Neural Response to Eye Gaze Differentiates ASD Diagnostic Status Among Adults Meeting ADOS-2 Criteria

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Background

- Individuals with autism spectrum disorder (ASD) process social information differently from typically developing (TD) individuals.
- These differences include significantly longer latencies of the N170 event-related potential, a marker of face-sensitive processing (McPartland et al., 2004).
- The N170 has not yet been characterized in individuals who were clinically referred for disorders involving social communication (such as ASD and schizophrenia (SCZ)) and received non-ASD diagnoses compared to those receiving ASD diagnoses.
- The objective was to examine the relationship between N170 response to faces and social communication symptoms in a clinically heterogeneous population of individuals with TD, ASD, SCZ, and other diagnoses.

Method

Participants

Group	n (female)	ASD	SCZ	Other	TD	Mean Age	Mean IQ
		Final Diagnosis (DX)					
Met ADOS, ASD DX	20 (4)	20	0	0	0	24.2	103
Met ADOS, Non-ASD DX	11 (2)	0	10	1	0	22.6	98
Did not meet on ADOS, No ASD DX	52 (22)	0	11	10	31	25.9	111

- Groups were matched on age and nonverbal IQ ($ps>0.05$) but did differ significantly on full scale IQ ($p<0.05$).
- The "Other" diagnostic category includes individuals who received primary diagnoses of anxiety disorders ($n=4$), depressive disorders ($n=4$), and obsessive-compulsive and related disorders ($n=3$).

Clinical characterization

- All participants received an ADOS-2 Module 4. "Met ADOS" is used to describe individuals who met 'autism spectrum' or 'autism' criteria on the original algorithm (Lord et al., 1999).
- Participants also received the Mini-International Neuropsychiatric Interview (MINI), and selected portions of the Structured Clinical Interview for DSM-IV to determine diagnosis.
- Eight participants met criteria for current substance abuse or substance dependence on the MINI, but results did not change when these participants were excluded.

