Visual Exploration in Autism Spectrum Disorder: Exploring Age Differences and Dynamic Features Using Recurrence Quantification Analysis


Eye-tracking studies have demonstrated that individuals with autism spectrum disorder sometimes show differences in attention and gaze patterns. This includes preference for certain nonsocial objects, heightened attention to detail, and more difficulty with attention shifting and disengagement, which may be associated with restricted and repetitive behaviors. This study utilized a visual exploration task and replicates findings of reduced number of objects explored and increased fixation duration on high autism interest objects in a large sample of individuals with autism spectrum disorder (n = 129, age 6–54 years) in comparison with a typically developing group. These findings correlated with parent-reported repetitive behaviors. Additionally, we applied recurrent quantification analysis to enable identification of new eye-tracking features, which accounted for temporal and spatial differences in viewing patterns. These new features were found to discriminate between autism spectrum disorder and typically developing groups and were correlated with parent-reported repetitive behaviors. Original and novel eye-tracking features identified by recurrent quantification analysis differed in their relationships to reported behaviors and were dependent on age. Trial Registration: NCT022599700.

Lay Summary: Using eye-tracking technology and a visual exploration task, we showed that people with autism spectrum disorder (ASD) spend more time looking at particular kinds of objects, like trains and clocks, and look at fewer objects overall than people without ASD. Where people look and the order in which they look at objects were related to the restricted and repetitive behaviors reported by parents. Eye-tracking may be a useful addition to parent reports for measuring changes in behavior in individuals with ASD.

Keywords: autism spectrum disorder; eye-tracking; restricted repetitive behavior; visual exploration; recurrence quantification analysis; biomarkers

Introduction

Eye-tracking variability discriminates between autism spectrum disorder (ASD) and typically developing (TD) groups across paradigms, reliably showing gaze abnormalities in attention to social versus nonsocial stimuli (for a review, see Frazier et al., 2017). Findings include reduction in attention to social information, increase in attention to certain nonsocial stimuli, attention to detail, and difficulty with attention shifting and disengagement. This circumscribed attention is a type of repetitive behavior commonly occurring in ASD (Sasson, Turner-Brown, Holtzclaw, Lam, & Bodfish, 2008). Compared to TD, individuals with ASD over-focus attention to specific categories of nonsocial stimuli such as electronics, vehicles, and numbers, defined as objects of high autism interest (HAI, South, Ozonoff, & McMahon, 2005; Unruh et al., 2016). Sasson et al. (2008) developed a set of task stimuli, the visual exploration task (VET), to measure aspects of visual attention in ASD that may enable quantification of functional impairment arising from circumscribed interests. There is evidence that performance on...
VET is negatively impacted by rigid behavior patterns and circumscribed interests, with less exploration related to restricted and repetitive behaviors (RRB), in particular, restricted interests (Pierce & Courchesne, 2001 [n = 14 ASD, 14 TD]; Sasson et al., 2008 [n = 29 ASD, 24 TD]).

While prior work is informative, much is still unknown about visual scanning patterns in children with ASD, and conclusions are limited by the small sample sizes, targeted age, or IQ ranges (Chita-Tegmark, 2016; Frazier et al., 2017). It remains unclear whether differences in patterns of gaze hold stable through childhood and adolescence, and into adulthood. There is evidence that differences in visual attention emerge as early as within the first year in ASD (Ozonoff et al., 2008; Sasson & Elison, 2012; Chawarska, Macari, & Shic, 2013; Jones & Klin, 2013; Shic, Macari, & Chawarska, 2014), and a small study of children aged 2–5 years (n = 10 ASD, 14 TD) using VET indicated reduced or atypical object exploration in the ASD group compared to a TD (Sasson, Elison, Turner-Brown, Dichter, & Bodfish, 2011), which increases with age for both groups (Elison et al., 2012). Frazier et al.’s (2017) review did not find that gaze deficits in attention to social stimuli were moderated by age, sex, or cognition. However, some observations appear to not hold stable across age in ASD (Guillon, Hadjikhani, Baduel, & Roge, 2014). Therefore, it is unclear whether circumscribed attention is age-related. A developmental hypothesis suggests increasing differences between ASD and TD groups with age, due to compounding of the effect over time. Alternatively, the converse may be true in that skills do develop, albeit at a slower rate in ASD, making differences less evident in older individuals. In addition, compensatory strategies may be employed in behavioral therapies to increase visual exploration and improve social behavior and communication. Further studies across age groups are needed to understand age-related changes in circumscribed visual attention.

There is a clinical and research need for more objective measures of symptoms of ASD that can enhance diagnostic accuracy or help measure change in symptom severity, in a developmental context, and in response to intervention. For eye-tracking to translate into clinically valuable tools, we need to uncover both sensitive and specific features that effectively identify deficits in social attention across clinically relevant phenotypes and domains of functioning and age (Muriás et al., 2018).

