Dissociating Neural Response to Gaze Cues in ASD and Schizophrenia using Simulated Face-to-Face Interaction

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Background

Deficits in maintaining and interpreting social gaze are hallmark features of autism spectrum disorder (ASD). Individuals with ASD show reduced attention to direct gaze, attenuated sensitivity to gaze changes, and reduced use of gaze cues to facilitate facial communication. Atypical gaze processing is not unique to ASD and is evident in other disorders, including schizophrenia (SCZ). It is unknown whether specific abnormalities in gaze processing differ by diagnostic category, or whether they are general indicators of social dysfunction across neurodevelopmental disorders.

The N170 is a negative-going event-related potential (ERP) that is recorded over occipitotemporal scalp and indexes the earliest stages of face processing. It is sensitive to point of gaze on the face and is atypical in both ASD and SCZ. The P1 is an earlier, positive-going ERP that indexes preferential attention to low-level visual features of stimuli. Previous studies of ERP response to gaze-related cues are limited by their use of static faces, which have questionable ecological validity. This study utilizes novel methods, integrating eye-tracking (ET) and electrophysiology (EEG) to study social behavior and brain function during simulated face-to-face interactions in individuals with ASD, SCZ, and typical development (TD).

Objective: This study aimed to: (i) evaluate P1 and N170 responses to direct and averted gaze in adults with ASD, SCZ, and TD to determine between-group differences in neural processes associated with face decoding and (ii) examine transdiagnostic associations between neural response and social difficulties.

Method

Participant Demographics

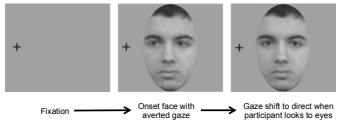
	N	Sex	Age (SD)	FSIQ (SD)
ASD	13	12M	22.96 (4.32)	101.92 (17.69)
SCZ	14	13M	30.45 (8.57)	96.07 (11.99)
TD	15	12M	26.92 (7.33)	109.67 (22.28)

*groups matched on sex and FSIQ

Experimental Paradigm:

- Participants were presented with 80 distinct photorealistic, animated faces matched for low-level visual features.
- Contingent upon participants' fixating on the face, stimuli responded by shifting eye gaze (either from direct to averted or averted to direct).

Fig. 1. Trial Structure. After participants fixated on a crosshair for ~300ms (panel 1), a face with either direct or averted gaze was presented (panel 2). After the participant looked to the face for at least 500ms, a second face with shifted gaze (panel 3) was presented for 600ms. The inter-trial interval ranged from 200-1200ms.



Clinical Measures:

To measure social and perceptual difficulties, participants completed:

- ***ASD diagnostic assessment:*** Autism Diagnostic Observation Schedule
- ***SCZ diagnostic assessment:*** Positive and Negative Syndrome Scale
- ***ASD self-report measures:*** Social Responsiveness Scale; Broad Autism Phenotype Questionnaire; Autism-Spectrum Quotient
- ***SCZ self-report measure:*** Schizotypal Personality Questionnaire
- ***Behavioral assessments:*** Benton Facial Recognition Test; Reading the Mind in the Eyes Test

Method

EEG and ET Data Acquisition and Collection:

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

ERP Preprocessing and Analysis:

- Data were filtered from 0.1-100 Hz. ICA was performed to remove ocular artifact, then data were segmented from -100ms to 600ms, artifact detected, referenced to average reference, and baseline corrected.
- P1 and N170 were extracted from electrodes over right occipitotemporal scalp from 70-120ms and 120-200ms, respectively. Peak amplitude and latencies were then included as dependent variables in repeated measures ANOVAs (with group as the independent variable), with follow-up one-way ANOVAs and t-tests to clarify effects.

