Dissociating Social Functioning in ASD and Schizophrenia using Clinical Assessment and Neural Response to Gaze Cues

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Background

Social difficulties, including deficits in maintaining and interpreting social gaze and in recognizing faces and emotions, are hallmark features of autism spectrum disorder (ASD). Atypical social functioning and gaze processing are not, however, unique to ASD. Both are also affected in schizophrenia (SZ), a disorder with genetic, neurobiological, and phenotypic commonalities with ASD. This study utilized novel methods, integrating eye-tracking and electrophysiology (EEG), to study social behavior and brain function during simulated face-to-face interactions in individuals with ASD and SZ.

Specifically, we evaluated N170 and P300 response to direct and averted gaze in adults with ASD, SZ, and typical development (TD) to determine between-group differences as well as transdiagnostic patterns in neural processes associated with face decoding. In parallel, we evaluated social functioning with a battery of diagnostic, clinical, and neurocognitive assessments. In this way, we evaluated whether specific abnormalities in gaze processing differed by diagnostic category or were general indicators of social dysfunction across neurodevelopmental disorders.

Objective: To evaluate relations among social function and dysfunction and neural markers of gaze processing during simulated face-to-face interactions in individuals with ASD, SZ, and TD controls.

Method

Participant Demographics

	N	Sex*	Age (SD)	FSIQ* (SD)
ASD	17	13M	21.89 (3.81)	102.56 (19.29)
SZ	14	13M	28.81 (8.30)	95.79 (11.56)
TD	13	9M	28.80 (7.69)	105.42 (20.47)

*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).

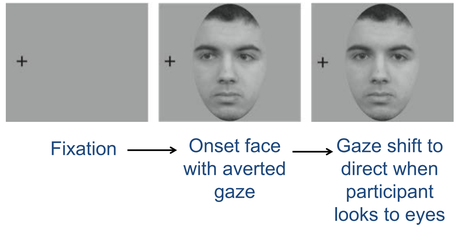

Figure 1. Trial Structure. After participants fixated on a crosshair for ~300ms (panel 1), a face with either direct or averted gaze was presented (panel 2). After the participant looked to the face for ≥500ms, a second face with shifted gaze (panel 3) was presented for 600ms. Inter-trial interval ranged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

Clinical Measures:

To measure social and perceptual difficulties, participants completed:

- ***ASD diagnostic assessment:*** Autism Diagnostic Observation Schedule
- ***SZ diagnostic assessment:*** Structured Clinical Interview for DSM Diagnosis; Positive and Negative Syndrome Scale
- ***ASD self-report measures:*** Social Responsiveness Scale; Broad Autism Phenotype Questionnaire; Autism-Spectrum Quotient
- ***SZ self-report measure:*** Schizotypal Personality Questionnaire
- ***Behavioral assessments:*** Benton Facial Recognition 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. Data were then rereferenced to average reference, segmented from -100ms to 400ms relative to shift in stimulus gaze, baseline corrected, and artifact detected.
- N170 was extracted from right occipitotemporal electrodes 130-250ms. P300 was extracted over fronto-central scalp from 250-400ms. Mean amplitude (N170, P300) and latency (N170) were included as within-subject variables in repeated measures ANOVAs (with group as the between-subject factor), with follow-up one-way ANOVAs and t-tests to clarify effects.

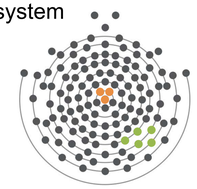

Figure 2. Recording sites. Fronto-central P3 and right occipito-temporal N170 were extracted from electrode clusters depicted.

Results

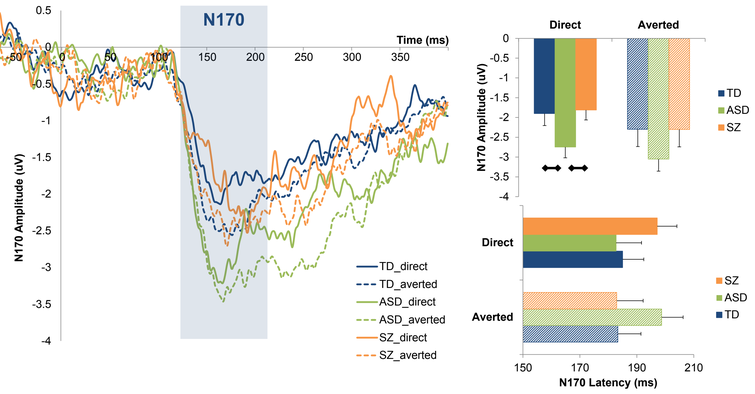

Figure 3. N170 response to direct and averted gaze in ASD, SZ, and TD. Main effect of Condition, $F(1,41)=7.79$, $p < 0.01$, indicating enhanced amplitude to averted vs. direct gaze in all groups. Particularly with gaze shift from averted to direct, individuals with ASD showed greater N170 amplitude relative to both SZ ($p = 0.019$) and TD ($p = 0.048$), whereas individuals with SZ and TD did not differ from each other ($p = 0.83$). There was a significant interaction with N170 latency, $F(1,41)=3.38$, $p = 0.04$, wherein latency to direct vs. averted gaze was equivalent in TD, delayed for direct in SZ, and delayed for averted in ASD.

