Visual social attention in SYNGAP1-related intellectual disability

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RESEARCH ARTICLE

Visual social attention in SYNGAP1-related intellectual disability

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Abstract

SYNGAP1-ID is a neurodevelopmental disorder caused by a mutation of the *SYNGAP1* gene. Characterized by moderate to severe developmental delay, it is associated with several physical and behavioral issues as well as additional diagnoses, including autism. However, it is not known whether social cognitive differences seen in SYNGAP1-ID are similar to those previously identified in idiopathic or other forms of autism. This study therefore investigated visual social attention in SYNGAP1-ID. Eye movements were recorded across three passive viewing tasks (face scanning, pop-out, and social preference) of differing social complexity in 24 individuals with SYNGAP1-ID and 12 typically developing controls. We found that SYNGAP1-ID participants looked at faces less than the controls, and when they did look at faces, they had less time looking at and fewer fixations to the eyes. For the pop-out task, where social and nonsocial objects (Phone, car, face, bird, and face-noise) were presented in an array, those with SYNGAP1-ID spent significantly less time looking at the phone stimulus as well as fewer fixations to the face compared with the typically developing controls. When looking at two naturalistic scenes side by side, one social in nature (e.g., with children present) and the other not, there were no differences between the SYNGAP1-ID group and typically developing controls on any of the examined eye tracking measures. This study provides novel findings on the social attention of those with SYNGAP1-ID and helps to provide further evidence for using eye tracking as an objective measure of the social phenotype in this population in future clinical trials.

Lay Summary

Individuals with SYNGAP1-ID often show social difficulties. In this study, we examined visual social attention in this population using eye tracking. We found that, in comparison to typically developing controls, those with SYNGAP1-ID showed different looking patterns, particularly to faces. These findings provide new insights into the visual social attention of individuals with SYNGAP1-ID and may help inform future clinical trials.

KEYWORDS
autism, eye-tracking, SYNGAP1-related ID, visual social attention

INTRODUCTION

SYNGAP1-related intellectual disability (hereafter SYNGAP1-ID) is a neurodevelopmental disorder caused by pathological variation of the *SYNGAP1* gene. Truncating mutations are the most commonly reported in the literature, though others including missense and microdeletions have also been described (Berryer et al., 2013). The *SYNGAP1* gene codes for SynGAP; a brain-specific, ras-GTPase activating protein highly

expressed at excitatory synapses, which plays a major role in synaptic development, function, and plasticity (Agarwal et al., 2019). The condition is characterized by moderate to severe intellectual disability (ID), epilepsy, attentional deficits, sleep issues, behavioral problems, sensory issues, and autism (Berryer et al., 2013; Holder et al., 2019; Mignot et al., 2016; Wright et al., 2022). First reported in patients in 2009, it is one of the most commonly recognized causes of sporadic ID (Hamdan et al., 2009).

Because of its recent recognition, much is still unknown about the detailed cognitive and behavioral phenotype of this condition. Currently, the phenotype of SYNGAP1-ID has been mostly described through parent-reported questionnaires, interviews, and examination of existing diagnostic labels. However, these methods provide limited and potentially biased information about behavior and cognition. Neurophysiological techniques offer the opportunity for more reliable and accurate phenotypic assessments. One such technique, eye-tracking, presents a potentially feasible way to study cognitive processes in real time. It has the ability to capture online processing with high spatial and temporal resolution, and has been well tolerated in other neurodevelopmental and infant populations, requiring little motor or behavioral interaction (Eckstein et al., 2017; Graziola et al., 2021; Key et al., 2020).

One important area, which has the potential to be investigated with eye tracking, is how people with SYNGAP1-ID process social information, in particular their attention to social stimuli. Social attention is the spontaneous attentional bias to socially relevant stimuli such as faces and people. In typically developing individuals, this tendency is demonstrated early in childhood and lasts into adulthood (Gliga & Csibra, 2007). Social attention acts as an aid to language acquisition and emotional recognition and is thus important in the development of social and communicative skills (Johnson, 2005). These skills are likely to be impaired in individuals with SYNGAP1-ID, given that autism diagnoses have been reported in approximately half of all patients (Vlaskamp et al., 2019; Wright et al., 2022) and parent-report questionnaires have shown that those with SYNGAP1-ID demonstrate significant social differences compared with typically developing controls (Naveed et al., 2023; Wright et al., 2023).