This Study

One aim of this study was to replicate existing VET results in a large sample across a broad age range, including children and adults aged 6–54, to establish whether visual exploration is impaired. We hypothesized that individuals with ASD would demonstrate reduced exploration (fewer images explored), more perseverance (longer fixation times per image explored), and more detail orientation (repeated fixations on the same objects), and that this would correlate with RRB severity. Further, the impact of eye-tracking features to age and sex was explored.

Novel features were created to compare the ratio of social vs. non-social images explored. An increased preference for nonsocial versus social images in ASD compared to TD was hypothesized and expected to be related to RRB.

Region of interest (ROI) metrics of gaze behavior are constructed by averaging spatial aspects of gaze behavior over time—discarding the more fine-grained temporal information inherent in eye-tracking behavior. These features do not account for the fact that eye movement behavior is a process that unfolds in sequence over time and may reflect active search and engagement strategies (Anderson, Anderson, Kingstone, & Bischof, 2015). The final aim of this study was to use Recurrence Quantification Analysis (RQA) (Marwan, Romano, Thiel, & Kurths, 2007) as a novel approach for characterizing dynamics of eye-scan patterns. As RQA characterizes both temporal and spatial aspects of eye movements, we hypothesized that this approach would lead to new ways of measuring and determining scan paths in ASD that reflect both within (association with RRB) and between group (ASD and TD) differences in visual processing.

RQA (Marwan et al., 2007) numerically assesses patterns of recurrence, previously characterized only graphically using Recurrence Plots (Eckmann, Kamphorst, & Ruelle, 1987). This methodology has demonstrated utility in autism research for quantifying social interactions (Fusaroli, Konvalinka, & Wallot, 2014), social motor coordination (Romero, Fitzpatrick, Schmidt, & Richardson, 2016), and stereotypical motor movements (Großekathöfer et al., 2017). The general application of RQA to analysis of eye movements has also been described (Anderson et al., 2015; Anderson, Bischof, Laidlaw, Risko, & Kingstone, 2013). However, to the best of our knowledge, it has not been used to quantify eye movements of individuals with ASD in general, or specifically during VET.

Methods

Ethical Practices

Institutional Review Boards approved the study protocol and amendments. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki, consistent with Good Clinical Practices and applicable regulatory requirements. Participants, their parents (for participants <18 years old), or legally authorized representatives provided written informed consent before joining the study. Participants also provided
assent. The study is registered at clinicaltrials.gov, NCT02299700.

**Participants**

**ASD sample.** The study enrolled participants aged ≥6 years with a confirmed diagnosis of ASD based on clinical examination and use of the Autism Diagnostic Observation Schedule, 2nd edition (ADOS-2) (Lord et al., 2012). Key exclusion criteria were a measured composite score on the Kaufmann Brief Intelligence Test-2 (KBIT-2) (Kaufman & Kaufman, 2004) of <60, and history of or current significant medical illness.

**TD controls.** As controls, the study enrolled participants, aged ≥6 years, with a score in the normal range on the Social Communication Questionnaire (SCQ) (Rutter, Bailey, & Lord, 2003), who did not meet criteria for major mental health disorder (Diagnostic and Statistical Manual of Mental Disorders, American Psychiatric Association, 2013, assessed using the Mini-International Neuropsychiatric Interview [MINI] or MINI-KID) (Hergueta, Baker, & Dunbar, 1998).

The study population, after exclusions due to technical or calibration failure, is shown in Table 1. More ASD participants were recruited due to our primary aim of establishing relationships to diagnostic scales. The population was divided into 2 age groups using 13 years-of-age as a cutoff. This separation corresponds with the Food and Drug Administration-mandated age for a specific upcoming interventional study. No significant difference in ages between TD and ASD is observed for the whole sample and 2 age groups.

**Materials**

**Visual exploration task.** We presented 12 arrays, comprised 24 static social and/or nonsocial images (see Sasson et al., 2008 for a full description of stimuli): 6 *social arrays* included 12 social and 12 nonsocial stimuli (either HAI objects or low autism interest [LAI] objects); 6 *object arrays* included a mix of 12 HAI and 12 LAI objects. Examples of slides containing social and nonsocial images are shown in Figures 1–4. This task was part of a large, observational, multicenter study conducted from 06 July 2015 to 14 October 2015 at 9 study sites in the US (Ness et al., 2017) consisting of passive viewing tasks. The total viewing time was around 40 min, including videos and other static stimuli presentations, divided into 3 sets, between which participants were allowed to take a break. VET arrays were interspersed between these other stimuli, presented for 10 s each, in groups of 2 or 3, with a random interstimulus interval of 1,900–2,100 msec. Each stimulus group consisted of different types of arrays. The interstimulus slide contained a cartoon image in the center designed to reorientate participants toward the screen.

