Brain-behavior relationships in autism spectrum disorder and typical development during an interactive social paradigm

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Background

- Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by impairments in social communication and the presence of restricted and repetitive behaviors. Atypical eye contact in individuals with ASD is present early in life.[1]
- Individuals with ASD exhibit slower neural response to faces during passive viewing,[2] and atypical gaze patterns during social scenes.[3] Neural response to dynamic eye contact allows for insight into face processing in more ecologically valid contexts.[4]
- Right- and left-handed individuals show different viewing patterns of faces,[5] but it is unclear whether handedness modulates neural response to face and gaze.
- We examined whether (1) behavior, namely handedness and patterns of viewing faces, differed between individuals with ASD and typical development (TD), (2) an event-related potential (ERP) associated with early face processing, the N170, differed based on handedness or diagnosis, and (3) brain and behavior were related.

Methods

Table 1. *Characteristics of the sample population.*

Group	Total *n* (male %)	Age *m* (σ)	IQ *m* (σ)	Edinburgh *n* (Right %)	EEG & Edinburgh *n*
ASD	132 (73%)	15.9 (5.7)	103 (18)	101 (82%)	57
TD	89 (60%)	16.9 (6.3)	109 (15)	70 (84%)	55

Sample population: (Table 1)
- All participants contributed eye-tracking (ET) data except for one individual in the ASD group due to file transfer error (Total *n*). The total ASD and TD groups were age-matched.
- A subset of these participants contributed to data on handedness (Edinburgh *n*). The final sample included those with handedness data that passed electroencephalography (EEG) artifact detection (EEG & Edinburgh *n*). The final ASD and TD group were age-matched.

Experimental Data Collection:
- Handedness was ascertained using the Edinburgh Handedness Inventory. Participants reported the hand used (e.g. always right hand, prefer right hand) to perform tasks (e.g. writing, brushing teeth). The Laterality Quotient (LQ) was calculated, and a LQ greater than 0 was considered right-handed.[6]
- EEG and ET were collected concurrently during gaze-contingent simulated eye contact. 112 faces,[7] matched on low-level visual features, were presented. The faces responded to the participant's gaze by making (direct gaze) or breaking (averted gaze) eye contact (Figure 1).
- EEG was collected at 1000 Hz using a 128-channel Geodesic Sensor Net.
- ET was collected with an EyeLink-1000 remote camera system.

ERP Preprocessing:
- Data were filtered between .1 and 30 Hz.
  - Re-referenced to average reference.
  - Segmented from -100 to 500 ms relative to gaze shift.
  - Baseline corrected and artifact detected.
- Trials were excluded if eye movement exceeded 1.5° of visual angle.
- The N170 (150–300 ms, post gaze shift) response was collected from occipitotemporal electrodes (Figure 2) in the left (58, 64, 59, 66, 65) and right (96, 95, 91, 84, 90) hemisphere.

ET and ERP Analysis:
Non-parametric data were analyzed with a Mann-Whitney U Test. Parametric data were analyzed with repeated measures ANOVA (rm-ANOVA) that included between-subject factors of diagnosis (TD or ASD) and handedness (right or left) and within-subject factors of condition (direct or averted) and hemisphere (EEG only; right or left). Follow-up tests included independent and paired sample *t*-tests, and brain-behavior relationships were analyzed with Pearson and Spearman correlations.

Figure 1. Trial Structure.
1. A crosshair appears. 2. When the participant fixates on the crosshair for ~300 ms, a face appears. 3. After looking at the eyes for ≥500 ms, the gaze shifts (to direct or averted) and remains onscreen for 600 ms.

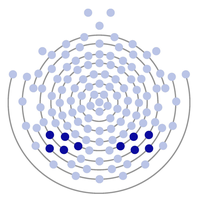

Figure 2. Occipitotemporal electrodes.

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Results

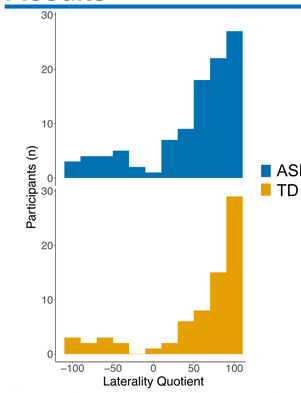


Figure 3. Handedness of individuals as measured by the LQ where 100 is always prefers right hand and -100 is always prefers left hand.

