Sex Differences in the Neural Processing of Interactive Eye Contact in Individuals with Autism Spectrum Disorder

Kathryn McNaughton, Adam Naples, Brianna Lewis, Talena Day, Ariel Chang, Max Rolison, Kimberly Ellison, Elzbieta Jarzabek, Julie Wolf, Sabrina Malak, Julie Trapani, Kayla Stinson, Jennifer Foss-Feig, James McPartland

Yale Child Study Center, New Haven, CT

McPartland Lab mcp.lab@yale.edu mcp-lab.org

Background

- Autism spectrum disorder (ASD) is characterized by difficulties in social interaction.
- Electroencephalography (EEG) techniques can be used to study social perception, with the P100 serving as an indicator of early visual processing and the N170 marking face-specific processing.
- Previous work from our group identified differences in neural processing of one type of dynamic social information, interactive eye contact, between individuals with ASD and typical development (TD).
- Sex differences in ASD exist in the processing of social information, including in the neural response to static faces (Coffman et al., 2015).
- The objective was to identify sex differences in neural processing of interactive eye contact in individuals with ASD and TD.

Method

Participants

Sex	Group	*n*	Mean Age	Mean IQ
Male	ASD	83	16.8	102
Male	TD	43	18.6	109
Female	ASD	30	16.8	106
Female	TD	35	17.0	110

- Sex and diagnostic subgroups did not significantly differ in age or IQ (*p*s>0.05).
- All participants contributed eye-tracking (ET) data. Sex and diagnostic subgroups for participants that contributed EEG data (*n*=114) also did not differ in age or IQ (*p*s>0.05).

Experimental Paradigm:

- Participants viewed 112 faces that shifted gaze (from direct to averted, or from averted to direct) in response to participant fixation on the eyes (Fig. 1).

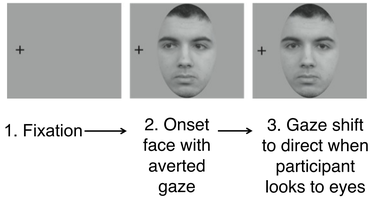

Figure 1. Trial Structure. Participants first fixated on a crosshair for ~300ms (Panel 1). Then a face displaying either direct or averted gaze was presented (Panel 2). After the participant looked to the eyes of the face for 500ms, the gaze of the face shifted (Panel 3) for 600ms (Naples et al., 2016).

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.

Event-related Potential (ERP) Analysis

- P100 (60-160ms) and N170 (150-300ms) 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 shift in stimulus gaze. Trials with eye movements greater than 1.5 degrees of visual angle were excluded.
- Peak amplitude and latency were analyzed for response to direct and averted gaze in repeated measures ANOVAs (with diagnostic group and sex as between-subject factors and gaze condition and hemisphere as within-subject factors).

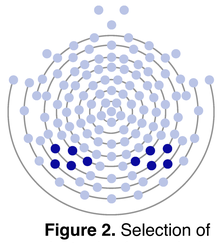

Figure 2. Selection of electrodes for analysis.

Results

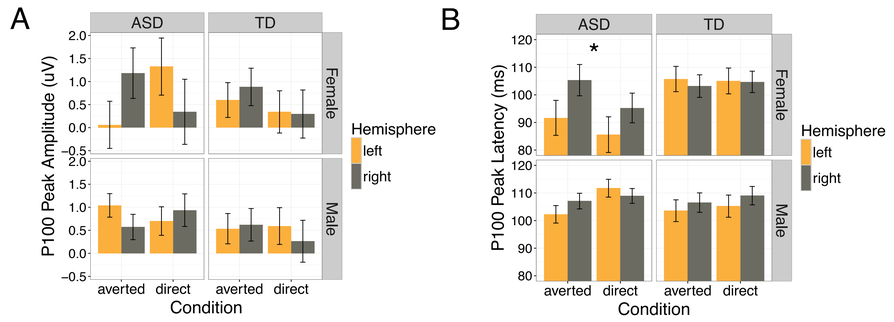

Figure 3. Differences in P100 amplitude (A) and latency (B) in response to faces displaying direct and averted gaze for males and females with ASD and TD (* = latency significantly faster than other sex by diagnosis subgroups, *p*<0.05).

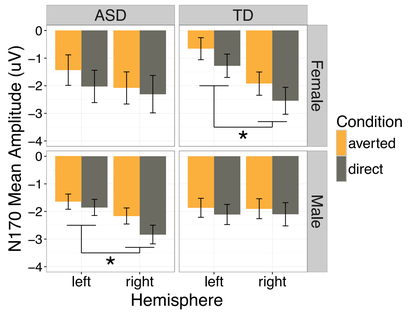

Figure 4. Differences in N170 amplitude in response to faces displaying direct and averted gaze for males and females with ASD and TD (* = significant difference between hemispheres, *p*<0.01).

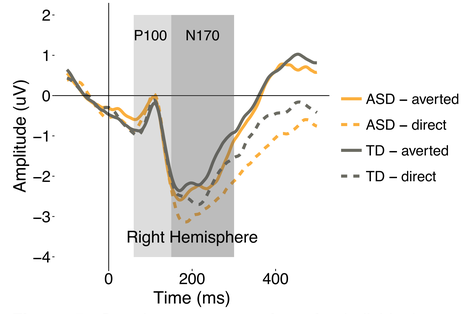

Figure 5. Grand average waveform for individuals with ASD and TD in response to direct and averted gaze.