**Parent-reported scales.** Parents or caregivers of individuals with ASD completed the following scales:

**Autism Behavior Inventory (ABI) (Bangerter et al., 2017)** is a rating scale developed to assess change in core and associated symptoms of autism. For this study, we focused on the ABI’s RRB domain, including subdomains corresponding to restricted interests, resistance to change, stereotypical behavior, and hypersensitivity.

**Social Responsiveness Scale 2nd (SRS-2)** (Constantino et al., 2003) identifies presence and severity of social impairment due to ASD. We considered SRS restricted interests and repetitive behavior (SRS RI and RB) subscores.

**Repetitive Behavior Scale—Revised (RBS-R) (parent)** (Bodfish, Symons, & Lewis, 1999) is a 43-item scale to indicate occurrence of repetitive behaviors and degree to which a behavior is a problem. The RBS-R assesses five categories of repetitive behavior (motor stereotypy, repetitive self-injury, compulsions, routines/sameness, and restricted interests). RBS-R Total Score and the RBS-R Restricted Behavior (RBS-R RB) Subscale were used.

The relationship between scales is shown in Table 2.

**Procedure.** Participants sat in a comfortable chair ~60 cm from a 23-in. computer screen (1,920 × 1,080 pixels). The height of the chair and screen were adjusted to ensure that participants’ eyes were level with the center of the screen. Eye-tracking data were collected using Tobii X2 eye tracker, with a sampling rate of 30 Hz, mounted below the screen. iMotions Biometric Research Platform (https://imotions.com/) was used for stimuli presentation, data synchronization, and automatic calibration. Participants were allowed to freely observe stimuli. Before each experimental set, a 5-point calibration procedure, consisting of presentation of animated cartoon characters paired with an auditory cue, was performed aiming for mean distance of measured gaze data from the target point of <0.5° (visual degrees).

**Analyses.** ROIs were manually drawn around each image allowing ~0.75° margins. Fixations were identified using a velocity-based Binocular-Individual Threshold algorithm (van der Lans et al., 2011), where minimum number of samples a fixation should consist of and maximum number of consecutive samples not tracked within a fixation were set to 3. The following spatial features were estimated: exploration (number of images fixated on per array), perseveration (sum of duration of fixation for each image), and detail orientation (average number of fixations per image explored); and they were averaged across selected stimuli/arrays.

Recurrence Plots are symmetric N × N matrices estimated for each participant and each VET array separately, where N is the number of fixations. Elements of these matrices r_{ij} are equal to 1 if i th and j th fixations have a distance between them less than a threshold, ε, and
0 otherwise. We chose $\varepsilon = 80$ pixels, which approximately corresponds to the size of images visualized in VET arrays. To quantitatively compare between different eye-scan patterns, the following RQA measures were used: recurrence rate (RR), center of recurrence mass (CORM), determinism (DET), and laminarity (LAM). These metrics

Table 1. Participant Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All participants</th>
<th>&lt;13 years old</th>
<th>≥13 years old</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ASD, $n = 129$</td>
<td>TD, $n = 40$</td>
<td>ASD, $n = 65$</td>
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<tr>
<td>Gender, $n$ (%)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>99 (76.7)</td>
<td>26 (65)</td>
<td>53 (81.5)</td>
</tr>
<tr>
<td>Female</td>
<td>30 (23.3)</td>
<td>14 (35)</td>
<td>12 (18.5)</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>14.5 (7.8)</td>
<td>16.4 (13.3)</td>
<td>9.4 (2.1)</td>
</tr>
<tr>
<td>Race, $n$ (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>106 (82.2)</td>
<td>33 (82.5)</td>
<td>56 (86.1)</td>
</tr>
<tr>
<td>Black or African American</td>
<td>5 (3.9)</td>
<td>2 (5)</td>
<td>1 (1.5)</td>
</tr>
<tr>
<td>Asian</td>
<td>4 (3.1)</td>
<td>0</td>
<td>3 (4.6)</td>
</tr>
<tr>
<td>Multiple</td>
<td>8 (6.2)</td>
<td>3 (7.5)</td>
<td>3 (4.6)</td>
</tr>
<tr>
<td>Other</td>
<td>4 (3.1)</td>
<td>0</td>
<td>1 (1.5)</td>
</tr>
<tr>
<td>Missing/unknown</td>
<td>2 (1.5)</td>
<td>2 (5)</td>
<td>1 (1.5)</td>
</tr>
<tr>
<td>ADOS CSS total score, mean (SD, range)</td>
<td>7.6 (1.7, [4–10])</td>
<td>–</td>
<td>7.5 (1.7, [4–10])</td>
</tr>
<tr>
<td>KBIT-2 IQ composite score, mean (SD, range)</td>
<td>99.4 (20.1, [60–140])</td>
<td>–</td>
<td>103.4</td>
</tr>
</tbody>
</table>

ADOS CSS = Autism Diagnostic Observation Schedule, 2nd edition, comparison score; ASD = autism spectrum disorder; KBIT-2 = Kaufmann Brief Intelligence Test-2; TD = typically developing.

