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Heart rate defined sustained attention relates to visual attention in autism and fragile X syndrome

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Social attention, including shared attention and social orienting, is essential for positive social interactions. Although early visual social attention is often quantified using eye tracking, these indices may not consistently reflect cognitive engagement. Heart rate defined sustained attention (HRDSA) is a physiological measure that can index cognitive engagement alongside visual attention, leading to more comprehensive assessments of attentional processes that are particularly important in young, neurodiverse children with high support needs, including those with autism and fragile X syndrome (FXS). The present study examined visual and heart-defined measures of social attention to the Selective Social Attention task, a video-based assay of social attention, in children with autism, FXS, and neurotypical development. Linear mixed models examined group and condition effects in multiple cardiac indices and overall looking at the scene. Findings suggest that, overall, children across all groups engaged similarly across the experiment in most dimensions of HRDSA, and consistent with previous work, autistic children spent less time visually attending to the scene than either other group. HRDSA was positively associated with visual social attention. Combining physiological and visual attention measures may elucidate the complex nature of social attention and be especially valuable for neurodiverse children when typical assessments are inaccessible.

Keywords Autism spectrum disorder, Fragile x syndrome, Social attention, Eye tracking, Heart activity

Social attention, including social orienting and shared social gaze, is essential for effective social interaction. Social attention emerges within the first few months of life¹ and can have cascading impacts on higher-order social skills including social cognition, language, theory of mind, joint attention, social motivation, and social learning, throughout development^{2–5}. Given its importance for functional outcomes, several studies have evaluated how social attention, primarily indexed through eye-tracking methodologies, manifests in neurodevelopmental disorders characterized by social differences, such as autism or fragile X syndrome (FXS)^{6–11}. Furthermore, eye-tracking has a long history of measuring social attention in infants and young children with autism and FXS, especially those with high support needs, due in large part to the fact that eye-tracking is relatively non-invasive and experiments can require very few task demands^{12–17}. This work is extremely valuable, as much autism research has excluded individuals who have high support needs (e.g., are nonspeaking or have intellectual disability), leading to a dearth of validated outcome measures for use in these populations^{15,18,19}. While eye-tracking methodologies have been highly useful in characterizing social attention in autistic children and children with FXS⁶ indexing visual attention alone has some limitations^{20,21}. As such, multimethod studies of social attention and engagement are essential to objectively quantify and understand social attention, particularly in children who have high support needs.

Autism spectrum disorder (ASD, or autism) is a neurodevelopmental condition defined by differences in social communication and the presence of restricted and repetitive interests and behaviors²². Autism is one of the most common neurodevelopmental conditions, with current prevalence estimates of 1:31 children diagnosed²³ although the causes of autism are largely unknown. Fragile X syndrome, a heritable condition affecting roughly 1:7,000 males and 1:11,000 females²⁴ is a single gene condition caused by a CGG repeat

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expansion mutation on the *Fragile X Messenger Ribonucleoprotein 1 (FMR1)* gene, suppressing the production of the fragile X messenger ribonucleoprotein (FMRP), a protein critical for neurodevelopment^{25,26}. There is a diagnostic co-occurrence with autism of approximately 60%²⁷, but both autism and FXS are characterized by a multitude of overlapping features, even when co-occurrence is absent^{27–30}. Atypical social attention is a prominent overlapping feature across non-syndromic autism and FXS that has been an important topic of research to date because of its potential cascading effects on important functional and developmental outcomes^{13,31}.

Given the complex and multi-faceted nature of social attention, there are numerous measurement approaches for young children with neurodevelopmental disorders^{29–31} with automatic eye tracking^{13,32,33} among the most common. Eye tracking provides an objective and efficient measure of attention with relatively high temporal and spatial precision³⁴. The Selective Social Attention (SSA) task is one of the most commonly used and validated eye-tracking assays in neurodevelopmental research³⁵. It is a brief, dynamic video that depicts an actress surrounded by four non-social distractors engaging in experimental probes that use child-directed speech and eye contact as bids for attention. Multiple studies using the SSA in infant through school-age populations have indexed unique profiles of social attention in autism and FXS as compared to neurotypical development or other non-autistic developmental delays^{13,36,37}. Furthermore, studies have associated visual social attention measured by the SSA with measures of observable social behavior, including autism features, adaptive behavior, naturalistic social attention, and play skills^{13,32,36,38}.

