

# Externalizing behaviors in autism spectrum disorder modulate neural responses during a novel interactive social paradigm

M. Zhou<sup>1</sup>, A. Naples<sup>1</sup>, T. Winkelman<sup>1</sup>, M. R. Altschuler<sup>1</sup>, D. Stahl<sup>1</sup>, E. Jarzabek<sup>1</sup>, J. Wolf<sup>1</sup> and J. McPartland<sup>1</sup>  
(1) Child Study Center, Yale University School of Medicine, New Haven, CT

## Background

- Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by (1) social and communication deficits and (2) restricted, repetitive behaviors
- Gaze direction is an important part of nonverbal social communication
  - Direct: analysis of faces; ↑ approach-oriented emotions (anger, joy)
  - Averted: orientation of spatial attention, shared attention; ↑ avoidance-oriented emotions (fear, sadness)
- EEG neural responses to gaze direction is atypical in both ASD and disorders associated with externalizing behavior (e.g., conduct disorder)
  - May be related to aberrant development of attention
- However, there have been few investigations into the potential influence of externalizing behaviors on neural responses to social information in ASD

Objective of study: to examine whether externalizing behavior modulates EEG derived event-related potentials (ERPs; N170, P100) to social information in individuals with ASD compared to typically developing (TD) controls

## Method

Sample characteristics:

	N	Sex	Age (SD)	IQ (SD)
ASD	40	6F, 34M	14.3 (2.8)	109.5 (21.6)
TD	41	19F, 22M	13.2 (2.6)	109.5 (12.6)

Questionnaire

- Externalizing symptomatology was measured using parent-report on the Child Behavior Checklist (CBCL) Externalizing scale

EEG Data Acquisition and Collection

- EEG was recorded at 1000 Hz with a 128-channel Hydrocel Geodesic Sensor net.

Trial Structure/Experimental Paradigm (Figure 1)

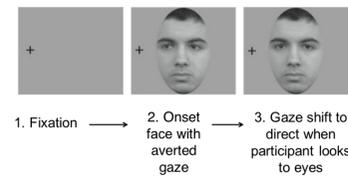
- EEG was recorded while the participant underwent a gaze-contingent viewing paradigm. Participants viewed 112 faces that were matched on low-level visual features. The faces responded to the participant's gaze by looking at (direct gaze) or away from (averted gaze) the participant.

Event-related potential (ERP) analysis

- The amplitudes and latencies of the N170 (150-300ms), a face sensitive ERP and P100 (60-160ms), an ERP associated with early sensory processing were extracted from electrodes over left and right occipitotemporal regions (see Figure 2)
- Data were filtered at 0.1 to 30Hz and segmented from 100 to 500ms relative to shift in stimulus gaze.

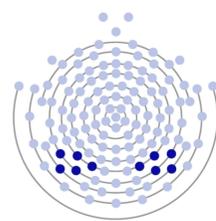
Statistics

- Group differences in externalizing behavior were examined using t-tests. Effects of diagnosis and gaze on ERPs were examined with two-way ANOVAs. Linear regression analyses were used to test whether externalizing behaviors significantly predicted neural responses.



**Figure 1: Trial Structure**

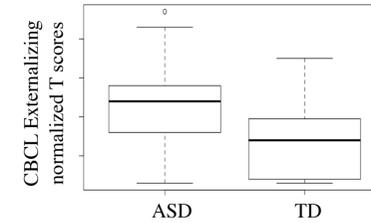
Participants first fixated on a crosshair for ~300ms (Panel 1). Then a face displaying either direct or averted gaze was presented (Panel 2). After the participant looked to the eyes of the face for ≥500 ms, the gaze shifted and remained onscreen for 600 ms (Panel 3).