Figure 1. RQA features: recurrence rate (RR). Circles surround examples of fixations, which will be considered as laying in close proximity to each other. Fixations, distanced less than a radius $\varepsilon$ of these circles, are considered as refixations and counted during RR estimation. While information of fixation proximity within blue circles contributes to detail orientation and to RR, red circles (centered at fixations #4 and 40), that span exploration of neighboring images, characterize contribution to RR only.
Figure 2. RQA features: center of recurrence mass (CORM). Red circles surround fixations, which are consequent in time (fixations #16–18 and fixations #8–9,11–14), and contribute to smaller CORM. Blue circles surround fixations, which are more distant in time. The latter indicates that it took more time for a participant to refixate on the same area, which led to increased CORM.

Figure 3. RQA features: determinism (DET). Eye-scan pattern within blue ellipsoid represents repeated shifting of gaze between images. For example, pairs of consecutive fixations #12–#13 (green) and #15–#16 (red) show the same repetitive gaze pattern, represented as diagonal element $r_{12,15^213,16}$ in recurrence plot. DET quantifies the relative amount of such repetitive patterns (diagonal element in recurrence plot) among all fixations.
quantify the relative number of refixation to the same area (RR) and measure whether refixations occur close or far apart in a fixation sequence (CORM). DET and LAM measure finer temporal structures, indicating sequences of saccades that are repeated (DET) and points at which detailed inspections of an image reoccur (LAM) (Anderson et al., 2013).

- **RR** was estimated as 
  \[ RR = 100 \frac{2R}{N(N-1)} \]
  where 
  \[ R = \sum_{i=1}^{N-1} \sum_{j=i+1}^{N} f_{ij} \]
  This measure described the percentage of recurrent fixations during observation of a stimulus (Fig. 1).

- **CORM**, estimated as 
  \[ CORM = 100 \frac{\sum_{i=1}^{N-1} \sum_{j=i+1}^{N} (j-i)f_{ij}}{(N-1)R} \]
  measured distance from center of gravity to the identity line on a recurrence plot, normalized to have the highest value of 100. CORM quantified averaged refixation timing, that is, smaller CORM indicates that refixations on the same area occurred closer in time than during the case when CORM is higher (Fig. 2).

- **DET**, estimated as 
  \[ DET = 100 \frac{|D_h|}{R} \]
  where \( D_h \) is the set of diagonal lines on a recurrence plot. This measure represents percentage of repeating gaze patterns during stimulus presentation. For example, Figure 3 shows that a participant first fixated on the image left to the center of the VET array (fixation #12) and then on the image in the upper right of the VET array (fixation #13). Later in time, he/she fixated on the same image to the left from the center of the VET array (fixation #)

### Table 2. Pearson Correlation Between RRB Scales and Subscale Considered for This Study

<table>
<thead>
<tr>
<th></th>
<th>ABI RRB restricted interests</th>
<th>SRS RI and RB</th>
<th>RBS-R total</th>
<th>RBS-R RB</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABI RRB</td>
<td>( r = 0.79, p &lt; 0.001 )</td>
<td>( r = 0.75, p &lt; 0.001 )</td>
<td>( r = 0.79, p &lt; 0.001 )</td>
<td>( r = 0.67, p &lt; 0.001 )</td>
</tr>
<tr>
<td>ABI RRB restricted interests</td>
<td>( r = 0.62, p &lt; 0.001 )</td>
<td>( r = 0.66, p &lt; 0.001 )</td>
<td>( r = 0.71, p &lt; 0.001 )</td>
<td>( r = 0.63, p &lt; 0.001 )</td>
</tr>
<tr>
<td>SRS RI and RB</td>
<td>( r = 0.71, p &lt; 0.001 )</td>
<td>( r = 0.63, p &lt; 0.001 )</td>
<td>( r = 0.84, p &lt; 0.001 )</td>
<td></td>
</tr>
<tr>
<td>RBS-R Total</td>
<td>( r = 0.79, p &lt; 0.001 )</td>
<td>( r = 0.67, p &lt; 0.001 )</td>
<td>( r = 0.84, p &lt; 0.001 )</td>
<td></td>
</tr>
</tbody>
</table>

ABI = Autism Behavior Inventory; RBS-R = Repetitive Behavior Scale - Revised; RBS-R RB = Repetitive Behavior Scale - Revised Restricted Behavior; RRB = restrictive repetitive behaviors; SRS RI and RB = Social Responsiveness Scale Restricted Interests and Repetitive Behavior
and then again on the same image in the upper right of the VET array (fixation #16) (i.e., the initial diagonal gaze pattern was repeated). Gaze patterns such as this lead to the diagonal elements $r_{12,15}/f_{13,16}$ on a recurrence plot, which can further be quantified using DET.