Eye tracking has been used to examine social differences in autism more broadly, but there has only been a limited investigation into these skills for those with SYNGAP1-ID. The only SYNGAP1-ID eye tracking study to date to examine social attention showed that these individuals demonstrated significant reductions in overall attention, attentional scanning, social attention and slower speed to faces and objects, as well as increases in nonsocial preference relative to typically developing controls (Frazier et al., 2023). In regards to ASD, meta-analytic findings of social attention in ASD have revealed that individuals with ASD spend less time looking at social stimuli (Chita-Tegmark, 2016) with this most affected for stimuli that had a high social content (e.g., showing more than one person (Chita-Tegmark, 2016)). They also paid less attention to the eyes and whole face regions from human interaction stimuli than typically developing controls (Frazier et al., 2017). Similar patterns have been observed in other neurodevelopmental disorders. Eye tracking studies have shown that participants with fragile X syndrome (FXS) avoid eye regions when viewing pictures of faces (Farzin et al., 2009) and look less at faces in real-time interactions (Hall et al., 2015).

Eye tracking in populations such as FXS has been suggested for use, and used (Farzin et al., 2011; Hessl et al., 2019) in clinical trials as a measure of visual attention and pupil reactivity by way of evidence of response to treatment. Given that eye tracking is an objective, quantitative measure, less affected by bias and placebo effects, and likely to more directly reflect underlying pathophysiology of the condition than standardized parental or clinical reports, this method could be a useful tool in evaluating the success and efficacy of future putative therapeutics. It is of interest to investigate whether such a potential exists for this measure in the SYNGAP1-ID population. As such, we were first interested in the feasibility of using a lab-based eye tracking methodology in this group. This would help identify whether eye tracking could be used to contribute more fine-grained phenotypic information on this population, and the possibility of utilizing it in future research and clinical trials as a measure of treatment success. Second, there is currently limited understanding about social attention in those with SYNGAP1-ID. As such, we aimed to characterize social attention differences in SYNGAP1-ID and how they might differ from that of typically developing controls. Given the high incidence of autism, we hypothesized that those with SYNGAP1-ID would demonstrate social attention differences compared to their typically developing counterparts.

METHODS

Participants

Ethical approval for the study protocol was obtained through NHS Scotland A Research Ethics Committee. Participants were recruited through patient and family organizations (SYNGAP1 Foundation and SynGap Research Fund), through our social media channels, and from our contact database. Written informed consent was obtained for all participants, either from a parent/caregiver or the participant themselves as appropriate. SYNGAP1-ID was confirmed via genetic reports supplied by parents/carers. We were unable to obtain genetic

reports from two families. Typically developing controls were excluded if they had a neurodevelopmental condition, ID, or were aged over 16 years. Testing took place either in Edinburgh or at an alternate visited research site in the UK.

Eye tracking procedure

Participants were seated on a chair approximately 60–70 cm from the eye tracking laptop on which the stimuli were presented. Participants who were unable to sit alone were positioned on their caregiver's lap, or in their own wheelchair. Stimuli were presented on a 15.6-inch laptop monitor (1920 × 1080; 30 Hz), while eye movements were monitored using the REDn scientific eye tracking system (SensoMotoric Instruments (SMI) GmbH) to an accuracy of 0.4°. SMIs Experiment Center software was used to present stimuli and to synchronize with recorded eye movements.

Eye tracking tasks

Participants completed three passive viewing tasks (face scanning, pop-out, and social preference). The stimuli and tasks were previously employed in studies of typically developing and preterm infants (Gillespie-Smith et al., 2016; Gliga et al., 2009; Telford et al., 2016).

Task 1—Face scanning

Six photographs of faces in color with neutral expressions were presented for 10 s each, with two stimuli in each block. Stimuli consisted of three male and three female faces. (Figure 1a).

Task 2—Pop-out

A circular array of five colored stimuli was presented on a white background on the screen (Figure 1b). The stimuli consisted of one natural face image, one "face-noise" image and three nonsocial stimuli. The face-noise stimulus was a scramble of the pixels of the face stimulus in the same array. In this way, it contained the same low-level visual properties as the face stimulus, without being recognizable as a face. The nonsocial stimuli were a bird, car, and a mobile phone. There were seven presentations in total, each lasting 10 s, with either two or three presentations per block.

Task 3—Social preference

Two photographs of real-world scenes were presented side-by-side (Figure 1c). One photograph was social in nature and as such contained one or more children, while the other was nonsocial and had no children in it. There were 12 of each, presented for 5 s with either four or five presentations per block.

