The Role of Anxiety in Looking Patterns Among Children with ASD: Results from the ABC-CT Feasibility Study

E. Hamo[1], A. Naples[1], B. Lewis[1], K. Chawarska[1], R. Bernier[2], S. Jeste[3], C.A. Nelson[4], G. Dawson[5], S.J. Webb[2], M. Murias[6], F. Shic[7], C. Sugar[3], J. McPartland[1]

(1)Child Study Center, Yale University School of Medicine, New Haven, CT, (2)Psychiatry and Behavioral Sciences, University of Washington, Seattle, WA, (3)University of California, Los Angeles, Los Angeles, CA, (4)Boston Children's Hospital, Boston, MA, (5)Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, NC, (6)Duke University, Durham, NC, (7)Center for Child Health, Behavior and Development, Seattle Children's Research Institute, Seattle, WA

Background

- Previous literature reports high rates of comorbid anxiety symptoms in individuals with autism spectrum disorder (ASD).
- Between 39.6%-84.1% of those with ASD have at least one comorbid anxiety disorder [1,2].
- It is important to understand how anxiety symptomology impacts responses to social stimuli, and whether this effect is different in clinical populations.
- Exploring these relationships may help explain the influence of anxiety symptomology on ASD symptoms and inform research and intervention.

Objective: To examine the relationship between anxiety symptomology and attention to social stimuli among children with and without ASD.

Methods

ABC-CT Study Details:
- Methodologically rigorous, multi-site evaluation of potential biomarkers in a large sample of children with and without ASD.
- Longitudinal study evaluating children across 6 months, including clinical assessment, video-tracking during play, electroencephalogram (EEG), and eye-tracking.

Inclusion/Exclusion Criteria:
- ASD Group: Age 4-11; met criteria for ASD based on ADOS-2, ADI-R, and DSM-5; IQ 50-150; stable medication for 8 weeks; no sensory or motor impairments; no epilepsy; no genetic or neurological conditions.
- Typically Developing (TD) Group: Age 4-11; IQ 80-150; stable medication for 8 weeks; no sibling with ASD; no sensory or motor impairments; no epilepsy; no genetic or neurological conditions; no clinically significant score on the *Child and Adolescent Symptom Inventory, 5th Edition* (CASI-5).

Participant Demographics:

	n (Female)	Age (SD)	IQ (SD)
TD	23 (8)	6.66 (1.95)	115.13 (8.96)
ASD	22 (5)	8.01 (2.23)	93.39 (18.26)

**Diagnostic groups did not differ on sex, [$\chi^2(1,46)$=.94, p=.33]. However, diagnostic groups significantly differed on full scale IQs as measured by the *Differential Ability Scales, Second Edition* (DAS-II), [$t(44)$=5.13, p<.01]. Age was significantly different between groups, [$t(44)$=-2.19, p=.03].

Measures:
- *Behavior Assessment System for Children, 3rd Edition* (BASC-3)
  - Parent-reported evaluation of behaviors and self-perceptions of their children.
  - Anxiety *T*-score
- *Child and Adolescent Symptom Inventory, 5th Edition* (CASI-5)
  - Parent-reported behavior rating scale for DSM-5 emotional and behavioral disorders in children.
  - Generalized Anxiety *T*-score and Social Anxiety *T*-score

Methods, cont.

Eye-tracking Acquisition:
- Binocular eye-tracking data were collected at 500 Hz using SR Eyelink 1000 Plus.

Eye-tracking Experiment:
- Children were presented with six trials of five images equidistant from the center of the screen (Figure 1) [3,4].
- Average looking time at the pre-defined regions (i.e. looking time at face vs. nonfaces) were calculated for valid gaze samples.

Figure 1. Trial included face, phone, bird, car, scrambled face and were matched for color and luminosity.

Statistical Analyses:
- Group differences on BASC-3 Anxiety *T*-score were examined using *t*-tests.
- Relationships between anxiety, social anxiety, and generalized anxiety symptoms and average looking time at the faces were examined with regression analyses. IQ was held as a constant in the regression model.

Results

- BASC-3 Anxiety *T*-scores were significantly higher in the ASD group than the TD group [$t(45)$=-2.76, p=.01] (Figure 2).
- CASI-5 Social Anxiety *T*-scores and BASC-3 Anxiety *T*-scores did not significantly predict average looking time at the faces when controlling for IQ in the ASD group (Figure 3).