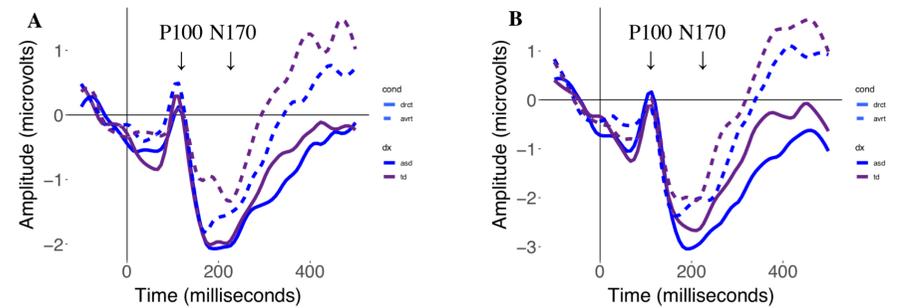
**Figure 2: Occipitotemporal electrodes**

## Results

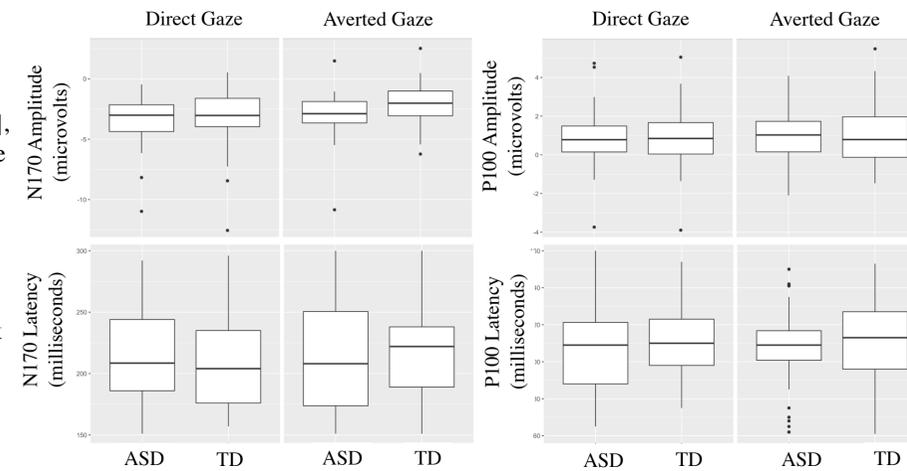
**Figure 3:** Participants with ASD exhibited significantly greater parent-reported externalizing maladaptive behavior than TD participants, as determined by the CBCL's Externalizing T-Scores [ $t(88)=3.56, p<0.001$ ].



**Figure 4:** N170 and P100 response to interactive gaze in the ASD and TD group over the (A) left hemisphere and (B) right hemisphere



**Figure 5:** Analysis of N170 peak amplitude revealed that there was a significant main effect of gaze [left hemisphere,  $F(1,158)=4.48, p=0.04$ ], which showed that across groups the N170 was enhanced in direct gaze compared to averted gaze [ $t(160)=-2.11, p=0.04$ ] but no main effect of group and no interaction between group and gaze ( $p>0.05$ ). The analysis of N170 latency, P100 peak amplitude and latency revealed that there were no main effects of group or gaze and no interaction between group and gaze ( $p>0.05$ ).

