

Background

- Restricted and repetitive behaviors are a core symptom of autism spectrum disorder (ASD), including motor stereotypies, cognitive rigidity, and problems with attentional processing.
- Several studies have noted differences in oculomotor movements such as blinks and saccades between individuals with ASD and their typically developing (TD) peers.
- Characteristics of these oculomotor movements have also been linked to behaviors and biological systems that may underlie the stereotypies and cognitive rigidities often seen in ASD; however, scant research has examined relationships between variability in spontaneous eye-movement and clinically meaningful individual differences.
- Spontaneous eye movements may provide a unique means of examining low-level neurotransmitter dynamics influencing autistic traits.
- Based on prior literature, we predicted differences in both blink rate and characteristics of spontaneous saccadic eye movements between children with ASD and TD children, such that spontaneous eye movements and blinks would be more frequent in children with ASD.
- We specifically expected to see differences in the 4-10 Hz frequency characteristics of eye movements, which have been associated with neural mechanisms of attentional control and cognitive flexibility, such that children with less cognitive flexibility would show a greater degree of regularity in eye movements.

Methods

Participants

- Clinical and eye-tracking data were collected from 51 participants (see Table 1) recruited from the New Haven, CT, Boston, MA, Los Angeles, CA, Durham, NC, and Seattle, WA metropolitan areas as a part of the Autism Biomarkers Consortium for Clinical Trials (ABC-CT) feasibility study.

Table 1

Group	n (n males)	Mean Age (Y)	Min. Age (Y)	Max. Age (Y)
ASD	25 (20)	7.77	4.42	11.3
TD	26 (17)	6.59	4.01	11.4

Behavioral Assessment:

- Stereotypy and rigidity were assessed using:
 - Aberrant Behavior Checklist (ABC) stereotypy standard score
 - Autism Impact Measure (AIM) frequency of restricted behavior subscale
 - Behavior Assessment System for Children (BASC-3) adaptability and attentional control subscales

Rigid and Stereotyped Behaviors

- Summary statistics are presented for measures of rigid and stereotyped behaviors for each group (Table 2).

Table 2 Measure	Mean (SD)		Welch t-test		
	TD	ASD	t	df	p
Full-Scale IQ (DAS-II)	114 (9.34)	91.1 (19.5)	-5.33	34.1	<0.01
ABC Stereotypy Standard Score	0.08 (0.39)	4.38 (3.33)	6.28	23.4	<0.01
AIM Frequency of Restricted Behavior	10.3 (2.92)	20.3 (7.37)	6.07	28.1	<0.01
BASC-3 Adaptability	58.3 (8.53)	42.0 (11.4)	-5.58	40.4	<0.01
BASC-3 Attentional Control	43.4 (7.33)	64.6 (6.19)	10.9	46.9	<0.01

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McPartland Lab, Yale Child Study Center, New Haven, CT mcp-lab.org

Methods

Eye-Tracking Data Acquisition, Pre-processing, and Analysis:

- Remote eye-tracking data were collected at 500 Hz using an SR Eyelink 1000+ while participants freely viewed static images of naturalistic social scenes (such as that depicted in Figure 1a).^{1,2}

Blink Rate:

- Blinks were identified using the SR's built-in blink detection algorithm, excluding blinks that were flagged as having a duration longer than 400 ms or shorter than 50 ms.
- Blink rate was calculated as the average number of blinks per second across all stimuli.

Saccadic Rhythmicity:

- Distance between gaze locus at each timepoint was examined in the frequency domain in order to assess rhythmicity of spontaneous saccadic eye movement. Schematic of process used to calculate saccadic rhythmicity is presented below in Figure 1.
- Power spectra were generated from 250 ms segments of data. Amplitude was extracted for frequencies from 4 to 10 Hz (see Figure 3); prior studies have identified attentional sampling and voluntary saccadic movements clustered around the 4-10 Hz frequency range and have linked eye movements to neural activity in this frequency band.

