude to mutual eye contact over development. (+) indicates marginally significant difference between correlations (*p*=0.06).

- Across development, individuals with TD had increasing right lateralization of N170 amplitude to dynamic faces compared to individuals with ASD (*p*<0.05).
- Individuals with ASD had significantly more negative N170 amplitudes to mutual eye contact with increasing age (*r*(50)=-0.41, *p*<0.01), but individuals with TD had no significant change over time (*r*(68)=-0.08, *p*>0.10). These two correlations differed marginally from each other (*p*=0.06), reflecting greater change over time for individuals with ASD than individuals with TD.

Conclusions

- Across diagnoses, there were significantly **stronger and faster N170 responses to mutual eye contact than to other gaze-contingent face movements**, consistent with previous findings in adults with TD (Naples et al., 2017).
- **Individuals with ASD had right-lateralized brain activity** in response to the gaze-contingent faces, while **individuals with TD had no significant lateralization** in N170 response. This finding, which contrasts with previous literature suggesting that individuals with ASD have reduced lateralization of brain response to faces (Senju et al., 2005), may reflect the dynamic nature of the gaze-responsive stimuli. Additionally, **lateralization patterns changed across development**, as older individuals with typical development demonstrated more right-lateralized patterns.
- **Older individuals with ASD had stronger brain responses to mutual eye contact**, while **individuals with TD had no changes** over the course of development. These developmental differences could reflect divergent patterns of circuit maturation or differences in intervention or treatment history across the course of development.
- As autism is a developmental disorder, future longitudinal work could better characterize developmental changes in social information processing and the relationship between neural and environmental changes.

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