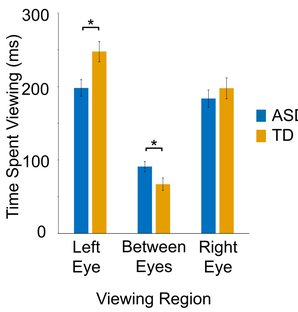
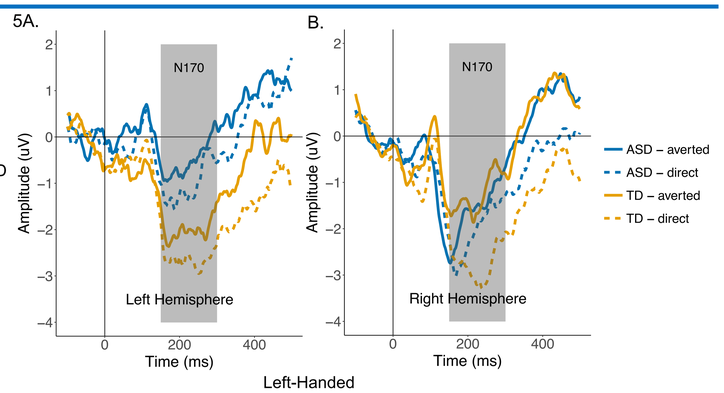


Figure 4. Time spent viewing various regions of the eyes by diagnosis.



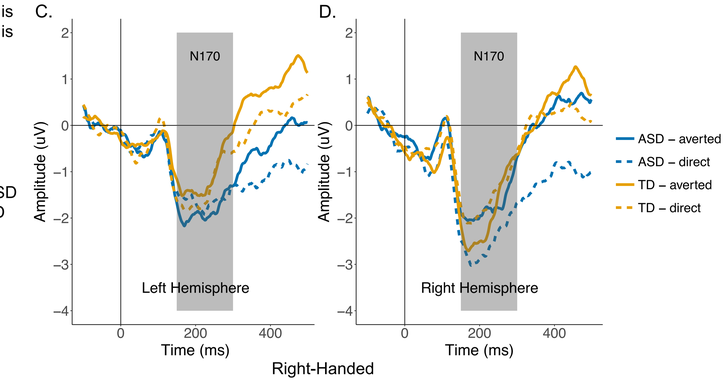


Figure 5. The N170 ERP to direct and averted gaze in left-handed (A, B) and right-handed (C, D) individuals. For each handedness group, left (A, C) and right (B, D) hemisphere, diagnosis and condition are depicted.

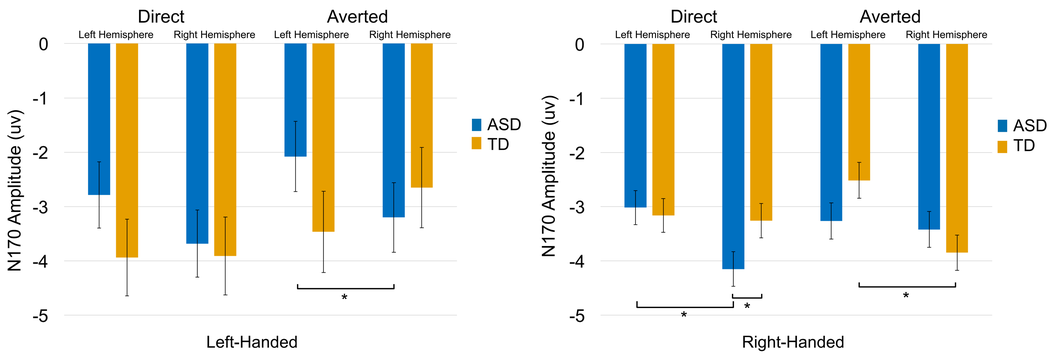


Figure 6. The N170 amplitude in the left- and right-handed groups in response to direct and averted gaze. Within direct and averted gaze, N170 amplitude is broken into hemisphere (left and right) and diagnostic group (TD and ASD).