Few studies to date have employed a multimethod approach to indexing social attention; that is, one combining eye-tracking with other objective measures of attention³⁹. This is particularly important, as visual attention does not consistently index cognitive engagement⁴⁰ and gaze aversion has been deployed in neurodiverse persons as a strategy for managing cognitive load⁴¹. Thus, the development and implementation of physiological indices of attention, such as heart activity, coupled with eye-tracking, may provide multidimensional insight into the cognitive states of social attention⁴². Heart activity has immense promise as part of a multimethod index of social attention⁴² given the clear evidence that cardiac indices of physiological regulation contribute to cognitive and social competency and hypotheses that physiological hyperarousal may underly difficulties in social, cognitive, and affective engagement^{27,43–45}. Cardiac indices of physiological regulation are also passive and relatively non-invasive measures, optimizing them for use in neurodevelopmental populations with high support needs^{39,46}.

Heart rate-defined sustained attention (HRDSA) is a well-validated physiological measure of sustained attention⁴⁰. It is defined by a period of sustained decrease in heart rate and heart rate variability following attentional orienting to a stimulus and is separate from phases of attention orienting and attention termination⁴⁷. This deceleration in heart rate occurs as activation of the sympathetic nervous system is withdrawn and/or the parasympathetic nervous system is activated to cognitively attend to a particular stimulus. Periods of sustained attention are associated with cognitive engagement^{43,48}. When paired with observed looking behaviors, HRDSA combines behavioral and physiological measures to index cognitive engagement alongside visual attention, increasing validity in capturing states of sustained visual attention. Previous research suggests that, compared to visual attention alone, HRDSA may provide differential insight into the development of social attention in neurotypical infants⁴⁹ leading to a more comprehensive measurement of attentional processes⁴⁰. Reflecting cognitive engagement during states of sustained visual attention, HRDSA offers a multidimensional and precise account of attentional processes, which, in a social context, are critical for social learning and the later development of higher-order social skills. Thus, including HRDSA paradigms may increase insight into the development and understanding of social attention in young children with high support needs, including those with autism and FXS.

Previous research with children with neurodevelopmental disorders supports the utility of HRDSA as a measure of social attention in this population. For example, shallower heart rate decelerations were associated with autistic features in a longitudinal sample of infant siblings of autistic children during an engaging, nonsocial viewing task⁵⁰ and marginally associated with autistic features in infants with FXS during a non-social visual attention task⁵¹. Tonnsen and colleagues⁵⁰ found that HRDSA was able to predict group status (i.e., infant siblings of autistic children and neurotypical infants) better than behavioral looking alone. It is important to note, however, that while these studies provide a unique insight into HRDSA as an index of attention, they primarily utilized manual coding of eye gaze to index behavioral states of attention rather than eye-tracking methods, which is a time- and labor-intensive process. Eye-tracking, on the other hand, has the potential to provide an automatic and precise estimate of time spent looking at a screen, although it does not record time that a child spends looking away. Nevertheless, a multi-method approach including eye-tracking and physiological indices offers the potential for quickly gathering precise insight into processes of social attention, greatly facilitating more widespread use of multimethod approaches⁴⁹. For example, Helminen and colleagues found a lack of orienting response to direct gaze in young autistic children with high support needs using both eye-tracking and heart rate-defined measures of orienting, highlighting the utility of this particular approach in neurodiverse populations³⁹.

Present study

In sum, although much existing eye-tracking research has assessed social attention in neurodevelopmental disorders using visual gaze, relatively few have incorporated heart activity as a supplemental measure. Also, there are limited multimethod studies of social attention in neurodiverse populations with high support needs, including those with low cognitive ability^{15,39}. Therefore, the present study aimed to (1) evaluate the potential difference in HRDSA between preschoolers with non-syndromic autism and intellectual disability (AS), FXS, and neurotypical (NT) development during a social eye-tracking task, and (2) determine whether HRDSA relates to visual social attention captured with eye-tracking. In line with prior eye-tracking work, we hypothesized that children with non-syndromic autism and those FXS would engage in less physiological social attention than