Event-related potential analysis

- EEG was recorded at 250 Hz with a 128-channel Hydrocel Geodesic Sensor net.
- N170 (120-270ms) was extracted from electrodes over left and right occipitotemporal regions (see Fig. 1). Data were filtered at 0.1 to 30Hz and segmented from -100 to 500ms relative to presentation of the face or house.
- Peak amplitude and latency were analyzed for response to faces and houses in repeated measures ANOVAs (with diagnostic group as a between-subject factor and stimulus type and hemisphere as within-subject factors). Follow up t-tests were used to determine between-group differences.
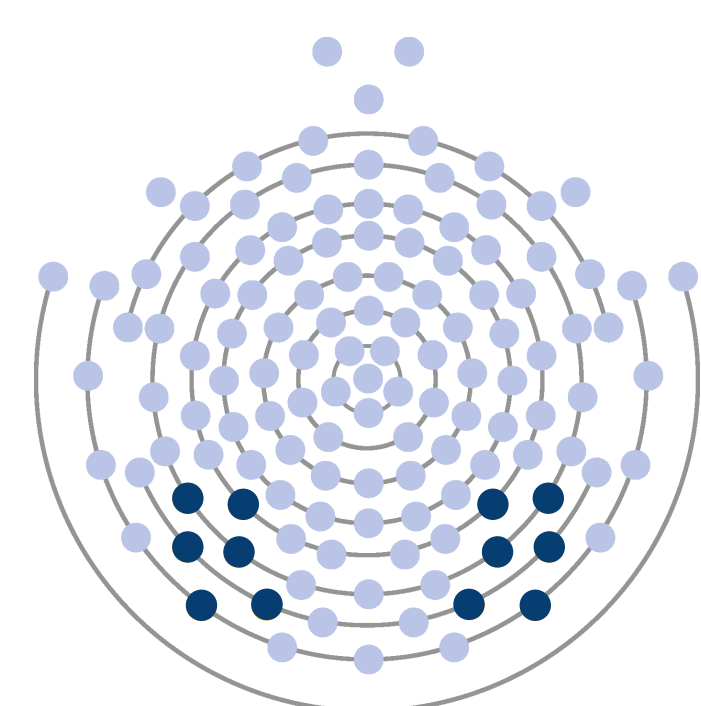
Figure 1. Selection of electrodes for analysis.
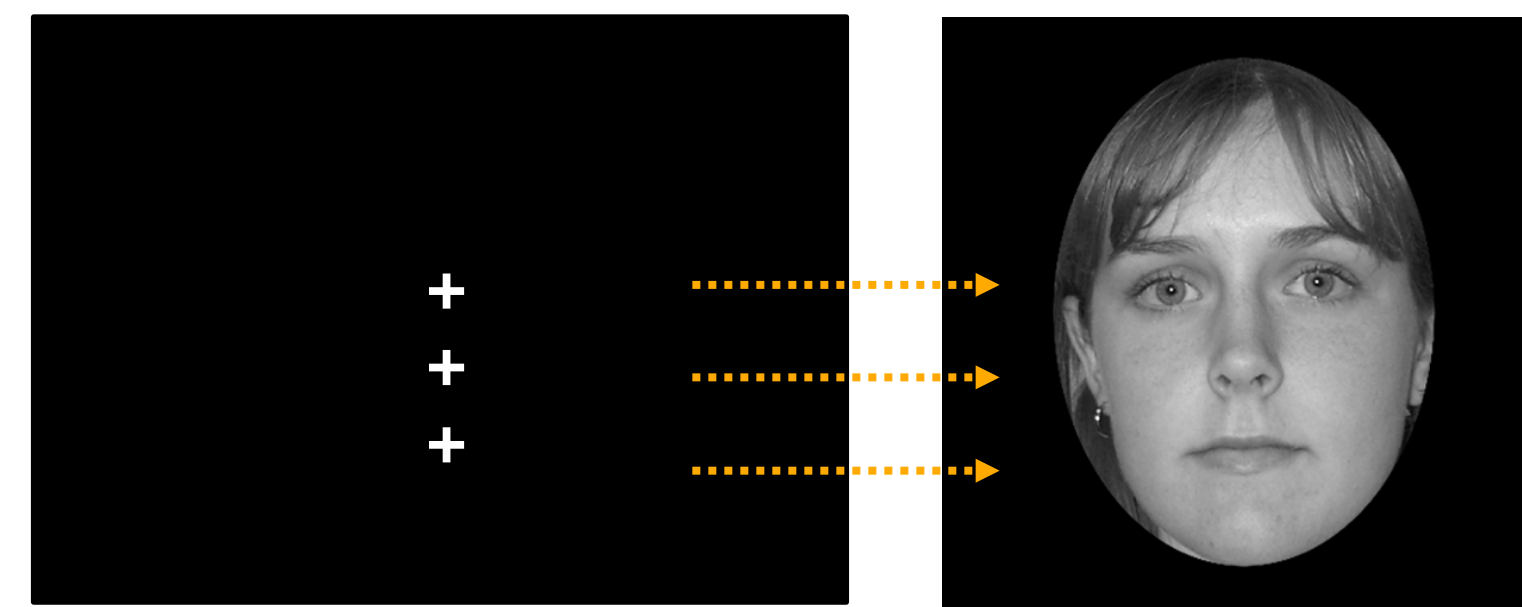
Experimental Paradigm