Prior to the start of the experiment, a five-point calibration and validation process was performed. Trials started with the presentation of an audio-visual animation (a moving geometric shape accompanied with a sound effect) presented for 1 s, which directed participants attention to the center of the screen; after which a stimulus from one of the three tasks was randomly presented. In total, there were 25 trials broken into three blocks. If required, short breaks were given between the blocks to allow the children to rest and help them focus on the task.

Standardized measures

To measure autistic traits, caregivers completed two questionnaires: (1) the Social Responsiveness Scale-2 (SRS) (Constantine and Gruber, 2005) to measure current autistic traits and (2) the Social Communication Questionnaire (SCQ)—lifetime (Rutter, 2003) to measure lifetime autistic traits.

The SRS is a parent completed questionnaire containing 65 items, which examines social abilities over the last proceeding 6 months. Each item is rated on a 4-point scale ranging from 0 (never true) to 3 (almost always true), with raw scores converted to gender-based *t*-scores. The higher the *t*-score the greater the degree of social difficulties. A *t*-score of 59 or lower is considered to be in the typical range; 60–65 mild range; 66–75 moderate range, and 76 or greater is in the severe range. *T*-scores on the SRS are classified into a total score and five symptom subscales: social awareness, social cognition, social communication, social motivation, and restricted interests and repetitive behaviors (RRB). Alongside these, there are two DSM-5 specific subscales: social communication and interaction (SCI) and RRB.

To estimate nonverbal IQ (NVIQ) the Leiter-3 International Performance Scale (3rd edition; (Roid et al., 2013)) was used. NVIQ was produced based on the scores obtained from the cognitive battery subtests (Figure ground, form completion, sequential order, and classification/analogies) of the Leiter-3. The raw scores from these subtests were converted to normalized scaled scores, which were then summed to produce an NVIQ composite.

Analysis

Areas of interest (AOI) were defined for each task (Figure 1). For the face scanning task, four AOIs were defined: eyes, nose and mouth, and nonfeature face regions (e.g., any part of the face not including eye, nose, and mouth). In the analysis, whole face denotes the