	%HRDSA		ΔIBI		IBI		%Looking	
	$\chi^2(df)$	<i>p</i>	$\chi^2(df)$	<i>p</i>	$\chi^2(df)$	<i>p</i>	$\chi^2(df)$	<i>p</i>
Intercept	64.0 (1)	<0.001	2.42 (1)	0.120	3793.0 (1)	<0.001	590.0 (1)	<0.001
Group	0.426 (2)	0.808	1.42 (2)	0.491	20.4 (2)	<0.001	10.8 (2)	0.005
Condition	6.162 (3)	0.485	15.2 (3)	0.002	13.3 (3)	0.004	6.88 (3)	0.076
Group*Condition	11.3 (6)	0.081	4.04 (6)	0.671	4.40 (6)	0.623	10.3 (6)	0.114

Table 1. Full model results for research question 1. Significant values are in [bold]. Note. %HRDSA = Proportion of time spent in periods of heart rate defined sustained attention. ΔIBI = Change in interbeat interval during periods of heart rate defined sustained attention. IBI = average interbeat interval during periods of heart rate-defined sustained attention. %Looking = Proportion of time visually attending to the eye tracking experiment.

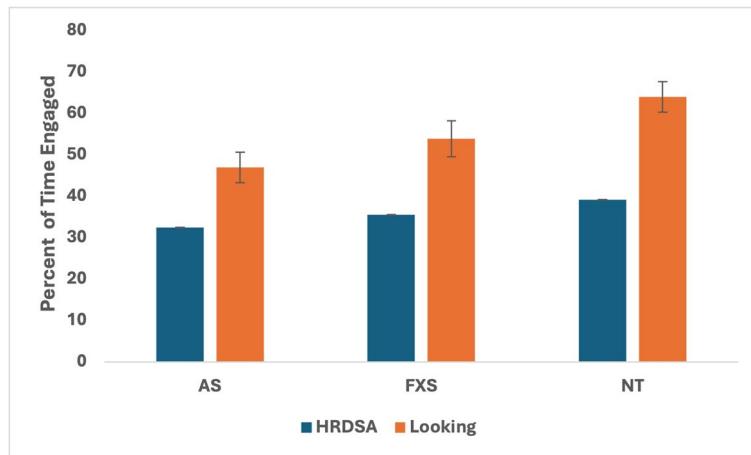


Fig. 1. Bar graph showing estimated marginal means for %HRDSA and %Looking with results collapsed across conditions. There were no group differences in %HRDSA. For %Looking, the AS group was significantly lower than the NT group, whereas the FXS did not differ from either group.

their neurotypical peers¹³. Relatedly, we hypothesized that physiological social attention would be closely linked in all groups⁴⁸.

Linear mixed models were estimated using the lmer package in R^{52,53}. Four within-child, between-group models of each of four primary variables were estimated: proportion of time spent in periods of HRDSA (%HRDSA); the change in inter-beat interval (IBI) during periods of HRDSA in milliseconds (ΔIBI); average IBI during periods of HRDSA (IBI); and the proportion of time visually attending to the eye-tracking experiment (%Looking). Effects of group, condition, and the group*condition interaction were also modeled. To evaluate the association between HRDSA and eye-tracked social attention, we estimated an additional mixed effects model. Specifically, %HRDSA was estimated with effects of %Looking, group, condition, and their two-way and three-way interactions. The estimated trend of the relationship between %HRDSA and %Looking was the primary outcome of interest.

Statistical power was estimated using G*Power⁵⁴. An estimated effect size of $d=0.9$ was used based on results reported in Tonnsen and colleagues' study of heart rate defined sustained attention in children at high and low likelihood of neurodevelopmental disabilities⁵⁰. Alpha was set to 0.05 and power to 0.80. With these parameters, the present study was powered to detect a significant between group difference with a sample of $n=19$ in each group, or $n=22$ in one group and $n=16$ in another, with an allocation of 1.4. These proposed sample sizes are comparable or larger than previous studies in this area^{39,50,51}.