Figure 2. Participants viewed black-and-white faces and houses preceded by a single crosshair in either the upper, middle, or lower portion of the screen. Gaze was thus directed to the eyes, nose, or mouth region of the face, and upper, middle, or lower region of the house. For analysis of the brain response to houses, all viewing positions were collapsed.
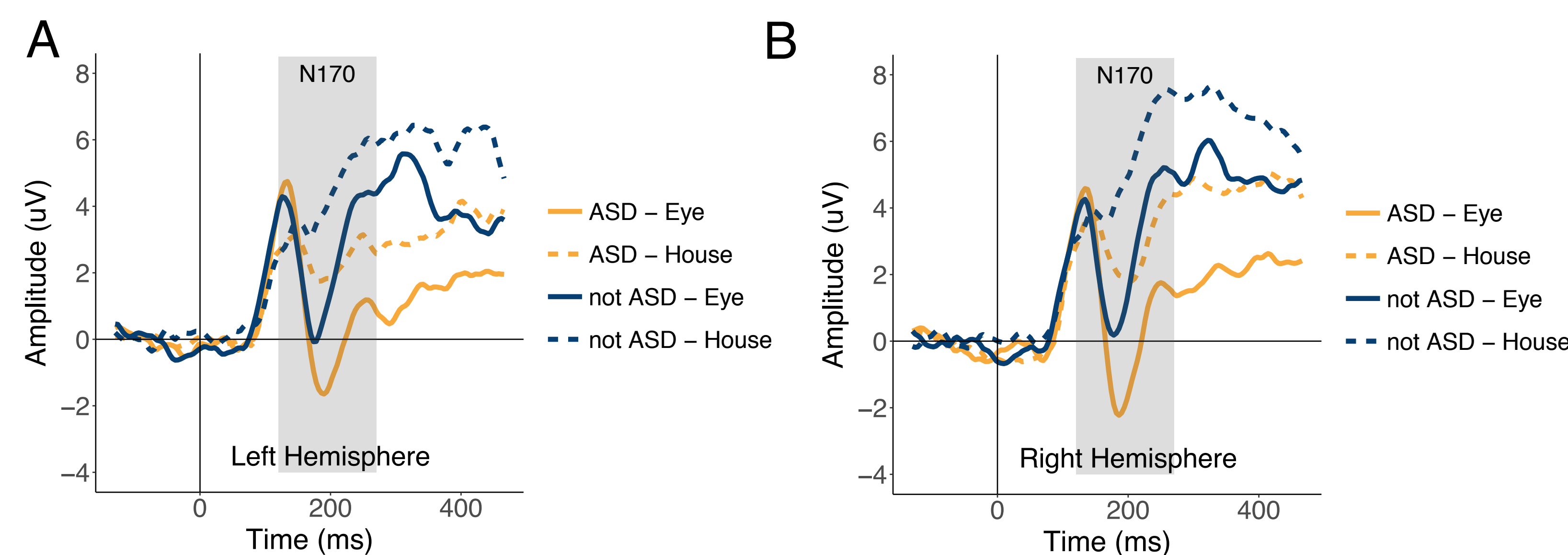
Results