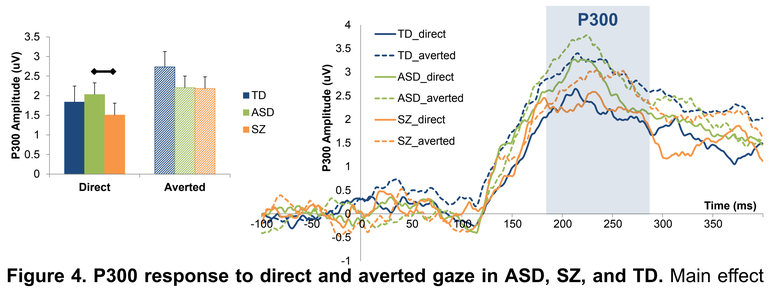

Figure 4. P300 response to direct and averted gaze in ASD, SZ, and TD. Main effect of Condition, $F(1,41)=12.27$, $p < 0.01$, wherein all groups showed enhanced amplitude to averted vs. direct gaze. For shift from averted to direct gaze, individuals with ASD showed increased P300 amplitude relative to SZ ($p = 0.043$), but no differences between ASD and TD or between SZ and TD were observed.

Results

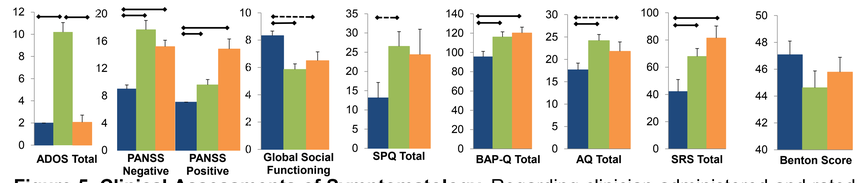

Figure 5. Clinical Assessments of Symptomatology. Regarding clinician administered and rated measures, ADOS scores and the PANSS positive symptoms scale differentiated ASD from SZ; however ASD and SZ patients were not well discriminated by the PANSS negative symptoms scale or the Global Social Functioning Rating. When administered self-report measures of ASD and SZ symptomatology, individuals with SZ and ASD did not differ from each other and both clinical groups endorsed elevated symptom levels relative to controls across measures.

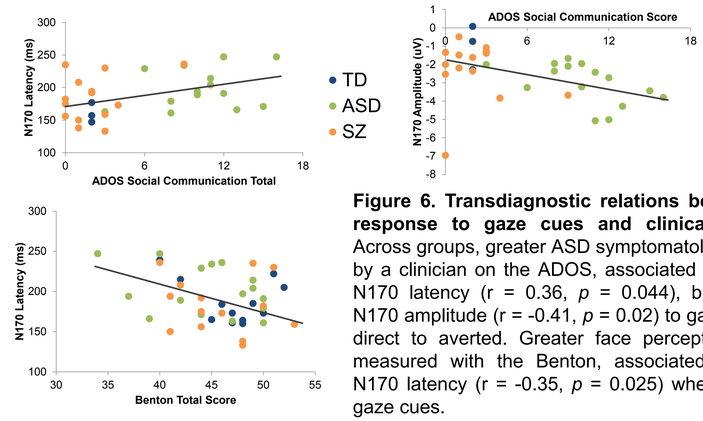

Figure 6. Transdiagnostic relations between ERP response to gaze cues and clinical variables. Across groups, greater ASD symptomatology, as rated by a clinician on the ADOS, associated with delayed N170 latency ($r = 0.36$, $p = 0.044$), but enhanced N170 amplitude ($r = -0.41$, $p = 0.02$) to gaze shift from direct to averted. Greater face perception skill, as measured with the Benton, associated with faster N170 latency ($r = -0.35$, $p = 0.025$) when perceiving gaze cues.

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 dysfunction across individuals with ASD and SZ.

- N170 latency is related to social function and dysfunction. Across groups, those with better face perception skills during clinical assessment had faster N170 latencies, whereas those with greater ASD symptomatology had more delayed N170 to gaze cues.
- Whereas previous literature has suggested attenuated N170 response in ASD, across groups ASD symptomatology was also associated with a larger N170 to gaze cues in the context of our novel, gaze-contingent face perception paradigm.

In contrast to ERP markers, clinical measures of ASD and SZ 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 difficulties that behavioral measures of overt symptomatology do not capture.

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