Results

Research question 1

Full model results are presented in Table 1. Results from linear mixed models indicated that there were no group or condition effects in %HRDSA, nor was there a significant interaction (all $p > 0.05$; Fig. 1). There was a significant main effect of condition on ΔIBI that was driven by the Sandwich condition ($\chi^2(df)=15.2(3)$, $p=.002$). That is, children exhibited shallower IBI decelerations during the Sandwich condition relative to all other conditions (Fig. 2). There were significant main effects of group and condition for average IBI. Specifically,

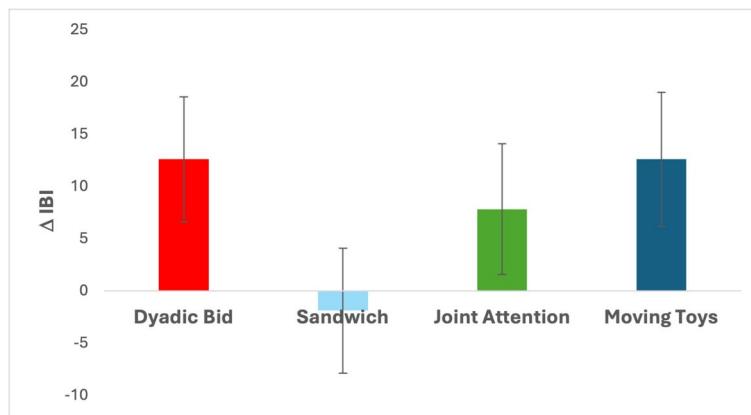


Fig. 2. Bar graph showing main effect of condition on change in IBI with results collapsed across groups ($p = .016$). Post-hoc analyses indicated that all children exhibited shallower IBI decelerations during the Sandwich condition relative to all other conditions.

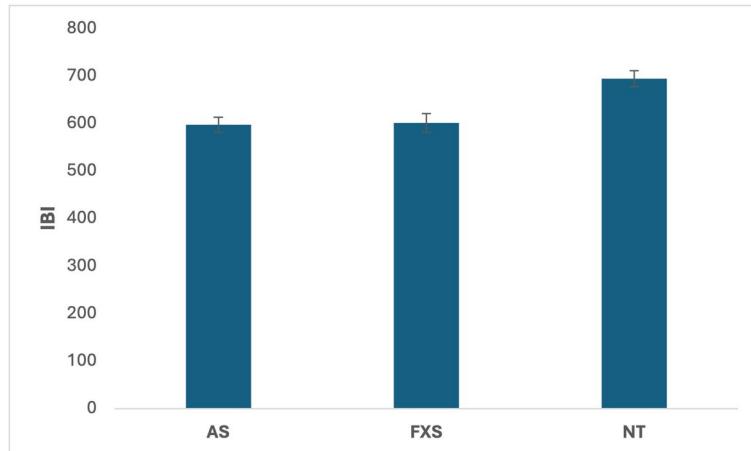


Fig. 3. Significant main effect of group averaged IBI averaged across conditions. The AS and FxS groups significantly differed from the NT groups, but not each other.

for the main effect of group, autistic children $t(df) = -4.17(52.1); p = .001$ and FxS $t(df) = -3.52(51.9); p = .000$ had significantly shorter average IBI during HRDSA periods relative to NT children, but not each other ($t(df) = -0.194(52.0); p = .846$; Fig. 3). For the main effect of condition, average IBI was shorter for all children during the Sandwich condition relative to the Dyadic Bid ($t(df) = -3.20(92.6); p = .0019$) and Moving Toys conditions ($t(df) = 3.024(92.4); p = .003$), but not for the Joint Attention Condition ($t(df) = 1.734(92.3); p = .086$; Fig. 4). Finally, for %Looking, there was a significant group effect, such that autistic children spent significantly less time visually attending to the scene throughout the experiment relative to NT children ($t(df) = -3.27(61.9.6); p = .002$). Children with FxS did not differ from either the AS $t(df) = -1.21(61.6), p = .232$ or NT $t(df) = -1.77(61.8), p = .081$ groups in their visual attention to the scene (Fig. 1).

Research question 2

Results from the model evaluating associations between HRDSA and eye-tracked visual attention across groups revealed a significant positive relationship between %HRDSA and %Looking ($B = 0.569, \chi^2(df) = 4.71(1), p = .03$), with no other significant model effects (all $p > 0.05$), suggesting an association between HRDSA and eye-tracked visual attention independent of group status and experimental condition (Table 2).

