

## Background

Region of Interest (ROI) analysis is the standard approach for eye tracking-based biomarker discovery in autism research. The approach identifies between-group differences between individuals with autism spectrum disorder (ASD) and typically developing (TD) peers based on percentage of time spent looking at specified areas. While powerful, ROIs are predefined by ET experts' hypothetical expectations for where ASD and TD gaze patterns should differ. Informative gaze pattern visualizations can be used as an investigatory tool to identify robust ROIs in ASD/TD stratification. Insight from expert clinicians can further improve the odds of identifying accurate visualization mechanisms and precise ROIs which would illuminate strategies used in ASD to capture scene content.

## Objectives

To identify clinically sound ROIs for ET-based stratification of ASD and TD, this study proposes multiple visualization mechanisms that allow better capturing of norm differences between groups based on their ET gaze patterns. We include input from expert clinicians on ROI definition with the ultimate goal of being insightful for that population.

## Methods

This study leverages ET gaze patterns from multiple paradigms (Biomotion Preference, Activity Monitoring (AM), Social Interaction (SI) Play, Static Social (SS) Scenes, Pupillary Light Reflex (PLR), and Visual Search (VS)) from the interim dataset (Summer 2018) of the Autism Biomarkers Consortium for Clinical Trials (ABC-CT) formed to investigate promising biomarkers for ASD.

The dataset consisted of three timepoints from 225 6-to-12-year-old children (TD:n=64;ASD:n=161). We investigate Timepoint1 only. Five visualization strategies were designed. Applying these strategies to multiple eye-tracking paradigms and considering groupings upon specific phenotypic measures [e.g. ASD vs non-ASD, lower IQ(LIQ) versus higher IQ(HIQ) ASD] provides new insights into information processing strategies employed by children with ASD and reveals temporal components of gaze patterns that can be overlooked in standard time-summary-based ROI analyses. The resultant visualizations were presented to a group of expert autism clinicians with combined clinical experience of 287 years (ARNP/RN=11,BCBA=2,MD=1,ClinPsych/Therapist=8, Family services/CRA=2).

## Results

The clinicians (14 out of 15) favored the proposed "Threshold-HeatMap" visualization above alternatives and confirmed several insights. For example, in AM,

### 1. in TD vs ASD,

- TD>ASD on looking at people/faces on overall (p-value<.001,Cohen'sD=0.97),
- TD>ASD on looking at peoples when
  - People reached for the object (p-value =.001, Cohen'sD = 0.94),
  - Actors were not talking and/or in anticipation of speech or activity (p-value <.001, Cohen'sD = .91),
- ASD>TD on looking at toys and the central activity(p-value < .001, Cohen's D=-1.07; p-value<.001, Cohen'sD = -1.06 during speech; p-value<.001, Cohen'sD = -1.09 during non-speech),
- ASD seemed more likely to reference faces after speech,
- ASD was slower to disengage from objects/people.

### 2. In ASD,

- LIQ>HIQ on looking at distractors(p-value<.001, Cohen'sD = .76),
- LIQ responded to conversation less in overall (p-value < .001, Cohen'sD = .82), and more slowly,
- LIQ showed more scattered gaze patterns,
- LIQ spent more time looking at background objects(p-value < .001, Cohen'sD =.59).