- LAM is estimated as $LAM = 100\frac{H_L + V_L}{2R}$, where $H_L$ and $V_L$ are the sets of horizontal and vertical lines on a recurrence plot, respectively (Fig. 4). Vertical lines on a recurrence plot represent areas that were fixated first in a single fixation and then rescanned in detail over consecutive fixations at a later time. Horizontal lines describe instances when a particular object was scanned in detail first and then was quickly revisited. The LAM measure numerically quantifies such a recurrence pattern during stimulus observation.

For further analysis, RQA measures were averaged across different types of stimulus-arrays (either social arrays, object arrays, or all arrays together) for each participant.

All participants were included in analyses, independent of time spent looking at the screen during the VET experiment.

**Statistical inference.** As some eye-tracking features did not follow a normal distribution (especially for ASD participants, where a skewed or asymmetric distribution was typical), and to be more robust to outliers, we performed statistical inference based on ranks. Partial Spearman correlations corrected for sex, age, and baseline IQ score were calculated in the ASD group to assess features extracted and their associations with RRB symptom scales. Age was treated both as a continuous variable and by age group (<13 years and ≥13 years). In the latter case, age was not used during model construction. To further check whether interactions with either age or sex were linear, corresponding second-order interactions were included in the model for post-hoc analysis. Differences between TD and ASD groups were assessed on ranks using a linear regression for post-hoc analysis. Differences between TD and ASD second-order interactions were included in the model when interactions with either age or sex were linear, corresponding to age and sex groups.

In the latter case, age was not used during model construction. To further check whether interactions with either age or sex were linear, corresponding second-order interactions were included in the model for post-hoc analysis. Differences between TD and ASD groups were assessed on ranks using a linear regression for post-hoc analysis. Differences between TD and ASD second-order interactions were included in the model when interactions with either age or sex were linear, corresponding to age and sex groups.

### Results

**Parent-Reported Restricted Repetitive Behavior by Age**

Table 3 shows parent-reported RRB for the 5 scales across age groups.

### Eye-Tracking

Ratio-of-time participants attended to the screen across the 2 groups had a mean of: 88% (TD) and 83.7% (ASD); and a median of: 90.6% (TD) and 88% (ASD). 1.6% and 13.2% participants with ASD and 0% and 5% of TDs attended to the screen <50% and 70%, respectively. Differences between groups in attention to the screen were significant ($P < 0.01$ for all ages, $P < 0.001$ for age group younger than 13, and nonsignificant $P = 0.2$ for older group). For this reason, relative exploration (i.e., number of images explored normalized by total valid time on screen) was used for analysis.

**TD versus ASD Comparisons**

Table 4 (Section 1) shows the statistical significance of differences between the TD and ASD groups across features. We were able to confirm that, irrespective of age group, exploration across all arrays is lower in ASD participants ($P < 0.001$) and perseveration on HAI across all arrays is higher in the ASD group ($P < 0.01$). Further analysis showed longer HAI looking time reflects preference for HAI in ASD ($P < 0.01$ [ASD vs. TD]) for both social and object arrays, rather than avoidance of social stimuli (nonsignificant [ASD vs. TD]) for social arrays both with HAI and LAI images). There was no difference in detail orientation across all arrays between TD and ASD groups, across all ages ($P = 0.67$) or for any age subgroup. Detail orientation decreased with age ($P < 0.001$) and was higher for males ($P < 0.01$), irrespective of group membership. A significant two-way interaction between group and age emerged for detail orientation ($r = 0.32$; $P < 0.05$), suggesting that detail orientation may vary disproportionately with age in the ASD group.