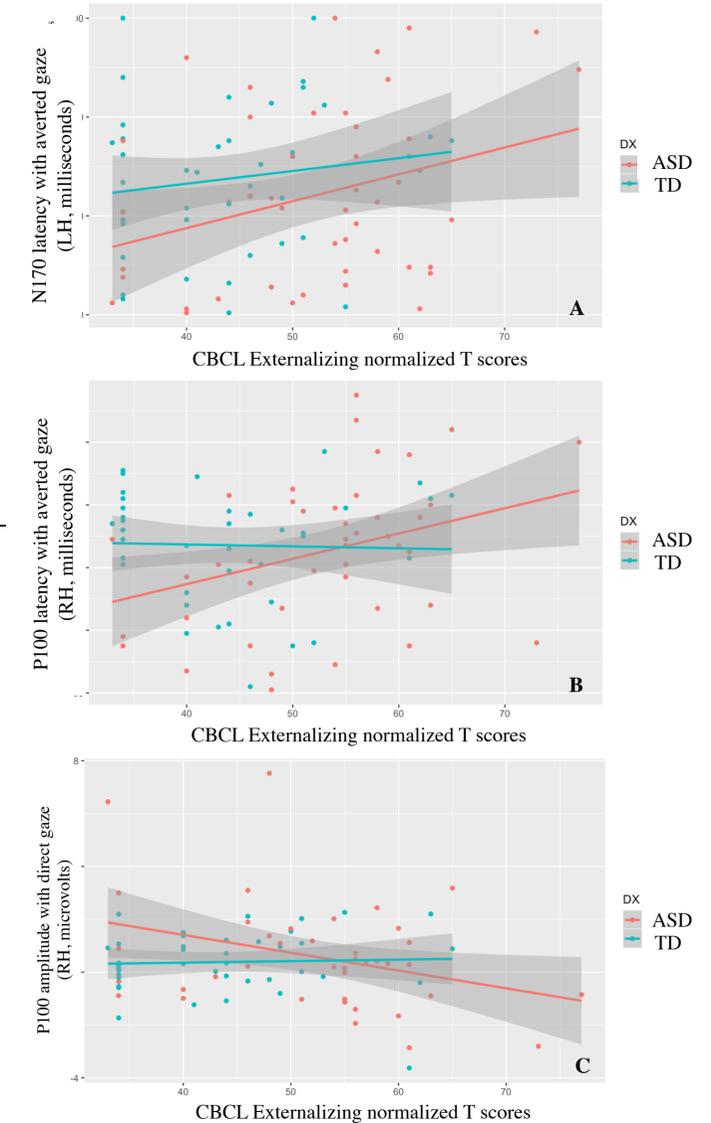


**Figure 6:** In ASD but not TD, externalizing maladaptive behaviors significantly predicted:

A. N170 latency with averted gaze [left hemisphere, ( $b=1.36, p=0.04$ ), ( $R^2=0.10, F(1,43)=4.53, p=0.04$ )]

B. P100 latency with averted gaze [right hemisphere, ( $b=0.81, p=0.02$ ), ( $R^2=0.13, F(1,43)=6.22, p=0.02$ )]

C. P100 amplitude with direct gaze [right hemisphere, ( $b=-0.07, p=0.01$ ), ( $R^2=0.11, F(1,39)=4.96, p=0.03$ )].



## References

- Adams, R. B., & Kleck, R. E. (2005). Effects of Direct and Averted Gaze on the Perception of Facially Communicated Emotion. *Emotion*, 5(1), 3-11. doi:10.1037/1528-3542.5.1.3
- Brislin SJ, Yancey JR, Perkins ER, et al. Callousness and affective face processing in adults: Behavioral and brain-potential indicators. *Personal Disord Theory, Res Treat*. 2018;9(2):122-132. doi:10.1037/per0000235
- Conty, L., N'Diaye, K., Tijus, C., & George, N. (2007). When eye creates the contact! ERP evidence for early dissociation between direct and averted gaze motion processing. *Neuropsychologia*, 45(13), 3024-3037. doi:10.1016/j.neuropsychologia.2007.05.017
- Coull J. Neural correlates of attention and arousal: insights from electrophysiology, functional neuroimaging and psychopharmacology. *Prog Neurobiol*. 1998;55(4):343-361. doi:10.1016/S0304-0082(98)00011-2
- Dodge, K. A., & Crick, N. R. (1990). Social Information-Processing Bases of Aggressive Behavior in Children. *Personality and Social Psychology Bulletin*, 16(1), 8-22. https://doi.org/10.1177/0146167290161002
- 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.
- Patrick CJ, Bernat EM, Malone SM, Iacono WG, Krueger RF, McGue M. P300 amplitude as an indicator of externalizing in adolescent males. *Psychophysiology*. 2006;43(1):84-92. doi:10.1111/j.1469-8986.2006.00376.x

## Acknowledgments

Work was supported by NIMH R01 MH100173 (McPartland), NIMH R21 MH091309 (McPartland), CTSA Grant Number UL1 RR024139 (McPartland), Autism Speaks Translational Postdoctoral Fellowship (Naples), Waterloo Foundation 1167-1684 (McPartland) and Patterson Trust 13-002909 (McPartland)

## Conclusions

- Enhancement of the face-sensitive N170 to direct gaze across diagnostic groups suggest similar response to mutual gaze at initial stages of face perception
- Externalizing behaviors were associated with gaze perception in children with ASD but not TD
  - In children with ASD, more severe externalizing behaviors were associated with slowed visual and facial processing in an avoidance-oriented social context and with more impaired visual processing in an approach-oriented one
- These findings suggest that externalizing behavior may be useful in guiding strategies to stratify a heterogeneous ASD population to advance the objective of individualized, targeted therapies