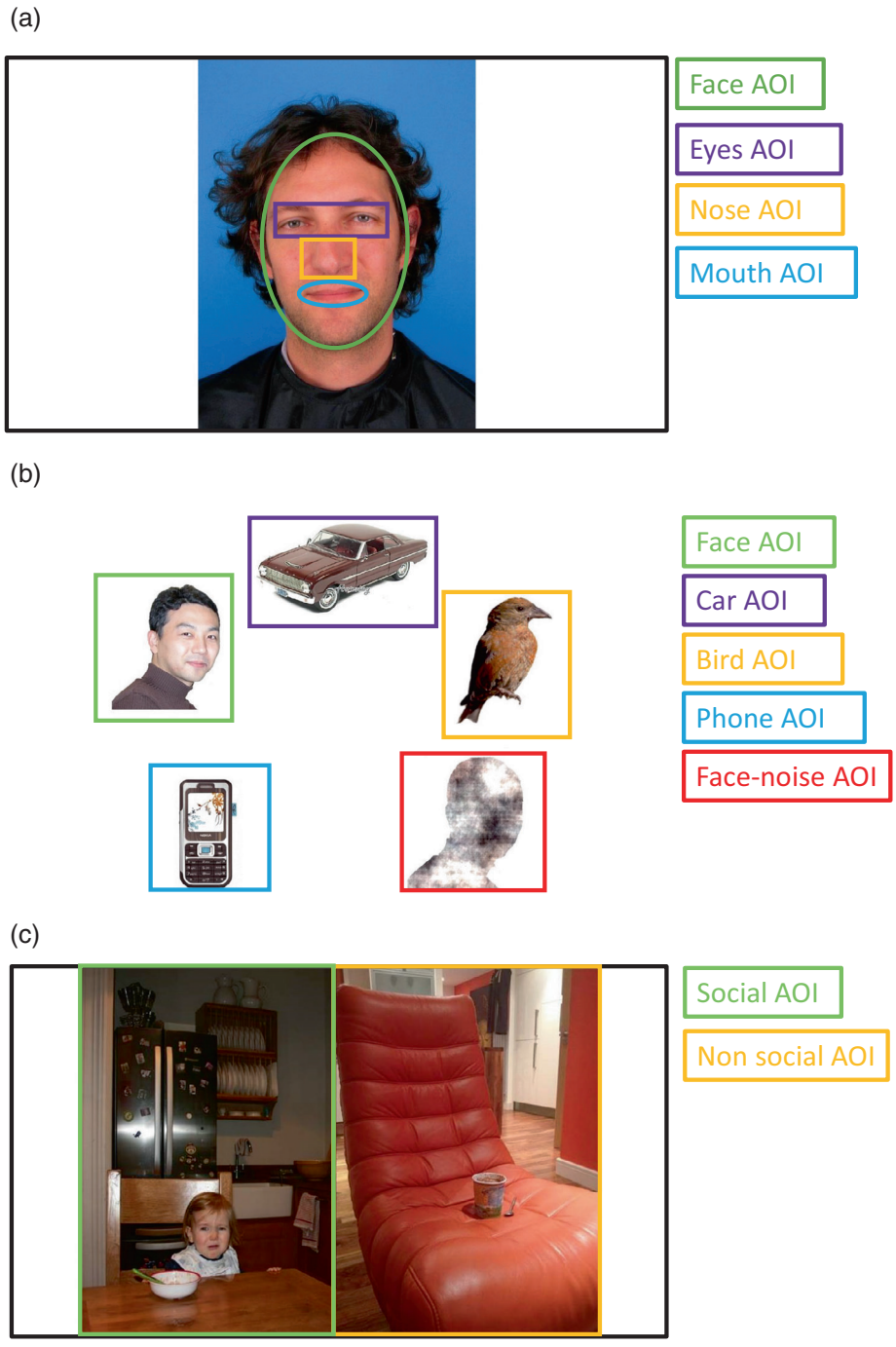

FIGURE 1 Examples of the stimuli presented and their defined areas of interests (AOIs). (a) Task 1—face scanning; (b) Task 2—pop-out; and (c) Task 3—social preference.

summed looking time (LT) to the eyes, nose, and nonfeature face regions. For the pop-out task, there were five AOIs: face, car, bird, phone, and face-noise, while for the social preference task there were two AOIs: social scene and nonsocial scene.

Fixations were identified using the event detection algorithm of the SMI BeGaze 3.7 software. Fixation detection parameters were set at a minimum duration of at least 80 ms with a maximum dispersion of two degrees. Further, any fixations of less than 500 ms were excluded, as this was considered insufficient time to denote a planned eye movement to a specific AOI (See Data S1 for analysis where fixations of less than 500 ms are not excluded). For each trial, fixations which started less than 100 ms after presentation onset were also excluded, as it is likely that these eye movements began prior to stimulus presentation and similarly failed to represent a planned movement to a specific AOI.

We examined three eye-gaze measures: proportional LT, fixation count, and time to first fixate. Proportional LT was determined as the ratio of LT at specific AOI's or AOI combinations to LT at the whole screen and was calculated as AOI LT/whole screen LT. Fixation count was determined as the sum total of the overall number of

fixations toward an AOI out of the total number of fixations during stimulus presentation multiplied by 100. Time to first fixation was calculated by averaging the time to first fixation for each AOI.

Normality was inspected both by visual inspection with QQ plots and using measures of skew. Nonnormally distributed data are reported here using medians and interquartile ranges (IQR). Given the nonnormality and small samples size, the Mann–Whitney U test was used for group-wise comparisons for each task, while Wilcoxon signed rank tests were used to examine any within group differences for AOIs. To correct for multiple comparisons, Bonferroni corrections were applied to each statistical test. Both uncorrected and corrected statistical results are reported due to the current rarity of SYNGAP1-ID eye tracking research and the difficulty in obtaining large samples for this population. Effect size (r) was calculated as the z value from the statistical test divided by the total number of observations squared.

To investigate the relationship between autistic traits and eye tracking measures for each task for those with SYNGAP1-ID, Spearman's rank correlations were computed between the eye tracking measures (proportional LT, fixation count, and time to first fixation) and the SRS summary scores (total, SCI and RRB scores).

RESULTS

Participants

A total of 24 individuals with SYNGAP1-ID and 12 typically developing controls participated in the study. See Table 1 for a breakdown of the characteristics of each group.

For the face scanning task, 23 SYNGAP1-ID and 11 typically developing controls were included in the analysis. For the pop-out task, 20 individuals with SYNGAP1-ID and 12 typically developing controls were included while for the social preference task there was 23 SYNGAP1-ID and 10 typically developing controls, respectively. We were unable to obtain SRS and SCQ scores from two individuals with SYNGAP1-ID and one typically developing control. A second typically developing control only had scores for the SRS. NVIQ was obtained using the Leiter-3 from 32 individuals (20 SYNGAP1-ID; 12 typically developing controls).