Discussion

Despite a wide body of literature demonstrating reduced visual social attention in children with non-syndromic autism and FxS relative to neurotypical controls, limited work has taken a biobehavioral, mixed methods approach to measuring social attention in this population. Hence, the present study had two primary aims. First, to evaluate potential differences in HRDSA between preschoolers with non-syndromic autism and ID, FxS, and neurotypical development during a social eye-tracking task. Second, to determine whether HRDSA relates to visual social attention to quantify and describe alternative approaches to understand social attention

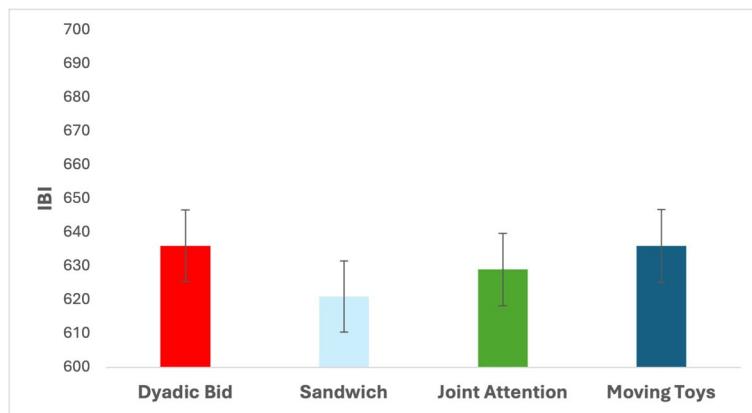


Fig. 4. Bar graph showing main effect of condition on IBI during periods of sustained attention. Average IBI was lower for all children during the Sandwich condition relative to the Dyadic Bid and Moving Toys conditions ($p < .01$).

	$\chi^2(df)$	<i>p</i>
Intercept	7.716 (1)	0.0055
%Looking	4.7068 (1)	0.0300
Group	0.1811 (2)	0.9134
Condition	5.2273 (3)	0.1559
%Looking*Group	0.5263 (2)	0.7686
%Looking*Condition	3.2594 (3)	0.3533
Group*Condition	3.3704 (6)	0.7611
%Looking*Group*Condition	6.1635 (6)	0.4051

Table 2. Model results for research question 2. Significant values are in [bold]. Note. %Looking = Proportion of time visually attending to the eye tracking experiment.

and engagement in these populations. Overall, our findings demonstrated unique patterns of social attention in children with autism and FXS relative to their neurotypical peers.

First, our findings did not indicate overall differences in the proportion of time spent in HRDSA in either clinical sample relative to neurotypical children. Our results also revealed distinct patterns of physiological differences in social attention across the course of our experiment that highlight the vulnerabilities present in children with autism and FXS. Interestingly, our finding of a condition effect, but not a diagnosis effect in change in IBI during periods of HRDSA, suggests that all children modulated their HRDSA in expected ways based on the experimental video content. That is, they exhibited significantly shallower IBI deceleration during silent, non-social conditions (e.g., when the actress was looking down and engaged in an activity) relative to the other experimental conditions, which were more social or visually/auditorily salient. However, both autistic children and those with FXS had shorter average IBI during periods of HRDSA relative to neurotypical children throughout the experiment. It is worth noting that the current study did not take into account overall baseline differences in IBI, so it is unknown whether the differences in IBI observed are task-specific or reflect global differences in arousal in autism and FXS. Nevertheless, our current findings are in line with an established “hyperarousal hypothesis” in children with FXS, as shorter IBI is indicative of overall ANS dysfunction⁴⁵. Although the research on hyperarousal in non-syndromic autism is mixed⁵⁵, the present study provides some evidence for physiological vulnerabilities in autistic children, particularly during periods of sustained attention.