Figure 3. Grand average waveforms of (A) left hemisphere and (B) right hemisphere N170 response to eyes and houses. All individuals included in waveforms met criteria on the ADOS for autism or autism spectrum, and received either an ASD diagnosis or another diagnosis.
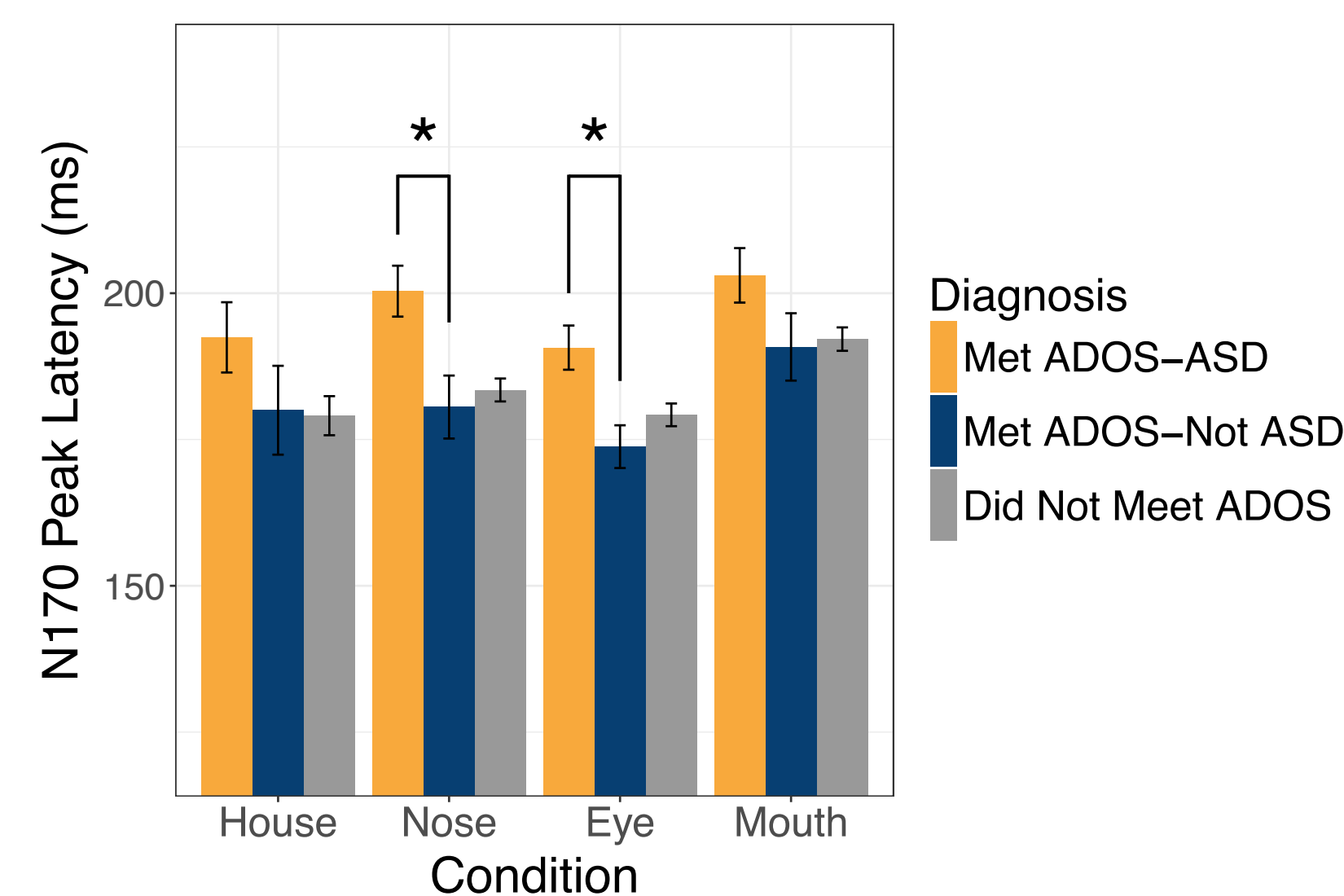