As expected, there were significant differences in SCQ and SRS scores between those with SYNGAP1-ID and typically developing controls (SCQ $U = 0$, $p < 0.001$, $r = 0.79$; SRS Total $U = 0$, $p < 0.001$, $r = 0.8$; SRS RRB $U = 0$, $p < 0.001$, $r = 0.81$; SRS SCI $U = 0$, $p < 0.001$, $r = 0.8$). There was no significant difference in age between the two groups, but there was a significant difference in NVIQ between those with SYNGAP1-ID and the typically developing controls ($U = 2$, $p < 0.001$, $r = 0.81$).

TABLE 1 Participant characteristics for each group included in the analysis.

	SYNGAP1-ID ($N = 24$)	Typically developing controls ($N = 12$)
Age (Mean)	6.6 years (SD 2.9)	6.6 years (SD 2.2)
Gender (N)	9 Male/15 Female	3 Male/9 Female
NVIQ	61.9 (SD 16.3)	107.7 (SD 13.2)
Autism formal diagnosis (N)	8	0
SCQ	19.1 (SD 6.6)	1.7 (SD 1.7)
SRS:		
Total (Mean t-score)	78.9 (SD 11)	43.6 (SD 3.6)
SCI (Mean t-score)	78.4 (SD 11.5)	43.5 (SD 4.2)
RRB (Mean t-score)	78.6 (SD 11.9)	45.3 (SD 4.2)
Total proportional looking time:		
Face scanning task (Mean)	0.17 (SD 0.11)	0.30 (SD 0.17)
Pop-out task (Mean)	0.17 (SD 0.14)	0.18 (SD 0.14)
Social preference (Mean)	0.25 (SD 0.17)	0.28 (SD 0.18)

Abbreviations: NVIQ, nonverbal IQ; RRB, restricted interests and repetitive behaviors; SCI, social communication and interaction; SCQ, Social Communication Questionnaire; SRS, Social Responsiveness Scale.

Deviation

Those with SYNGAP1-ID were found to have an average deviation of 5.0° (SD 3.3), while for typically developing controls the average was 1.1° (SD 1.7). There was a significant difference in calibration deviation ($U = 28$, $p < 0.001$, $r = 0.64$) between the groups. An additional analysis was therefore conducted limiting the groups only to those individuals with deviations of less than 2° (see Data S1).

For the face scanning task there was a significant difference in the number of valid trials (those in which participants looked at the screen; $U = 62$, $p = 0.017$, $r = 0.41$), with the SYNGAP1-ID group providing fewer valid trials for analysis than the typically developing controls. There was however a difference ($U = 63$, $p = 0.019$, $r = 0.4$) in proportional LT to the screen between the two groups for this task. For the pop-out and social preference tasks, there was no difference in number of trials included in analysis or in proportional LT at the screen between those with SYNGAP1-ID and the typically developing controls.

Task 1: Face scanning

For this task, those with SYNGAP1-ID spent proportionally less time looking at the eyes ($U = 50.5$, $p = 0.004$, $r = 0.49$) and the face ($U = 38$, $p = 0.001$, $r = 0.55$) than the typically developing controls (Figure 2a). They also made a smaller percentage of