Difference/ratio in perseveration between social and object images across social arrays showed that ratio

### Table 3. Parent-Reported RRB for the Five Scales Across the Age Groups Under 13 and 13 and Above

<table>
<thead>
<tr>
<th>Scale</th>
<th>Mean (SD)</th>
<th>&lt;13 years</th>
<th>≥13 years</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABI restrictive repetitive behaviors</td>
<td>2.4313 (1.2196)</td>
<td>2.1259 (1.1847)</td>
<td>0.080852</td>
<td></td>
</tr>
<tr>
<td>ABI RRB restricted interests</td>
<td>3.1947 (1.8164)</td>
<td>3.2789 (1.7316)</td>
<td>0.74399</td>
<td></td>
</tr>
<tr>
<td>SRS restricted interests and repetitive behavior</td>
<td>75.9688 (13.0614)</td>
<td>72.6429 (12.2426)</td>
<td>0.068759</td>
<td></td>
</tr>
<tr>
<td>RBS-R total score</td>
<td>32.1546 (22.1003)</td>
<td>23.602 (19.5526)</td>
<td>0.004663</td>
<td></td>
</tr>
<tr>
<td>RBS-R restricted behavior subscale total</td>
<td>4.1856 (3.3239)</td>
<td>3.2959 (2.954)</td>
<td>0.049576</td>
<td></td>
</tr>
</tbody>
</table>

ABI = Autism Behavior Inventory; RRB = restrictive repetitive behaviors; RBS-R = Repetitive Behavior Scale – Revised; SRS = Social Responsiveness Scale.
(P < 0.05) and difference (P < 0.05) in perseveration on social vs. non-social images is lower in the ASD than TD group across the two age groups. For RQA features, only RR was different between TD and ASD groups (P < 0.001), where ASD participants showed higher recurrence rate, regardless of age. No other RQA measure provided statistically significant differentiation between TD and ASD groups. However, all remaining RQA measures changed with age in both groups (with increase for LAM [P < 0.001] and CORM [P < 0.05], and decrease for DET [P < 0.001]), and were not dependent on sex.

Correlation Analyses Within the ASD Group

Table 4 (Section 2) shows the P values obtained while assessing statistical significance of the relationship between eye-tracking features and the five RRB scores within the ASD group, and we use relationship with RBS-R Total as an example in the text. In the case of the features derived from Sasson et al. (2008), only perseveration on HAI across all arrays showed a relationship with RRB scores across all ages (r = 0.16, P < 0.05). This relationship appears to be primarily driven by participants <13 years (r = 0.18 and P = 0.07). No relationship between perseveration on HAI across all arrays and RRB scores was seen for the older group (≥13 years). In addition, detail orientation showed a relationship with RRB scores for the older group only (r = 0.31, P = 0.01), but not for the younger group or across all ages.

All RQA measures showed a correlation with scores for the older group (≥13 years), but not for the younger group (<13 years). In addition, RR (r = 0.22 and P < 0.01) and CORM (r = 0.35, P < 0.05) showed a relationship with RRB across all ages, which was mainly driven by correlation in the older group (r = 0.35, P < 0.01 for RR, and r = 0.24, P < 0.05 for CORM).

Relationship Between TD and ASD With High RRB Score

As individuals with ASD vary in the extent and nature of RRB, we conducted exploratory analyses to determine if eye-tracking features found to correlate with RRB scores could discriminate between TD and ASD for participants with severe RRB. Accordingly, we split the ASD group into 2 subgroups based on a cutoff score of 80 on the SRS RI and RB scales. The subgroup with ≥80 (n = 68: 36 for <13 years and 32 for ≥13 years) was expected to differ from the TD group in RRB behavior. Table 4 (Section 3) shows statistical significance of differences between TD and the severe RRB group for all eye-tracking features considered in this study. The same features, which showed difference between TD and ASD, appear able to discriminate between TD and the severe RRB group. This pattern appeared to hold in general for both age groups. In addition, severe RRB participants had higher CORM values than TD (P = 0.06). This difference was mainly driven by the older group (P < 0.05), rather than younger (P = 0.46), suggesting developmental differences. We also found that primary object arrays yield a difference in the
CORM feature between the TD and severe RRB groups ($P = 0.01$ for all ages, $P = 0.01$ for $\geq 13$ years, and $P = 0.25$ for $< 13$ years).

**Analysis of Relationship Between of Eye-Tracking Features**

The biplot in Figure 5, constructed for features normalized to zero mean and unit variance, shows that all features used in this study could be grouped into three clusters. The first cluster included features such as exploration across all arrays, detail orientation across all arrays, perseveration on HAI across all arrays, LAM, DET, and RR. Exploration was negatively correlated with all other features within this cluster. For example, the correlation between RR and exploration was $r = -0.47$; between perseveration on HAI and exploration, the correlation was $r = -0.50$. The second cluster included novel features describing difference/ratio in perseveration between social and object images across social arrays. These two features were highly correlated with each other ($r = 0.90$), but at the same time were “orthogonal” to almost all other features (correlations with almost all other features were at a level of $|r| < 0.1$)[i.e., nonsignificant with $P > 0.1$] and the only significant correlation was at level $|r| = 0.18$ with perseveration on HAI and exploration. The third cluster included only one CORM feature. CORM was “orthogonal” to almost all features ($|r| \leq 0.04$); significant correlations were only with DET and LAM ($r = 0.26$).