Figure 4. Differences in N170 latency for individuals who met and did not meet ADOS criteria. * = different from both groups that did not receive an ASD DX ($p<0.05$).
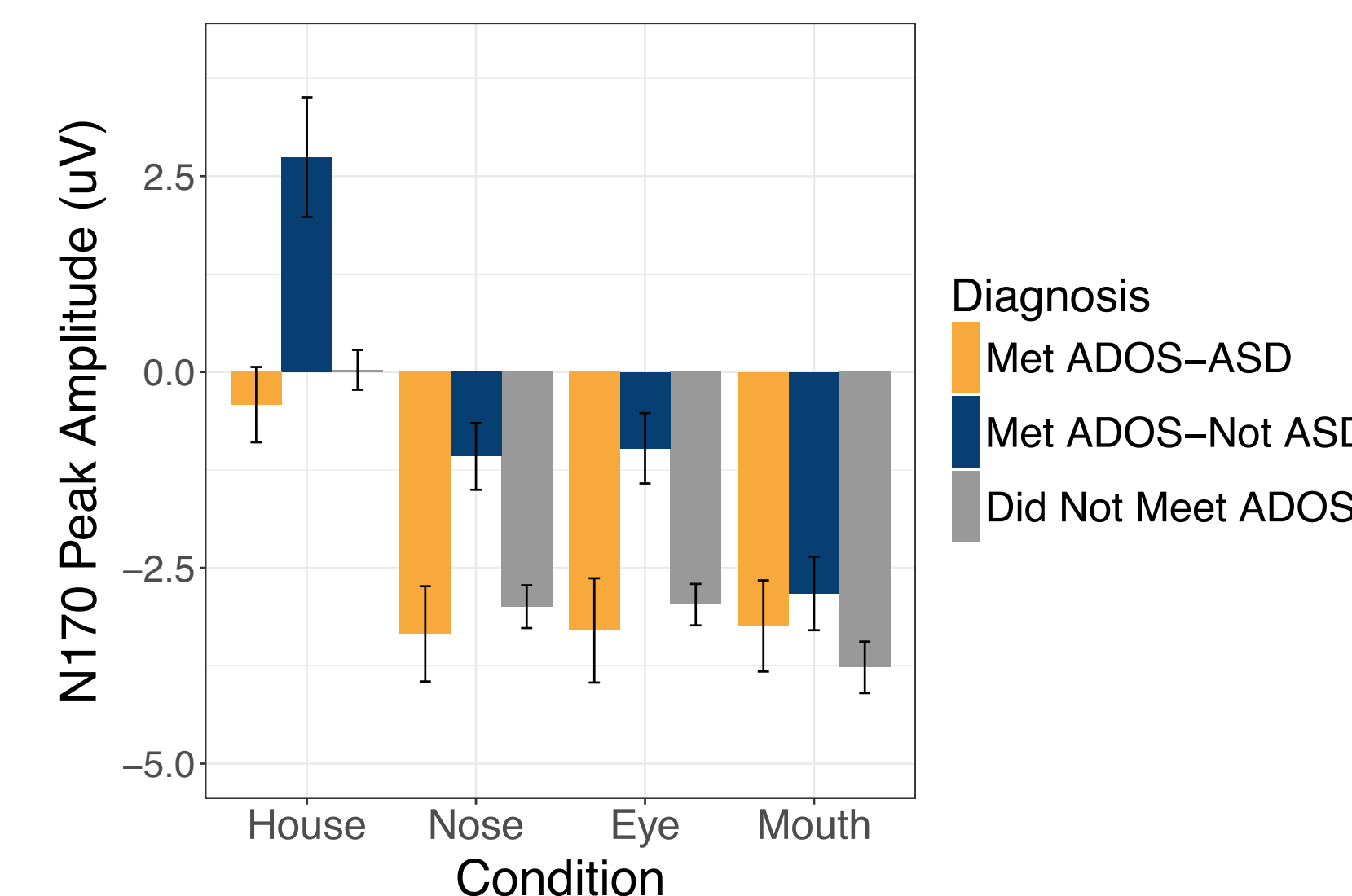
Figure 5. Differences in N170 amplitude in response to faces and houses for individuals who met and did not meet criteria on the ADOS.