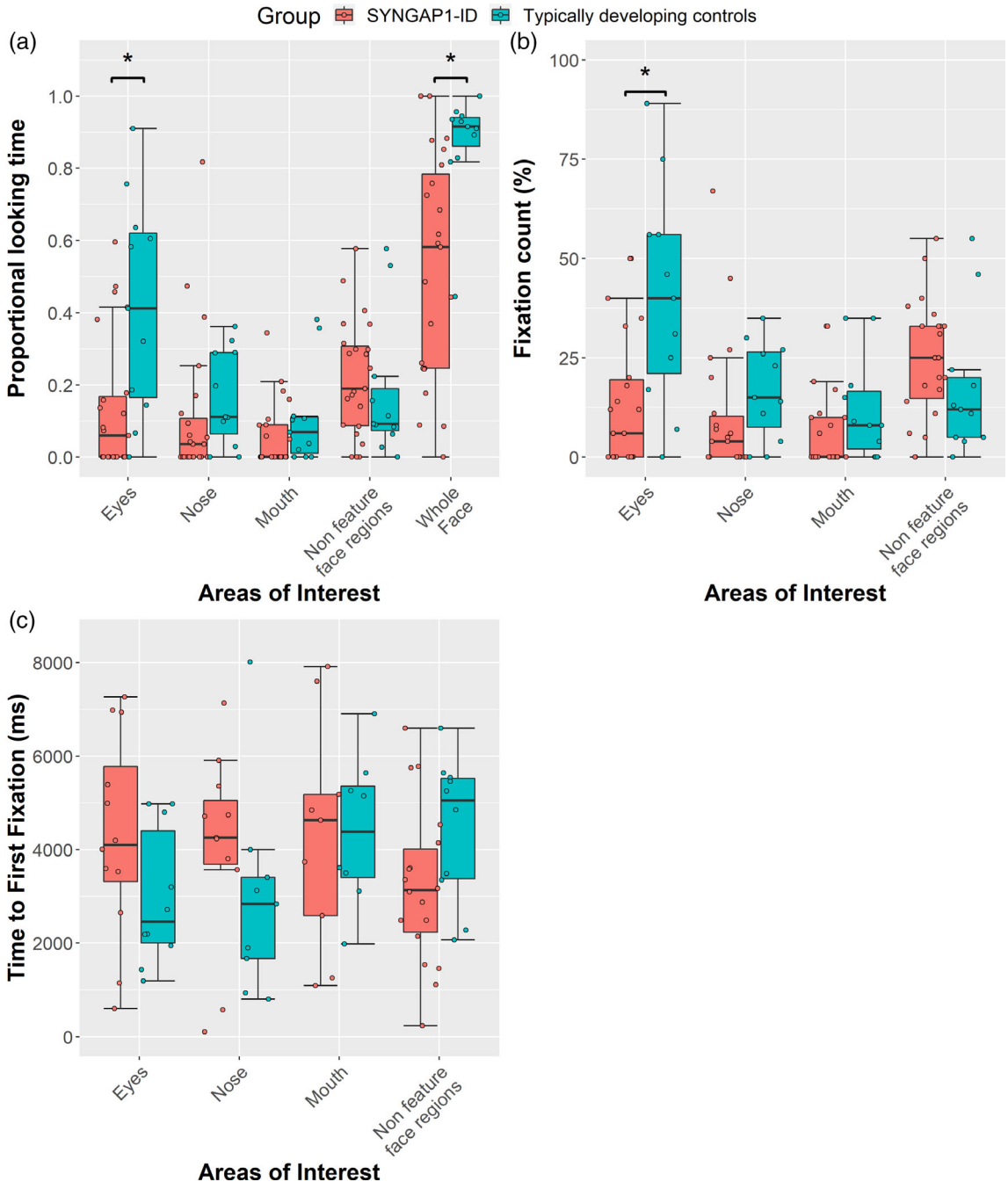

FIGURE 2 Face scanning task for those with SYNGAP1-ID and typically developing controls. (a) Proportional looking time to each defined area of interest (AOI); (b) fixation count for each defined AOI; and (c) time to first fixate on each defined AOI. *$p \leq 0.05$.

fixations to the eyes ($U = 48.5$, $p = 0.005$, $r = 0.5$) (Figure 2b). There was a significant difference in the proportion of time spent looking at the eyes compared with the time spent looking at the face between the groups ($U = 61.5$, $p = 0.014$, $r = 0.41$), with those with SYNGAP1-ID looking less at the eyes.

For those with SYNGAP1-ID on the face scanning task, there was a positive correlation between fixation count of the mouth region and SRS SCI ($r(20) = 0.447$, $p = 0.048$), indicating that those with more difficulties in SCI spent more time looking at the mouth.

Task 2: Pop-out

For the pop-out task, those with SYNGAP1-ID spent proportionally less time looking at the phone than the typically developing controls ($U = 68$, $p = 0.039$, $r = 0.36$; Figure 3a). It is worth noting that proportional LT to the face was on the boundary of statistical significance ($U = 70$, $p = 0.051$, $r = 0.34$). Those with SYNGAP1-ID also made a smaller percentage of fixations ($U = 64$, $p = 0.042$, $r = 0.36$) to the face stimulus than the typically developing controls (Figure 3b).