## Conclusions

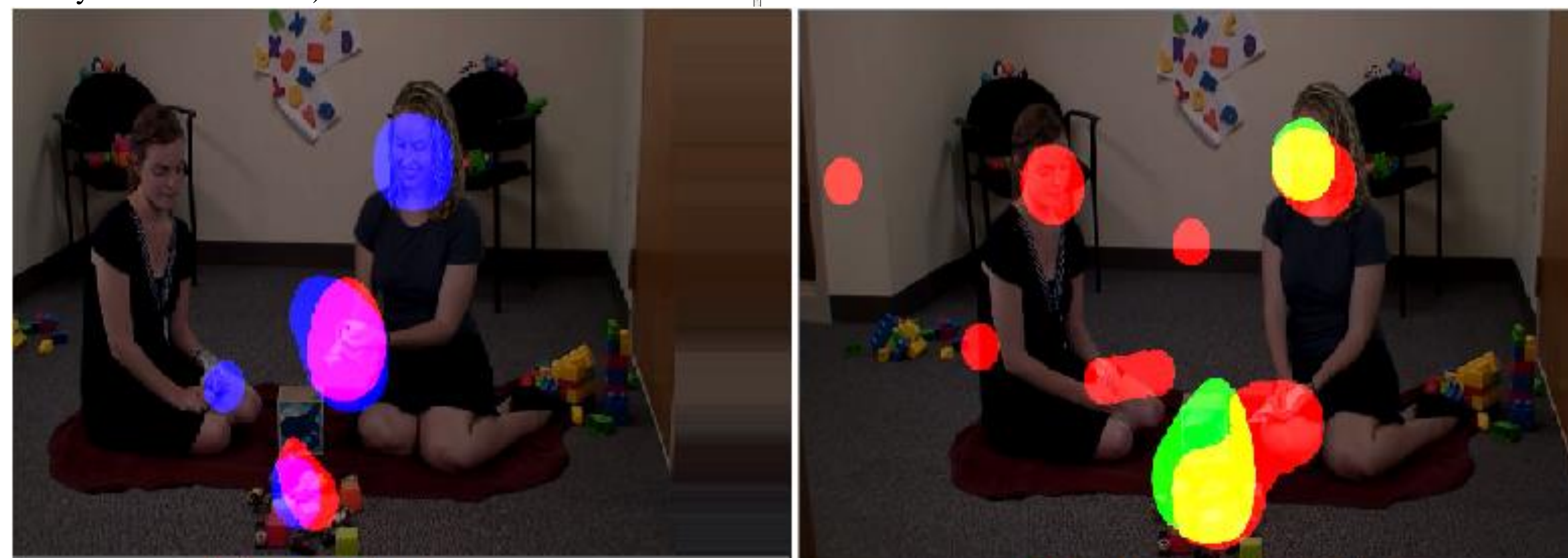
Results indicated suitability of proposed heatmap-based visualizations and the importance of incorporating expert clinicians' insights in defining robust ROIs. Moreover, a strong agreement on the importance of temporal information—often ignored in ROI analysis which uses summation of looking durations—indicates more advanced analysis approaches are required to better capture the temporal dysfunction in ASD ET gaze patterns.

## Bibliography

- Bernier, R., Mao, A., & Yen, J. (2010). Psychopathology, families, and culture: Autism. *Child and Adolescent Psychiatric Clinics of North America*, 19(4), 855–867.
- Bernier, R., & Gerdtz, Jennifer. (2010). *Autism spectrum disorders : A reference handbook* (Contemporary world issues). Santa Barbara, Calif.: ABC-CLIO.
- Bronheim, S. M. (2015). Considering culture in autism spectrum disorders. *LEND Brief*, 3–7.
- Croen, Lisa A., Grether, Judith K., Hoogstrate, Jenny, & Selvin, Steve. (2002). Descriptive Epidemiology of Autism in a California Population: Who Is at Risk? *Journal of Autism and Developmental Disorders*, 32(3), 217-24.
- Mandell, David S., Iitenbach, Richard F., Levy, Susan E., & Pinto-Martin, Jennifer A. (2007). Disparities in Diagnoses Received Prior to a Diagnosis of Autism Spectrum Disorder. *Journal of Autism and Developmental Disorders*, 37(9), 1795-1802.
- Mandell, Listerud, Levy, & Pinto-Martin. (2002). Race Differences in the Age at Diagnosis Among Medicaid-Eligible Children With Autism. *Journal of the American Academy of Child & Adolescent Psychiatry*, 41(12), 1447-1453.

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■ ASD ■ TD ■ LIQ ASD ■ HIQ ASD  
Figure 1. Threshold-HeatMap visualization