**Discussion**

In this large-scale study, we validate previous findings (Sasson, 2008, 2012) that typically-developing (TD) and autism spectrum disorder (ASD) groups differ in perseveration on objects shown to be of high interest to individuals with ASD and exploration during a visual exploration experiment, suggesting that the ASD group explore significantly fewer images and spend more time looking at each high-autism-interest (HAI) image than the TD group. These features also differ between the TD and ASD group with severe restricted and repetitive behaviors (RRB). At the same time, no between-group difference was found on the detail orientation feature, suggesting that the groups do not differ in number of fixations per image explored.

We also introduced several novel features: difference/ratio in perseveration between social and object images across social arrays and a set of Recurrent Quantification Analysis (RQA) measures (RR, LAM, DET, and CORM). Difference/ratio in perseveration between social and object images across social arrays showed that perseveration on social versus nonsocial images is significantly lower in the ASD group, including those with severe RRB, as compared to individuals with typical development, suggesting that those with ASD and severe RRB, contrary to the TD group, explore nonsocial objects longer than social ones. A significant between-group difference in recurrence rate indicated that the ASD group, including those with severe RRB, return to the same image more often than
their TD peers. Additionally, for the group with more severe RRB, it takes significantly more time to refixate on the same image (CORM feature) than for the TD group. This is common for individuals with RRB, who show persistence and inability to move on from an object or topic of interest (Sasson et al., 2008; South et al., 2005).

Correlation analyses showed that relationships between features and scales are dependent on age: spatial features (perseveration on HAI objects, or difference/ratio in perseveration between social and object images) showed a stronger relationship with scales for the younger (<13 years) group, while spatiotemporal features (as RR, DET, LAM, and CORM) and detail orientation correlated more strongly with scales in the older (≥13 years) group. The general pattern observed appears to be that within the ASD group, those reported as having more severe RRB look at HAI for a longer time, and return to the same image more often and after a longer period of time compared to TD. This suggests that adults with ASD may improve in one aspect of social attention, but continue to have deficits in other, perhaps more subtle aspects, despite intervening training and experience. These deficits, then, may reflect persistent underlying sensory or neurologic deficits in ASD, which might improve with behavioral intervention, perhaps in combination with medication.

We further analyzed the relationship between the novel features to understand whether they provided additional information. We found that features proposed by Sasson et al. (2008) together with RR, LAM, and DET exhibited high degrees of relation between each other, suggesting they describe to some extent the same information. At the same time, difference/ratio in perseveration between social and object images across social arrays and CORM were orthogonal to the rest of the features and between each other, suggesting that they provide additional, previously uncharacterized information.

Application of RQA Techniques

Application of RQA may hold some advantages in that it does not require drawing of prespecified ROIs, but there are other features of the analysis that need to be predetermined when applying the approach outside of an exploratory context. For example, RQA analysis depends on the selection of \( \varepsilon \) used for construction of recurrence plots. In our analysis, we used \( \varepsilon = 80 \), which approximately corresponds to the size of images on the arrays. We also performed analyses using \( \varepsilon = 64 \) and \( \varepsilon = 48 \). While similar conclusions were reached with \( \varepsilon = 64 \) and \( \varepsilon = 80 \), several relationships disappeared when the lowest value was used, suggesting \( \varepsilon = 48 \) might be too small. This finding suggests proper selection of \( \varepsilon \) is important in RQA feature discovery for eye-tracking data. Anderson et al. (2013) proposed a method that could be used for selection of \( \varepsilon \) values, which might be considered in future studies. In addition, Anderson et al. (2013) proposed incorporating fixation durations in RQA estimation, but we did not observe any differences in our results when reanalyzing using this approach. Therefore, reporting results from a simpler approach was more parsimonious.

Limitations

This experiment was part of a larger study designed to develop measures of change in ASD. One focus was on obtaining quality data across a number of tasks, and biosensors within the ASD population, and given the heterogeneity of this group the aim was to maximize the collection of data from this sample. A TD group was added for comparison, but this was not the main focus of the study. This lead to a smaller, unbalanced, and less well characterized TD group; for example, this group was assumed to have an IQ within the normal range, and although sex was balanced across the group as a whole, the older TD group included significantly more females (\( \chi^2(1) = 5.3221, P = 0.02 \)). Frazier et al. (2017) did not find that IQ or sex differences were a mediating factor in determination of effect sizes in social attention in ASD. However, it is important to be aware of these limitations.

IQ was available for the ASD group and was included as a covariate in the model when considering relationships to scales.