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Results

Handedness Findings (Figure 3):
- The ASD group (*m*=49.9, σ=57.7) and the TD group (*m*=59.0, σ =59.4) marginally differed on handedness (*U*=3003, *p*=.09).

ET Findings (Figure 4):
- No interaction effects between time spent viewing a region and handedness emerged. Subsequent rm-ANOVAs excluded handedness. Between-subjects effects revealed the ASD group spent less time viewing the left eye [*F*(1, 217)=7.7, *p*<.01] and more time viewing between the eyes [*F*(1, 217)=4.8, *p*=.03] compared to the TD group.

ERP Findings (Figures 5 and 6):
- N170 Amplitude: There was a main effect of hemisphere [*F*(1,108)=6.5, *p*=.01], with a more negative N170 in the right hemisphere, and condition [*F*(1,108)=3.8, *p*=.05], with a more negative N170 to direct gaze. Interaction effects between diagnosis, handedness and hemisphere [*F*(1,108)=3.9, *p*=.05], and diagnosis, handedness, hemisphere and condition [*F*(1,108)=4.9, *p*=.03] emerged.
  - Follow-up *t*-tests revealed in the left-handed group:
    - In the ASD group, there was a more negative N170 in the right, compared to the left, hemisphere to averted gaze [*t*(11)=2.5, *p*=.03] .
  - Follow-up *t*-tests revealed in the right-handed group:
    - The ASD group had a more negative N170 to direct eye contact in the right hemisphere compared to the TD group [*t*(89)=-2.1, *p*=.04].
    - In the ASD group, there was a more negative N170 in the right, compared to the left, hemisphere to direct gaze [*t*(44)=3.8, *p*<.01].
    - In the TD group, there was a more negative N170 in the right, compared to the left, hemisphere to averted gaze [*t*(45)=4.3, *p*<.01].
- N170 Latency: An interaction effect between hemisphere and condition [*F*(1,108)=4.1, *p*<.05], and handedness, hemisphere, and condition [*F*(1,108)=34.0, *p*<.05] was revealed.
  - Follow-up *t*-tests indicated in the left-handed group, the N170 was faster in the right, as compared to the left, hemisphere [*t*(20)= 2.2, *p*=.04].

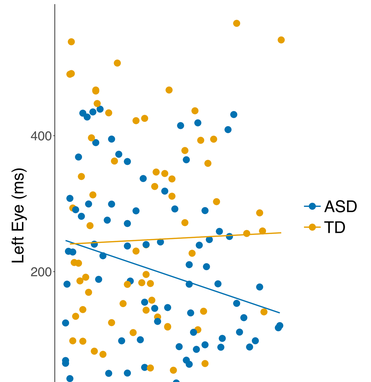

Figure 7. The relationship between right N170 latency and time spent viewing the left eye in the averted condition

Brain-Behavior Findings (Figure 7):
- Significant relationships between neural response and viewing patterns did not emerge in the left- or right-handed group.
- In the ASD group, faster N170 latency in the right hemisphere was related to more time spent looking at the left eye in response to averted gaze [*r*(74)=-.26, *p*=.03, r_s(74)=-.23, *p*<.05), but not in the TD group [*r*(69)=-.01, *p*>.10, r_s(69)=.01, *p*>.10].

Conclusions

- The distribution of handedness between individuals with ASD and TD was marginally different. This adds to the body of literature that atypical handedness, or weaker handedness, is present in individuals with ASD.[8]
- In a constrained viewing setting, individuals with ASD look to the left eye less and between the eyes more than individuals with TD. Individuals with TD demonstrate left gaze bias when viewing faces. Individuals with ASD may be missing key social cues during dynamic social interactions even when cued to look specifically to a region like the eyes due in part to differences in left gaze bias.
- Handedness impacts lateralized neural response as evidenced by the interaction between handedness and hemisphere in ERPs. Right-lateralized neural response to direct gaze was present in right-handed individuals with ASD and to averted gaze in left-handed individuals with ASD and right-handed individuals with TD. Handedness should be considered when examining lateralized brain response to faces.
- Relationships between neural response and viewing patterns did not emerge in left-handed or right-handed individuals. Together, individuals with ASD demonstrated a faster neural response as time spent viewing the left eye increased. Viewing specific regions of the face may lead to more efficient face processing specifically in ASD.