In terms of visual social attention, our results align with prior work and suggest that autistic children, but not those with FXS, spend less time visually attending to social information than their neurotypical peers^{13,35,36}. That is, children with FXS did not differ from neurotypical or autistic children in their overall visual attention to social scenes. This finding is particularly interesting in light of the lack of observed group differences in physiological social attention (i.e., HRDSA). Nevertheless, our findings do provide evidence that these two measures are moderately related in all groups and experimental conditions and thus may provide complementary information about overall social engagement. Taken together, these findings provide evidence for the utility of integrated measurements of attention and engagement. Future studies should continue to look beyond pure measures of looking behavior to index social attention. This is particularly important in light of research aligned with supporting neurodiverse perspectives highlighting the negative cognitive and social consequences of sustained eye contact^{21,41,56}. The present study could thus offer a supplemental measure of social attention that is potentially more affirming of neurodivergent strategies and not reliant on looking behavior alone.

	AS	FXS	NT
<i>n</i> (% Male)	23 (86.9)	16 (50)	22 (81.1)
Age [years]	4.74 (1.35)	5.45 (1.44)	5.70 (1.28)
Ethnicity			
%Not Hispanic/Latino	86.9	100	100
%Hispanic/Latino	0	0	0
%Unknown	13.1	0	0
Race			
%White	86.9	75.0	90.9
%Black	13.1	18.7	4.5
%Other	0	6.3	0
%More than One Race	0	16.7	4.5

Table 3. Participant characterization.

The present study takes an integrated biobehavioral approach to measuring social attention using eye-tracking and physiological measures, and findings offer an important extension of our current understanding of social attention in autism and FXS. Nevertheless, it is not without its limitations. First, we took a categorical approach to defining our diagnostic groups; future work could consider examining continuous measures of autism features and other aspects of phenotypic variability (e.g., intellectual ability, language) as correlates of social attention. Second, the present study examined only global measures of social attention across the duration of the experiment and therefore could not draw specific conclusions about how shifts in visual social attention or attention to specific regions (e.g., faces) manifest as changes in HRDSA beyond broader between-condition effects. Future research should take a more fine-grained approach to examine the temporal aspects of social attention, especially considering evidence that there are temporal differences in visual attention in FXS specifically⁵⁷. Additionally, the present study was unable to address potential confounds related to heart rate variability and respiration, which could impact the interpretation of the findings. Future research should include measures such as respiratory sinus arrhythmia or respiration to better distinguish and isolate attentional processes from general autonomic reactivity.

Taken together, the present study demonstrates that HRDSA can provide unique and valuable information about social attention in neurodevelopmental disorders and suggests that looking behavior is correlated with physiological measures of attention. Combining physiological and behavioral measures of attention may be particularly important in children with neurodevelopmental disabilities for whom typical assessments may not be accessible.

Methods

Participants

Data were collected from preschoolers with non-syndromic autism (AS; *n* = 23), FXS (*n* = 16), and neurotypical controls (*n* = 22) who were participants in longitudinal studies of early development at the University of South Carolina (National Institutes of Health R01MH90194; R01MH107573; PI: Roberts). Children were included in the present study if they had complete data on relevant measures. Inclusion criteria included gestational age ≥ 37 weeks, English as the primary language in the home, and no uncorrected hearing or vision impairments. Recruitment was primarily conducted through research medical sites and social media networks specializing in autism or FXS. A majority of the current sample (80%) overlaps with that of a previous study, which did not include HRDSA measures or examine visual social attention across the entire SSA task¹³. A detailed description of participant demographics can be found in Table 3.

Group assignment was made at intake using existing genetic or psychological reports. Those in the FXS group were confirmed through a review of a genetic report documenting > 200 repeats of the CGG sequence on the *Fragile X messenger ribonucleoprotein 1 (FMR1)* gene. Those in the AS group had an existing community diagnosis of autism and evidence of developmental delays. Although no formal genetic testing was done to rule out underlying genetic syndromes in the AS group, participants in the AS group were required to have no known genetic syndromes. Intellectual ability was assessed using the Mullen Scales of Early Learning (MSEL) Early Learning Composite^{58,59} and autism diagnoses were informed by the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2)⁶⁰. Autism diagnosis and the presence of co-occurring intellectual disability (i.e., Mullen Early Learning Composite score of 70 or below) in the FXS and AS groups were confirmed at enrollment using Clinical Best Estimate (CBE) procedures²⁷. Participants enrolled in the neurotypical group were required to have no family history of autism and were confirmed not to have autism or developmental delay (i.e., Mullen Early Learning Composite scores greater than 70) through study participation.