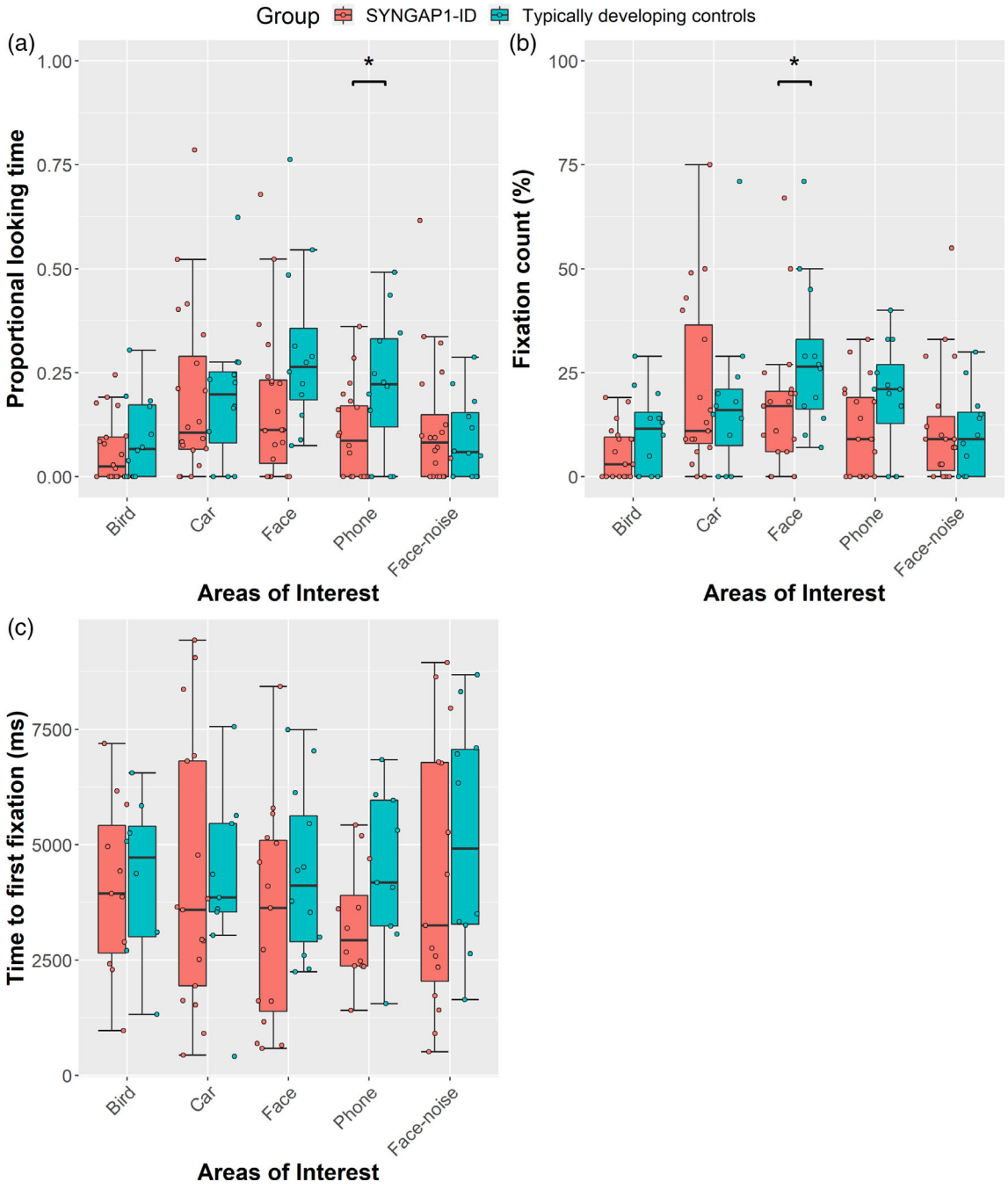

FIGURE 3 Pop-out task for those with SYNGAP1-ID and typically developing controls. (a) Proportional looking time to each defined area of interest (AOI); (b) fixation count for each defined AOI; and (c) time to first fixate on each defined AOI. *$p \leq 0.05$.

However, these did not survive after multiple comparisons correction.

For the phone stimulus, proportional LT ($r(19) = 0.514$, $p = 0.024$) and percentage of fixations ($r(18) = 0.484$, $p = 0.042$) were positively correlated with total SCQ score. For the face-noise stimulus, the percentage of fixations that those with SYNGAP1-ID made to this stimulus were significantly negatively correlated with SRS SCI ($r(18) = -0.495$, $p = 0.037$) score, while time to first fixate was negatively correlated with SRS RRB ($r(14) = -0.567$, $p = 0.034$).

