Associations between the pupillary light reflex and anxiety symptoms, ADHD symptoms, and sensory behaviors in autistic children: Results from the Autism Biomarkers Consortium for Clinical Trials (ABC-CT)

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Background

- The pupillary light reflex (PLR) is the natural constriction and redilation of the pupil in response to light and reflects autonomic nervous system (ANS) function.[1]
- Autistic children demonstrate differences in the PLR, including delayed latency to constriction, reduced relative pupil constriction (RPC), and faster constriction and redilation times than neurotypical peers, suggesting differences in ANS function.[2]
- Autistic children with more sensory behaviors show decreased RPC compared to autistic children with fewer sensory behaviors.[3]
- Attention-deficit/hyperactivity disorder (ADHD) and anxiety symptoms, also relate to ANS function and associate with the PLR.[4,5]
- Very few studies have examined how the PLR may associate with these co-occurring clinical features in autistic children.

Aim

- Investigate relationships among sensory, anxiety, and ADHD features and the PLR in autistic children.
- It was hypothesized that children with more co-occurring symptoms would have a shorter latency, faster constriction time, and smaller RPC.

Methods

Participants
- Participants were 207 autistic children (74% male, 68% White), ages 6-11 (M=8.42±1.65 years) taking part in the ABC-CT.

Clinical Measures
- Autism diagnoses were confirmed using the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2) and clinical judgement based on the DSM-5.
- ADHD and generalized anxiety symptoms were assessed via parent-report on the Child and Adolescent Symptom Inventory, Fifth Edition (CASI-5).
- Sensory behaviors were assessed via parent-report on the Pervasive Developmental Disorder Behavior Inventory (PDDBI).
- Autism characteristics were assessed via parent-report using the Social Responsiveness Scale, Second Edition (SRS-2).

Table 1. Clinical characteristics of the sample.

Subscale T-score (Instrument)	Mean (SD) Range
Generalized Anxiety (CASI-5)	67.67 (15.92) 43.55 – 126.30
ADHD Combined (CASI-5)	74.12 (12.92) 46.88 – 113.42
ADHD Inattentive (CASI-5)	73.07 (12.41) 44.71 – 104.15
ADHD Hyperactive/Impulsive (CASI-5)	69.67 (14.13) 40.36 – 110.47
Sensory Behaviors (PDDBI)	47.04 (9.32) 34.00 – 83.00
Autism Characteristics (SRS-2)	73.03 (10.42) 43.00-107.00

Pupillary Light Reflex
- Participants viewed nine flashes of light on a dark screen during an eye-tracking experiment (Figure 1a).
- PLR was measured at 500 Hz with an SR Eyelink-1000+ binocular remote camera system.

Methods

- PLR dependent variables included mean constriction time, latency to constriction, RPC, and redilation time (Figure 1b).
- Meter readings of ambient light in the room were taken prior to each session to ensure standard luminance across participants.
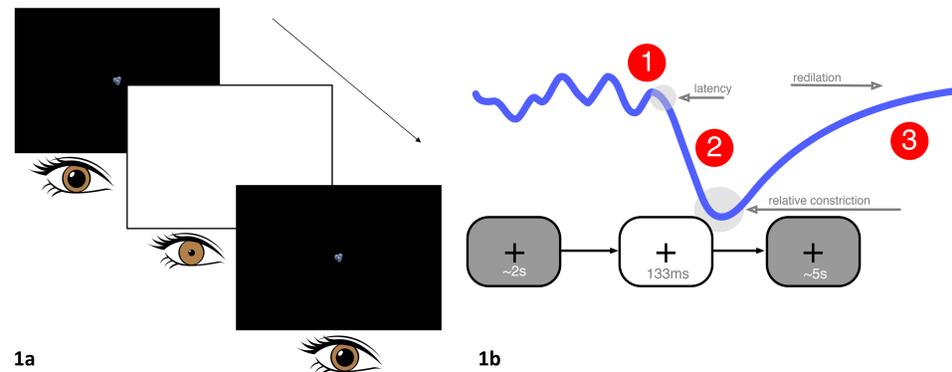

Figure 1a. PLR was elicited by a bright white screen that appeared for 133ms between two black screens. Figure 1b. Graphical depiction of the PLR including (1) latency (onset) to constriction, (2) RPC (change in pupil size), and (3) redilation.

Analysis
- Mean latency was log transformed.
- One extreme mean constriction time outlier was removed.
- Separate linear regressions explored relationships among T-scores on each clinical variable and each PLR measure.
- Ambient light and autism characteristics (SRS-2) were included in each model.