Procedures

As a part of their participation, children completed a battery of measures including intellectual/developmental ability, autism features, and multiple indices of social attention. All procedures were approved by the Institutional Review Board at the University of South Carolina, and parents provided written informed consent before enrollment in the study, and all experiments were performed in accordance with relevant guidelines and regulations.

Measures

Heart-rate defined sustained attention (HRDSA)

Heart activity was collected during the eye-tracking presentation via electrocardiogram (ECG) with an Actiwave Cardio Monitor (Alive Technologies; CamNtech Ltd., Cambridge, UK) at 1024 Hz. Trained research assistants edited ECG data to correct false heart periods and artifacts using CardioEdit software, and only $\leq 10\%$ of beats were edited⁶¹. Interbeat interval (i.e., IBI, the time in milliseconds between consecutive heartbeats) series data were extracted from CardioEdit and used to determine HRDSA.

The start of the eye-tracking task was synced to the heart activity data using audio cues from behavioral video. Baseline IBI was defined as the median IBI of the first 5 beats of the eye-tracking video. The start of HRDSA began after 5 successive beats with IBIs longer than baseline IBI, and HRDSA terminated after 5 successive beats with IBIs shorter than baseline IBI. HRDSA was quantified using three primary variables: proportion of time in HRDSA (%HRDSA), average heart rate deceleration during HRDSA in milliseconds (Δ IBI), quantified as the average change in IBI from baseline during periods of HRDSA, and average IBI during HRDSA overall (IBI). While measures of HRDSA have typically investigated phasic heart rate decelerations time-locked to discrete stimuli over short durations^{39–45} this application was grounded in prior literature demonstrating that extended heart rate deceleration can reflect sustained attention during continuous, engaging stimuli^{50,62}.

Visual social attention

Visual social attention was measured as the total time looking at any point on the screen (%Looking) during the presentation of the Selective Social Attention (SSA) task³⁵. The experimental stimulus depicted a 3-minute dynamic video scene depicting an adult female actress seated at a table surrounded by four mechanical toys³⁵. Interspersed throughout the video were four experimental conditions designed to evoke different patterns of looking behavior: (1) the actress engaged the viewer in child-directed speech (*Dyadic Bid*); (2) the actress looked down at the table and made a sandwich without direct gaze or speech (*Sandwich*); (3) the actress looked up briefly at the camera and said ‘uh-oh’ as she turned toward one of the toys (*Joint Attention*); and (4) after the actress looked up at the camera, a toy began to move and make noises (*Moving Toys*).

Eye-tracking data were collected on an SR Eyelink 1000 Plus eye tracker. The stimulus was built and presented with SR Experiment Builder using monocular, remote eye tracking on a 24-inch widescreen LCD monitor with a 60-Hz refresh rate, 16:9 (1366 \times 768 pixel) aspect ratio, and a 65 cm participant eye-to-monitor distance. Children were shown a cartoon to adjust to the experimental setting. A five-point calibration preceded the experiment for all participants, and five-point validation and calibration quality were assessed through a manufacturer-defined five-point validation⁶³. A behavioral camera recorded the child’s face and the monitor to allow for syncing of heart rate data with the eye-tracking stimulus presentation. Participants were excluded from analyses if the amount of valid eye-tracking data was less than 20%.

Eye-tracking data were processed with custom Matlab software that accommodated standard techniques for processing eye-tracking data including blink detection, data calibration, and Region of Interest (ROI) analysis⁶⁴. Data reduction and analysis were carried out through programs written in R⁵³.

Data availability

The datasets analyzed during the current study are available from the corresponding author upon reasonable request.

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Author contributions

All authors contributed to the design of the study. KS, FS, and BK developed the procedures for analyzing the data. CAW made extensive contributions to the analysis and interpretation of the data, and CAW and KS drafted the manuscript. The remaining authors were extensively involved in revisions. All authors have given final approval for the version to be published.

Competing interests

FS consults for Roche, Janssen, and MindMed pharmaceutical companies. The remaining authors declare that they have no competing interests.

Additional information

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