N170

- **Latency:** There was a significant main effect of stimulus ($F(3, 240)=6.90$, $p<0.01$), such that longer N170 latencies were elicited by mouths relative to other parts of the face. There was also a significant main effect of diagnostic group ($F(2, 80)=4.74$, $p<0.05$). Individuals who met ADOS criteria for autism and received an ASD DX had significantly slower N170 latencies than individuals who met ADOS criteria for autism and received a non-ASD DX ($p<0.05$), and individuals who did not meet ADOS criteria for autism ($p<0.05$). These latency differences were specific to the eye and nose conditions ($ps<0.05$).
- **Amplitude:** There was a significant main effect of stimulus ($F(3, 240)=67.73$, $p<0.01$), such that more negative N170 amplitudes were elicited by faces than houses. There was a marginal main effect of diagnostic group ($F(2, 80)=2.96$, $p<0.10$), such that individuals who met ADOS criteria for autism but received a non-ASD DX had less negative amplitudes than individuals who received an ASD DX or individuals who did not meet ADOS criteria.
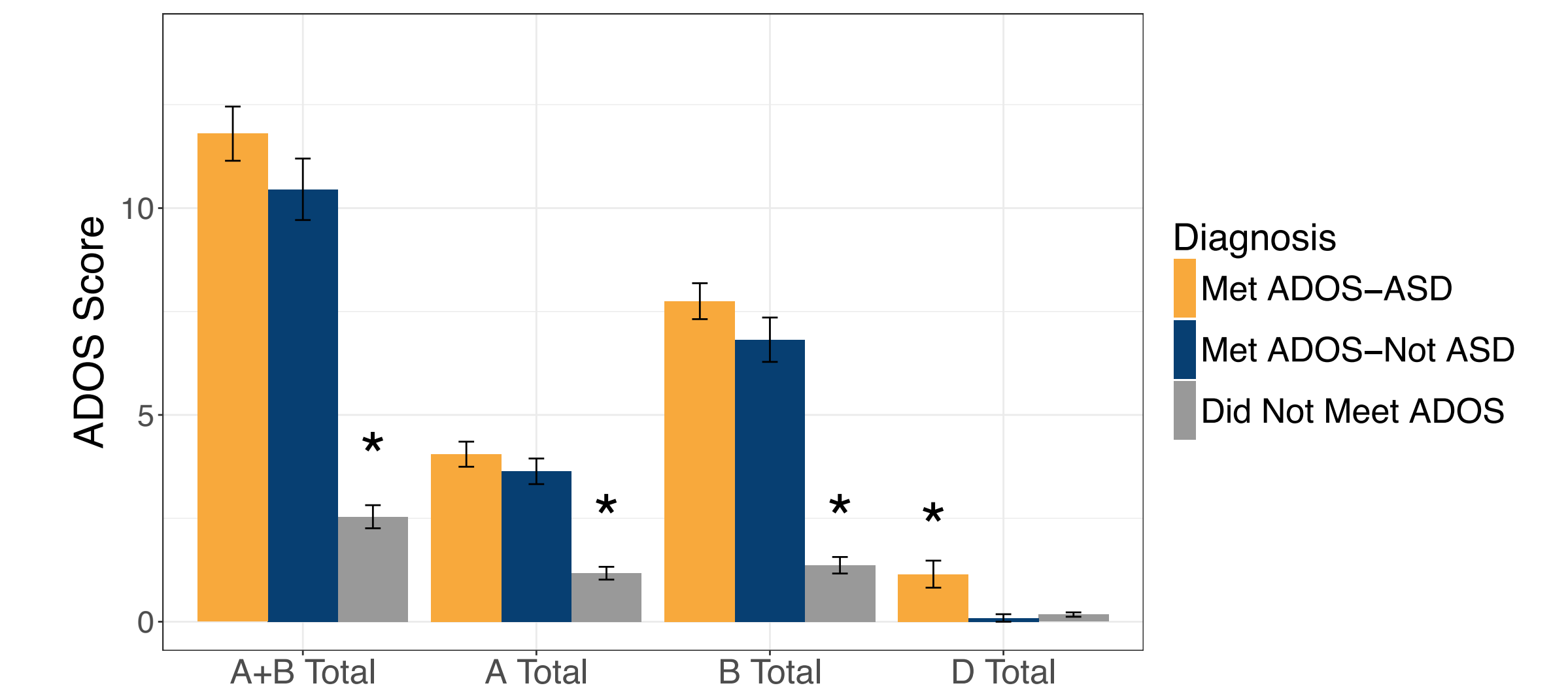
Results

Figure 6. ADOS total scores for participants that met and did not meet ADOS criteria. A+B Total = Communication + Social Interaction Total, A Total = Communication Total, B Total = Social Interaction Total, D Total = Stereotyped Behaviors and Restricted Interests Total. * = different from other two groups ($p<0.01$).

ADOS

- For communication total, social interaction total, and communication + social interaction total, participants who met on the ADOS and received an ASD DX did not differ from participants who met on the ADOS and received a non-ASD DX. Both groups that met on the ADOS differed from individuals that did not meet ($ps<0.01$).
- For stereotyped behaviors and restricted interests, participants who received an ASD DX differed from participants who did not receive an ASD DX ($ps<0.01$).

Conclusions

- Among individuals who met ADOS criteria, N170 latency to the eyes and nose of the face distinguished those who received an ASD DX from those who received a non-ASD DX.
- Brain-based measures of social functioning provide complementary information to commonly used clinical assessments such as the ADOS.
- As the current sample was comprised largely of individuals with ASD and SCZ, future research will examine N170 latency to faces in other diagnoses such as anxiety to confirm the specificity of this biomarker to ASD.

References:
McPartland, J., Dawson, G., Webb, S. J., Panagiotides, H., & Carver, L. J. (2004). Event-related brain potentials reveal anomalies in temporal processing of faces in autism spectrum disorder. *Journal of Child Psychology and Psychiatry, 45*(7), 1235-1245.
Lord, C., Rutter, M., DiLavore, P. S., & Risi, S. (1999). *Autism Diagnostic Observation Schedule (ADOS)*. Los Angeles, CA: Western Psychological Services.

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