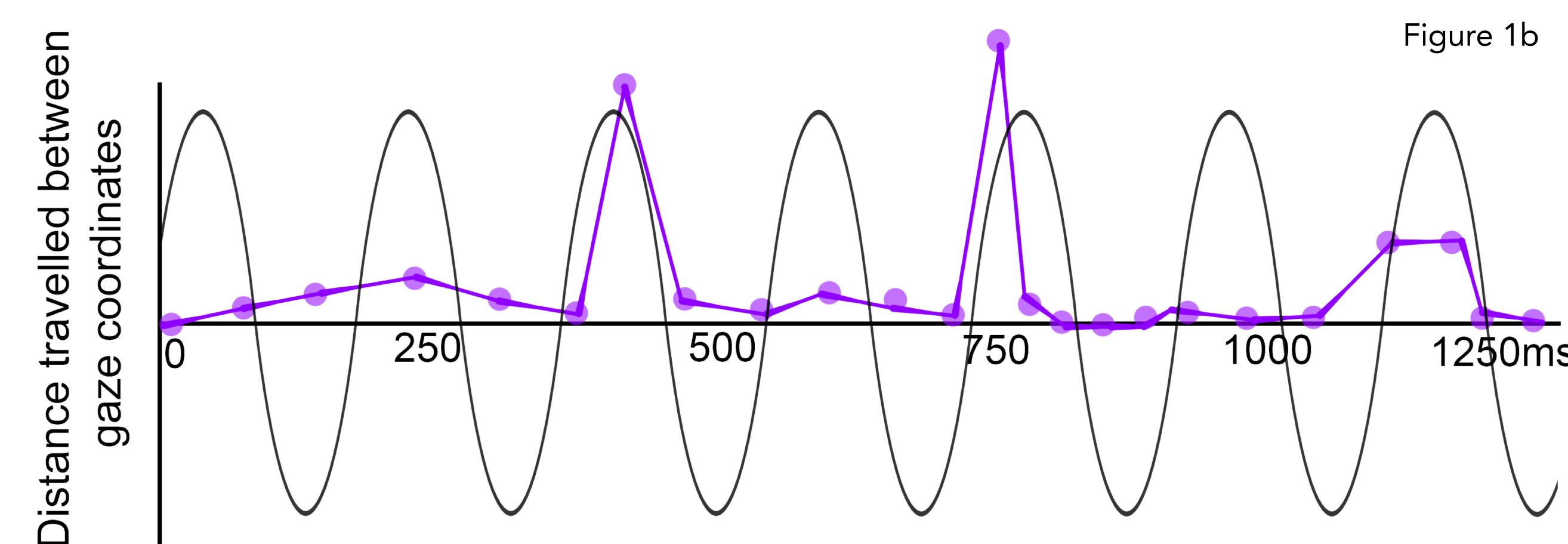
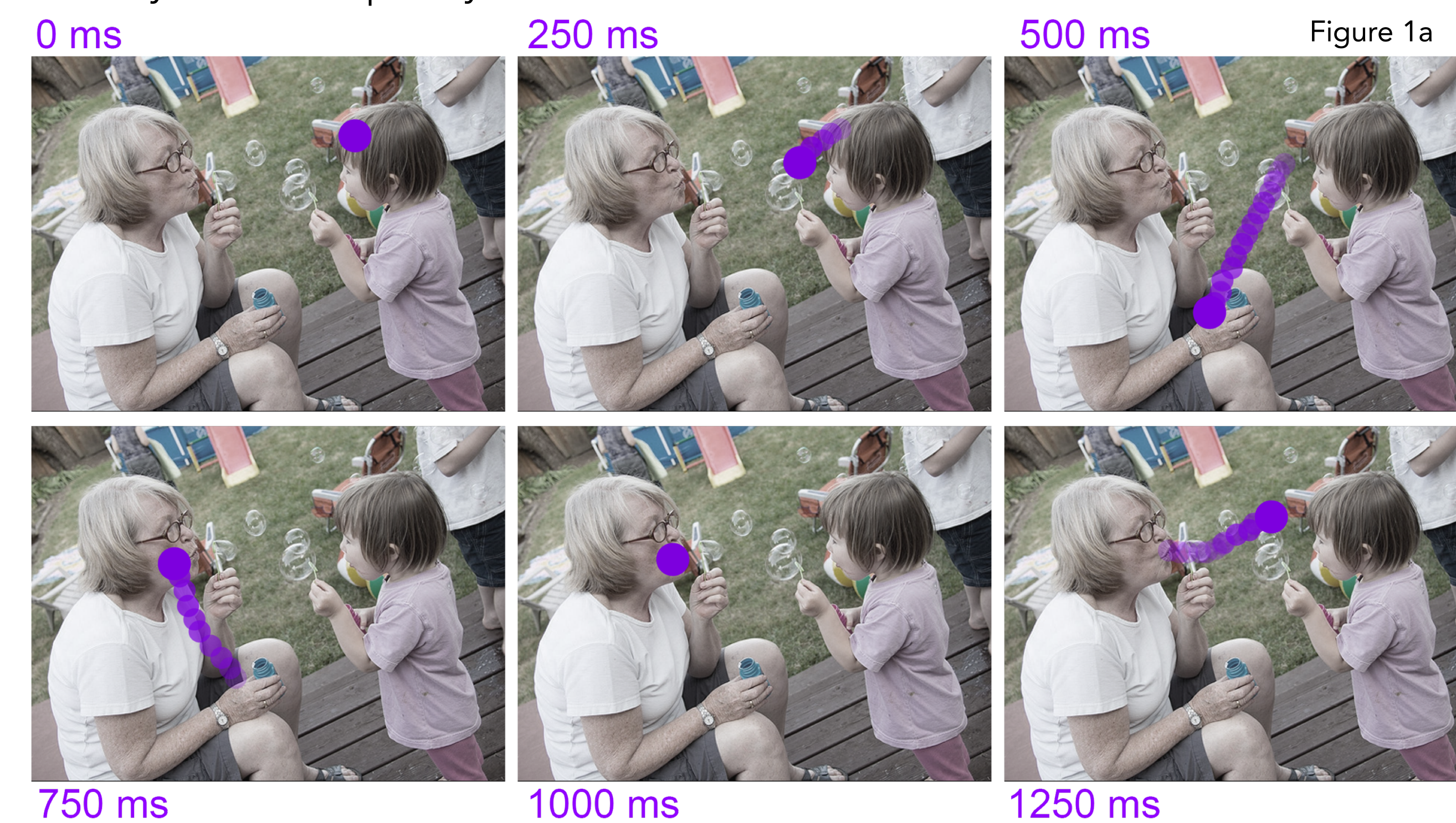