No control for multiple comparison was performed in our analyses. Hypotheses around exploration, detail orientation, and preservation were prespecified, and as such analyses could be viewed as confirmatory, replicating previous findings. Novel RQA features, although showing promising results, still need further validation. This may include more complex images or dynamic videos which could establish the usefulness of RQA in quantification of eye-tracking in ASD across a range of contexts.

For correlation analyses, we used RRB scales, which are related as shown in Table 2. However, the relationship between them is not perfect, suggesting that each scale characterizes additional information and may quantify RRB in slightly different ways. We kept all five RRB scales for comparison with eye-tracking feature assessment, to account for variation between scales. If, for example, when using only one scale, correlation with an eye-tracking feature is found, this estimated relation could characterize common variance between scales (i.e., RRB factor contributing to all scales) and variance specific to this particular scale. However, when a relationship between eye-tracking features and all scales is observed, this should increase confidence that the eye-tracking feature relates to a common RRB factor. Additionally, the extent to which the relationship is specific to RRB needs to be explored further and may not be specific. For
example, there is also a relationship between social impairment and overall severity of ASD (RR and perseveration on HAI relates to SRS social communication and interaction \( p < 0.01 \), and to ADOS total score \( p < 0.01 \)). VET stimuli used in this study were developed over 10 years ago, and included dated image quality and icons. For example, an old game boy may hold specific interest for the adult group who used to own one, regardless of whether they have ASD or restricted interests. We opted to maintain the original Sasson et al. (2008) image set to replicate and validate reported findings, but researchers should be mindful that attention to specific images may be disproportionately increased in both TD and ASD groups. Given that VET worked well in discriminating between groups and correlated with RRB, we will seek to establish in future studies whether up-to-date and higher quality images yield the same results.

Another potential challenge with stimuli used in this study was matching visual complexity of the images. For example, the small image sizes made it difficult to ascertain if participants were orienting to faces or eyes versus clothes (e.g., brightly colored shirt, plaid pants). As such, this may not be a true example of social orientation and could mask greater between-group differences in social orientation.

Summary and Conclusions

Using the visual exploration task (VET), we replicated findings of reduced exploration and increased perseveration on HAI objects in a large sample of individuals with ASD, including older children and adults with ASD.

The application of RQA enabled identification of new eye-tracking features which accounted for temporal and spatial differences in viewing patterns. Both existing and novel features discriminated between ASD and TD across age groups, but different eye-tracking features were correlated with RRB in different age groups indicating that viewing patterns change with age, but maintain an association with RRB in ASD. The application of RQA features was exploratory. While it will require replication in future studies, it may provide an alternative approach for analysis of eye-tracking data in ASD, across a number of paradigms.

The inclusion of dynamic features derived from RQA has the potential for better characterization of shifting of visual attention in ASD. Limitation of analysis to static features, such as duration of attention or number of fixations, does not take into account potential global level deficits in allocation of attention, such as reduced processing speeds (Richard & Lajiness-O’Neill, 2015, Keehn, Lincoln, Müller, & Townsend, 2010) and impaired spatial orienting, which might contribute to higher level or domain-specific deficits in social communication or repetitive behaviors. Increased understanding of domain general and domain specific differences in allocation of attention could lead to more targeted intervention.

Taken together, this study provides evidence that specific components of eye-tracking may be useful endpoints in measuring diagnostic and clinical symptomology, and considered as a potential biomarker for identification and change of behaviors in ASD over the course or maturation and in response to intervention.

Disclosures

N.V.M., A.B., M.C., S.N., D.L., A.S., M.B., and G.P. are the employees of Janssen Research & Development, LLC and hold company stocks/stock options. M.G. has received research and consulting funding from Janssen Research & Development, LLC. G.D. is on the Scientific Advisory Boards of Janssen Research and Development, LLC and Akili, Inc., a consultant to Roche, has received grant funding from Janssen Research and Development, LLC. and PerkinElmer, and receives royalties from Guilford Press and Oxford University Press. R.H. received reimbursement for consultation from Janssen Research & Development, LLC. B.L. has received research grant funding from the NIH, is a consultant to Janssen Research and Development, LLC and the Illinois Children’s Healthcare Foundation, and is a board member of the Brain Research Foundation. F.S. is on the Scientific Advisory Board of and is a consultant to Janssen Research and Development, LLC, and has received grant funding from Janssen Research and Development LLC, and Roche. L.M. has nothing to disclose.

Author Contributions

M.C., A.B., S.N., D.L., A.S., N.V.M., and G.P. were involved in study design, data collection, analysis, and interpretation. All authors were involved in the interpretation of the results.

All authors had full access to all the data in the study and take responsibility for integrity of the data and the accuracy of the data analysis. All authors meet ICMJE criteria and all those who fulfilled those criteria are listed as authors.

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