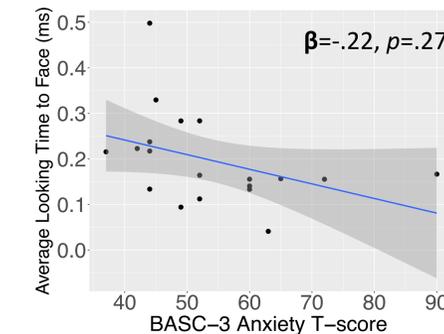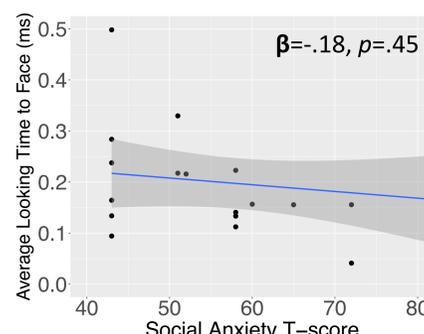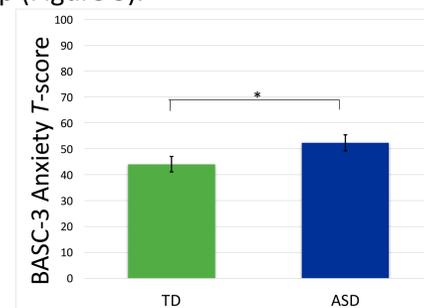**Figure 2 (right).** Group differences in BASC-3 Anxiety *T*-scores between diagnostic groups.

Figure 3. The relationship between CASI-5 Social Anxiety and BASC-3 Anxiety *T*-scores and average looking time at the faces when controlling for IQ in the ASD group.

Results, cont.
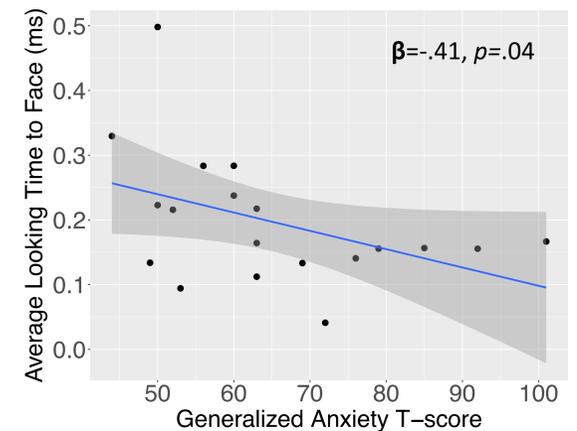

β=-.41, p=.04

Figure 4. The relationship between CASI-5 Generalized Anxiety *T*-scores and average time looking at the faces when controlling for IQ in the ASD group.

- Higher CASI-5 Generalized Anxiety *T*-scores predicted lower average looking time at the faces when controlling for IQ in the ASD group.
- Anxiety subscales were not significantly related to average looking time at the faces in the TD group.

Discussion

- Results reveal a relationship between higher generalized anxiety symptomology in children with ASD and decreased looking patterns toward social stimuli.
- Social anxiety was not associated with looking patterns in the ASD group, suggesting that the results may not be specific to anxiety toward social stimuli.
- Significant relationships between anxiety and looking patterns were not found in the TD group; however, clinically significant levels of anxiety were exclusionary for the TD group.
- These findings suggest that anxiety symptomology may be a significant factor in existing ASD symptomology.
- Further, these results suggest that the CASI-5 may be a more sensitive tool in capturing anxiety symptomology in relation to social biomarkers of ASD.
- Limitations include a small sample with a wide range of age and IQ. Age may be a confounding factor, however the ongoing study will expand on this pilot data to address sample limitations.

References

1. Muris, P., Steerneman, P., Merckelbach, H., Holdrinet, I., & Meesters, C. (1998). Comorbid anxiety symptoms in children with pervasive developmental disorders. *Journal of Anxiety Disorders, 12*(4), 387-393.
2. van Steensel, F., Bögels, S., & Perrin, S. (2011). Anxiety Disorders in Children and Adolescents with Autistic Spectrum Disorders: A Meta-Analysis. *Clin Child Fam Psychol Rev, 14*(3), 302-317.
3. Gliga, T., Elsabbagh, M., Andravizou, A., & Johnson, M. (2009). Faces attract infants' attention in complex displays. *Infancy, 14*(5), 550-562.
4. Loth, E., Charman, T., Mason, L., Tillmann, J., Jones, E.J., Wooldrige, C., …, & Banaschewski, T. (2017). The EU-AIMS Longitudinal European Autism Project (LEAP): Design and methodologies to identify and validate stratification biomarkers for autism spectrum disorders. *Molecular Autism, 8*(1), 24.

ABC-CT
abc-ct@yale.edu
medicine.yale.edu/ycci/researchers/autism/

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