Figure 1a shows an example of how gaze may move across a static image over time: at some points, viewers fixate, deviating from a point only slightly, while at others, they quickly saccade to another part of the image. 1b plots distance travelled by the viewer between gaze points at any given time, enabling examination of the time-frequency components of eye movements. A sine wave in the 4-10Hz range is overlaid.

1 Loth, E., Charman, T., Mason, L., Tillmann, J., Jones, E. J., Wooldridge, 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.
2 Shic, F., Bradshaw, J., Klin, A., Scassellati, B., & Chawarska, K. (2011). Limited activity monitoring in toddlers with autism spectrum disorder. *Brain research*, 1380, 246-254.

Results

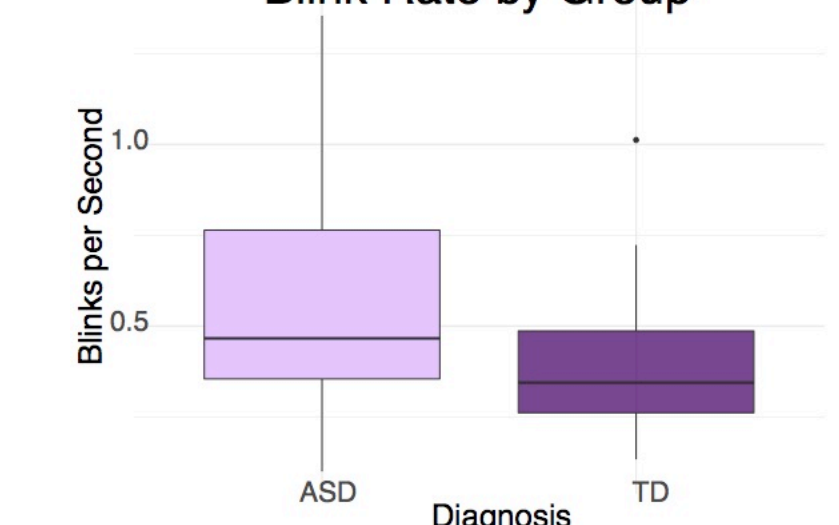
Blink Rate and RRBs:

- Table 3 shows summary statistics for blink rate in each group.
- One-way ANOVA indicated a statistically significant difference in blink rate between diagnostic groups, such that individuals with ASD blinked more than TD controls. ($F(1,48)=5.96, p=0.018$). See Figure 2.
- No main effects of stereotypy or rigidity were seen in multiple regression models examining the effect of diagnosis, behavioral measures, and their interactions on blink rate.

Table 3

Group	Blinks per second [Mean (SD)]
ASD	0.58 (0.34)
TD	0.39 (0.2)

Figure 2 Blink Rate by Group



Saccadic Rhythmicity and RRBs:

- Log-transformed power spectra for each group are presented in Figure 3.
- A one-way ANOVA showed a significant difference in the power of the 4-10 Hz frequency component between diagnostic groups ($F(1,49)=25.67, p<0.01$).
- Saccadic rhythmicity was associated with frequency of restricted behavior as measured by the AIM. Among individuals with ASD, those with more regular eye movements in the 4-10 Hz frequency band scored higher on the AIM ($\beta=45.57, p=.034$; Figure 4).
- No independent effect of restricted or stereotyped behavior on saccadic frequency was seen across diagnostic groups when models accounted for group differences in power.