P100

- Amplitude: There were no significant differences for P100 amplitude (*p*s>0.05) (Fig. 3A).
- Latency: There was a significant main effect of sex(F(1, 110)=6.17, p<0.05) and a significant interaction between sex and diagnosis (F(1, 110)=3.98, p<0.05), such that females with ASD had a faster P100 response to gaze than the other sex by diagnosis subgroups (*p*s<0.05). There was also a significant interaction between sex and condition (F(1, 110)=4.56, p<0.05), such that males had a significantly faster P100 response to averted gaze (p<0.05) while females trended towards a faster P100 response to direct gaze (Fig. 3B).

N170

- Amplitude: A significant interaction was found between sex, diagnosis, and hemisphere for N170 mean amplitude (F(1, 110)=5.73, p<0.05). Females with TD and males with ASD displayed significant right lateralization of the N170, indicated by a more negative amplitude for the right hemisphere N170 compared to left hemisphere N170 (*p*s<0.01), while left and right hemisphere N170s for females with ASD and males with TD did not differ significantly (Fig. 4). There was also a main effect of hemisphere, such that N170 exhibited more negative amplitude over the right hemisphere (F(1, 110)=14.98, p<0.01), and a main effect of condition, such that N170s had a more negative amplitude to direct than to averted gaze (F(1, 110)=5.42, p<0.05).
- Latency: There were no significant differences between groups or conditions for N170 latency (*p*s>0.05).

Results

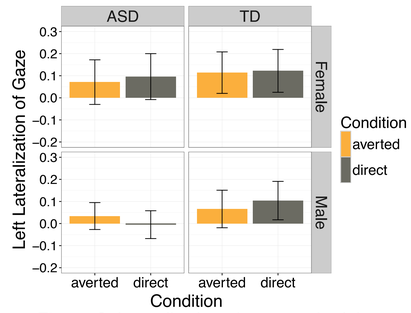

Figure 6. Lateralization of gaze to the left eye for males and females with ASD and TD.
Note: lateralization of gaze = [(time spent looking at left eye)-(time spent looking at right eye)/(time spent looking at both eyes)]

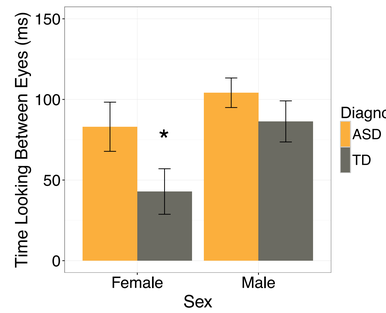

Figure 7. Amount of time spent looking between the eyes during each trial for males and females with ASD and TD.
(* = significantly different from other sex by diagnosis subgroups, *p*<0.05)

Eye-tracking

- There was a marginally significant interaction between sex, diagnosis, and condition for lateralization of gaze (F(1, 187)=2.73, p=0.10). Females with TD looked more to the left eye than the right eye of the stimulus face, while males with ASD did not show a preference (Fig. 6).
- There were significant main effects of sex (F(1,187)=6.14, p<0.05), and diagnosis (F(1,187)=4.95, p<0.05) for time spent looking between the eyes (Fig. 7). Females with TD spent significantly less time looking between the eyes than each of the three other sex by diagnosis subgroups (*p*s< 0.01).

Conclusions

- Males and females with ASD differed in terms of their neural and behavioral responses to faces displaying direct and averted gaze.
- Females with ASD had faster neural responses to gaze shift, and less lateralized response to gaze shift than males with ASD and females with TD. They also displayed stronger gaze lateralization patterns, in line with typically developing peers, than males with ASD.
- Sex-specific brain activity and looking patterns in individuals with ASD highlight the importance of considering sex as a variable in understanding ASD and suggest distinct mechanisms underlying social perception in females with ASD.
- Future work will examine correlations between the neural responses to direct and averted eye contact and other clinical measures of social responsiveness to examine potential sex differences in these relationships.

Funding sources: NIMH R01 MH100173 (McPartland), CTSA Grant Number UL1 RR024139 (McPartland), NIMH K23 MH086785 (McPartland), NIMH R21 MH091309 (McPartland), Autism Speaks Translational Postdoctoral Fellowship (Naples), Waterloo Foundation 1167-1684 (McPartland), Patterson Trust 13-002909 (McPartland), NIMH R01 MH107426 (McPartland, Srihari), NIMH R01 MH100173-02S1 (McPartland).

References:

Naples, A., Rolison M., Foss-Feig, J. H., Chang S. A., Stavropoulos K. K., Winkelman T., Stinson K., Jarzabek E., Ellison K., McAllister T., McPartland, J. (2016, May). Attention and Brain Response during Simulated Social Interactions in ASD. Poster presented at the International Meeting for Autism Research, Baltimore, MD.

Naples, A. J., Wu, J., Mayes, L. C., & McPartland, J. C. (2017). Event-Related Potentials Index Neural Response to Eye Contact. *Biological Psychology*.

Coffman, M. C., Anderson, L. C., Naples, A. J., & McPartland, J. C. (2015). Sex differences in social perception in children with ASD. *Journal of autism and developmental* disorders, 45(2), 589-599.