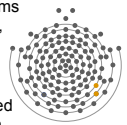
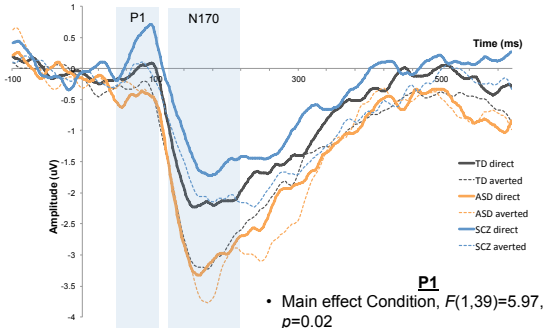
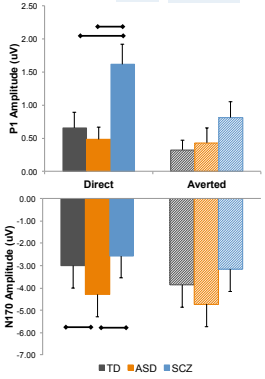


Fig. 2. Recording sites. P1 and N170 were extracted from the average of two electrodes over the right hemisphere.

Preliminary Results





P1

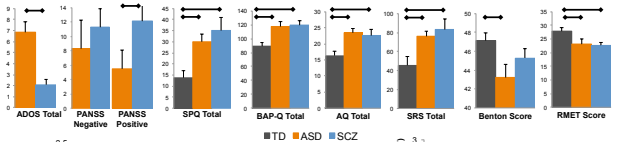
- Main effect Condition, $F(1,39)=5.97$, $p=0.02$
- Main effect Group, $F(2,39)=5.49$, $p=0.008$
  - In response to direct gaze, P1 amplitude did not differ between ASD and TD ($p=0.64$). However, individuals with SCZ exhibited enhanced P1 response relative to both ASD and TD groups ($ps<0.01$).
- No group differences in P1 latency

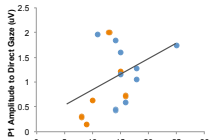
N170

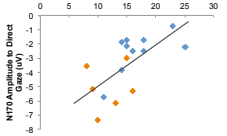
- Main effect Condition, $F(1,39)=5.9$, $p=0.009$
  - Enhanced amplitude to averted vs. direct gaze across all groups
- Across conditions, individuals with ASD showed greater N170 amplitude relative to both SCZ ($p=0.014$) and TD ($p=0.06$), whereas individuals with SCZ and TD did not differ from each other ($p=0.49$).
- No group differences in N170 latency

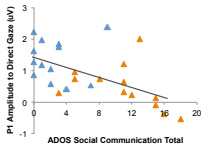
Preliminary Results

- ADOS scores differentiated ASD from SCZ, though 3 of 14 participants with SCZ met criteria for ASD on the ADOS-2.
- Individuals with SCZ and ASD did not differ on any of the self-report measures of social functioning, autistic symptomatology, or schizophrenia traits.
- Both individuals with ASD and SCZ had difficulty with behavioral assessments of emotion recognition, but only those with ASD had difficulties with face recognition.









Correlations

- Across clinical groups, positive symptoms of SCZ were associated with greater P1 ($r=0.577$, $p=0.019$) and attenuated N170 responses to direct gaze ($r=0.642$, $p=0.007$)
- Higher levels of ASD symptoms were associated with attenuated P1 response to direct gaze ($r=-0.344$, $p=0.079$)

Conclusions

In line with a dimensional approach to understanding neurodevelopmental disorders, preliminary results of this study suggest that neural response to gaze-contingent shifts in eye gaze is a reliable marker of social and perceptual dysfunction across individuals with ASD and SCZ.

- Greater P1 response is related to higher levels of positive symptoms of SCZ and lower levels of ASD symptoms. Whereas early sensory responses are intact in ASD, adults with SCZ show amplified P1 response relative to both TD and ASD.
- More robust N170 response to direct gaze is associated with fewer positive symptoms of SCZ. Whereas neural response associated with face processing in SCZ is similar to that in TD, individuals with ASD show enhanced N170 amplitude relative to both TD and SCZ.

In contrast to ERP markers, clinical measures of ASD and SCZ symptomatology are variably effective in differentiating the two clinical populations. Specifically, though self-report measures are reliable in differentiating clinical populations from TD, they are ineffective in differentiating between diagnostic categories.

These preliminary findings suggest that, across multiple neurodevelopmental disorders, neural indices of social processing can reveal differences in gaze processing related to clinically-relevant social and perceptual differences that behavioral measures of overt symptomatology do not capture.

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