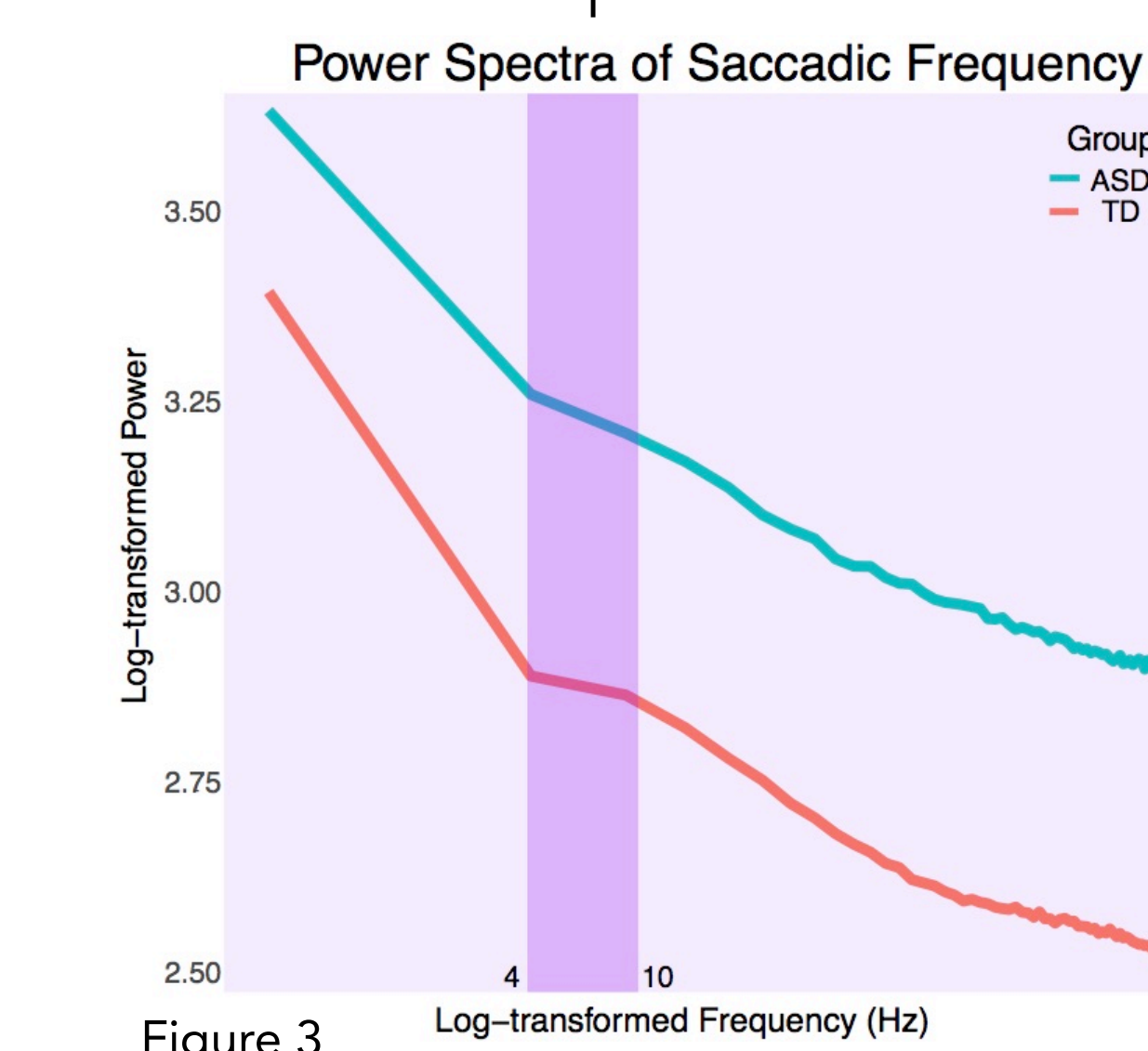


Figure 3

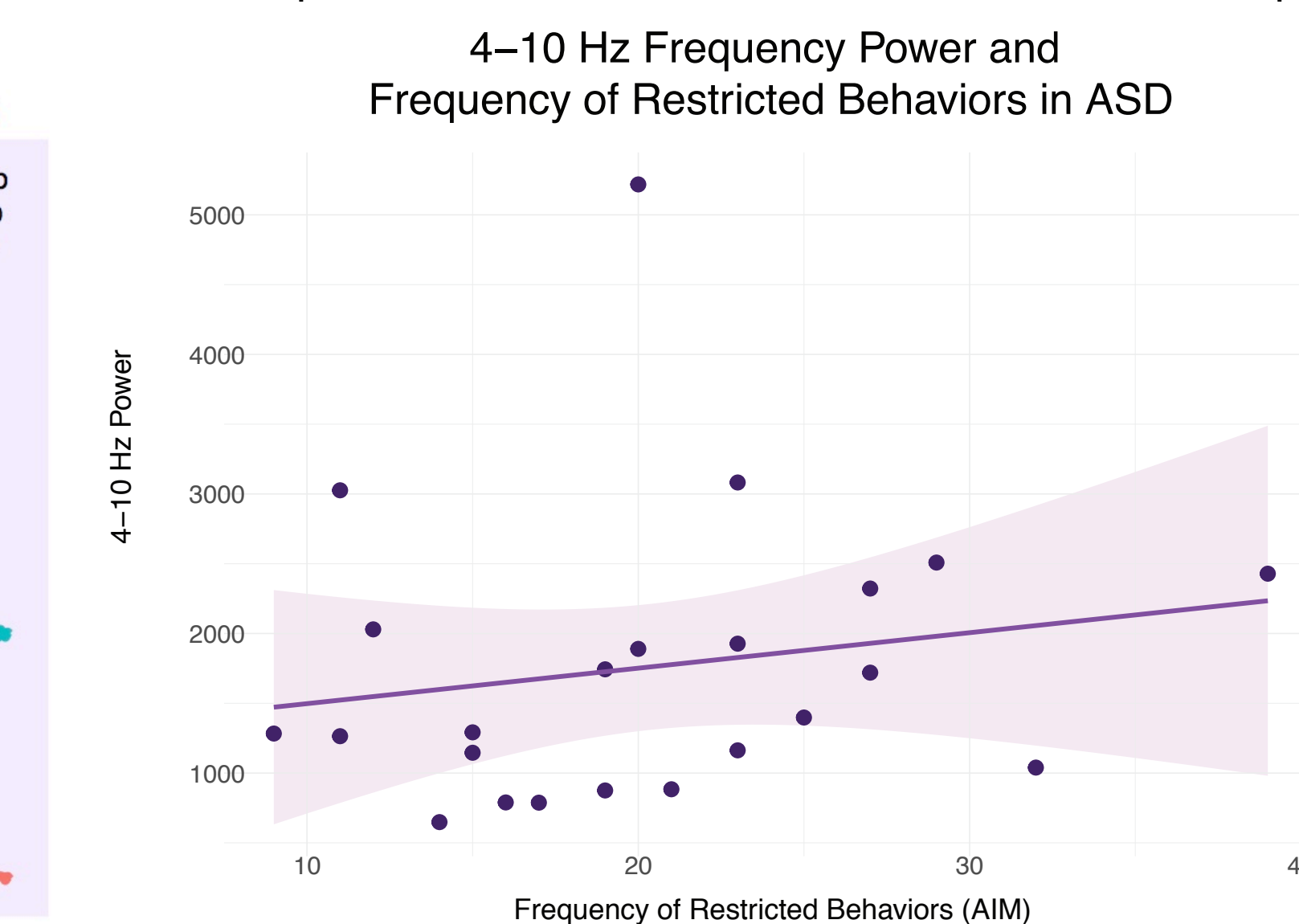


Figure 4

Conclusions

- These data suggest that the blink rate and frequency dynamics of spontaneous eye movements in children with ASD differ from that of their TD peers.
- Among children with ASD, eye movement rhythmicity exhibited a stronger frequency component from 4-10 Hz, which was further modulated by the degree of restrictive behavior displayed.
- That this frequency band has been implicated in attentional processing and cognitive control suggests that further examination of spontaneous oculomotor dynamics in this range may have potential as a biomarker of processes relevant to RRBs.
- Future research should examine relationships between the frequency dynamics of oculomotor movements and stereotypy and rigidity in ASD in both spontaneous and more structured eye-tracking paradigms.
- Frequency-spectrum-wide group differences in power suggest a possible confounding influence of noise in data; future research should aim to reduce noise in data collection and to further characterize any systemic differences in data quality between groups.