Results

- Greater sensory (Figure 2), generalized anxiety (Figure 3), ADHD hyperactive/impulsive (Figure 4), and ADHD combined (Figure 5) symptoms each significantly predicted shorter pupil constriction times when controlling for autism characteristics and ambient light (ps<.05).
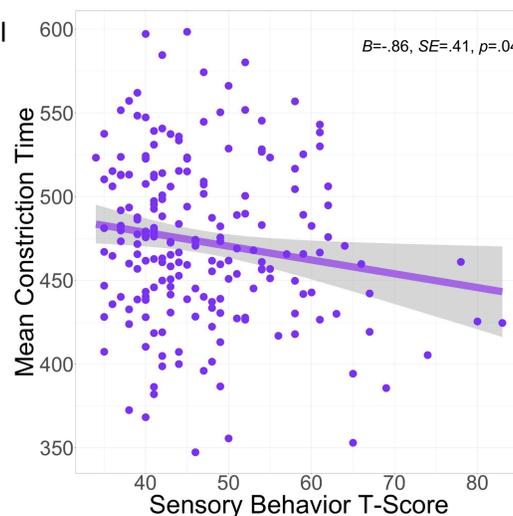

Figure 2. Relationship between sensory behavior T-Score on the PDDBI and mean pupil constriction time.
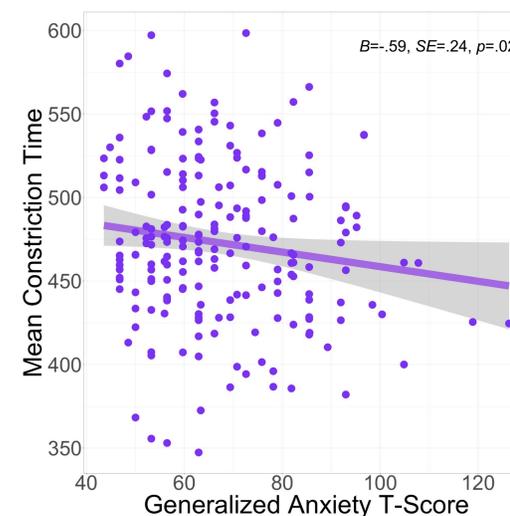
Figure 3. Relationship between generalized anxiety T-Score on the CASI-5 and mean pupil constriction time.

Results
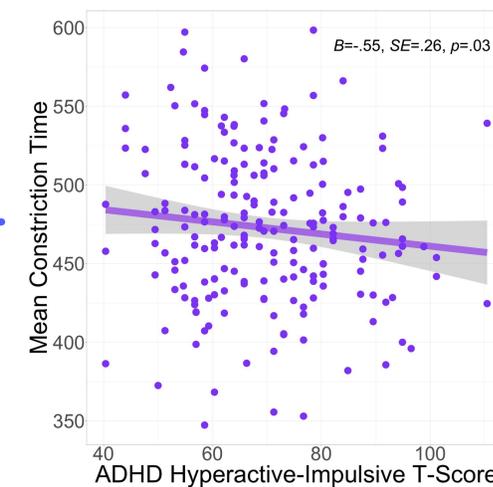
Figure 4. Relationship between ADHD hyperactive/impulsive T-Score on the CASI-5 and mean pupil constriction time.
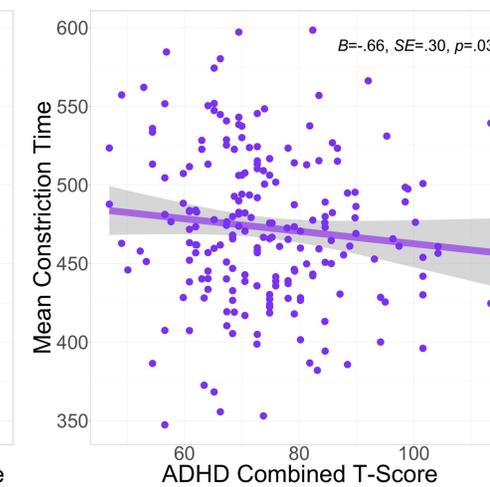
Figure 5. Relationship between ADHD combined T-Score on the CASI-5 and mean pupil constriction time.

- Generalized anxiety symptoms also approached significance as a predictor of redilation time, with greater symptoms predicting a shorter redilation time (B=-1.02, SE=.55, p=.07).
- Co-occurring symptoms were not significantly associated with PLR latency or RPC (ps>.05).

Conclusions

- Significant associations between increased co-occurring sensory, ADHD, and anxiety symptoms and shorter pupil constriction time in autistic children indicates relevance of PLR constriction time in understanding neural correlates of individual differences in autism.
- Autistic children with greater ADHD, anxiety, and/or sensory symptoms may experience more ANS dysregulation.
- No associations were found with latency to constriction or RPC suggesting these measures may not be related to co-occurring psychopathology symptoms in autism.
- Future research should examine longitudinal relationships among PLR and clinical features to clarify the utility of PLR as a predictor of clinical attributes.

References

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