Task 3: Social preference

There were no significant differences in eye tracking measures between those with SYNGAP1-ID and typically developing controls, with both showing similar patterns

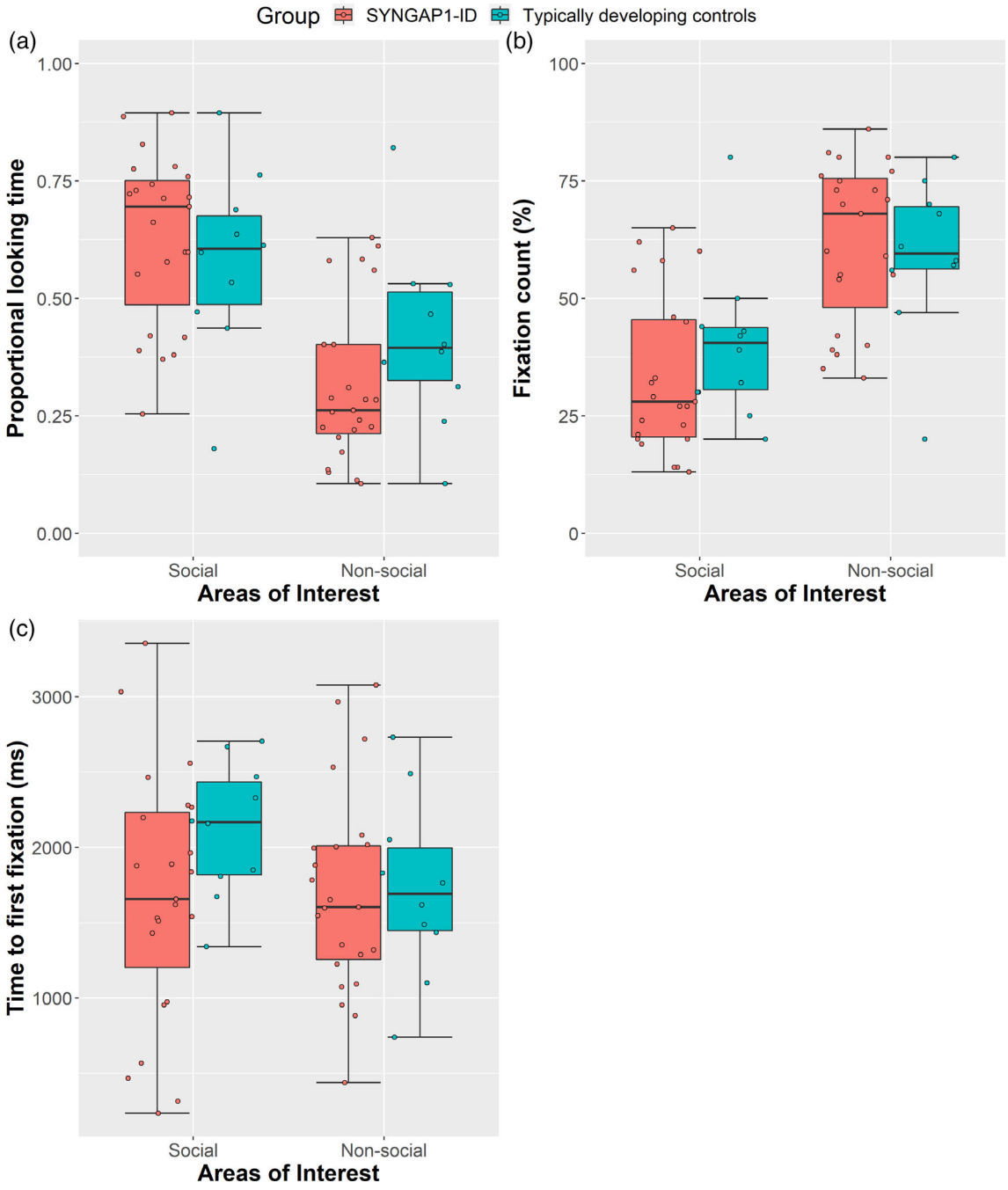

FIGURE 4 Social preference task for those with SYNGAP1-ID and typically developing controls. (a) Proportional looking time to each defined area of interest (AOI); (b) fixation count for each defined AOI; and (c) time to first fixate on each defined AOI.

of bias (Figure 4). Further, there were no significant correlations for the social preference task with scores on either the SRS or SCQ for those with SYNGAP1-ID.

DISCUSSION

In this study, we used eye tracking to examine social attention in those with SYNGAP1-ID. Social attention is likely to be impaired given that a diagnosis of autism has been reported in around 50% of this population while parent-reported questionnaires have highlighted that they exhibit social difficulties (Wright et al., 2022). However, there has only been a limited investigation into these difficulties.

We found that SYNGAP1-ID participants spent much less time overall looking toward images of faces than typically developing controls. Research has regularly reported a lack of this social attentional bias in autism, with a tendency toward reduced attention to

faces compared with controls (Fletcher-Watson et al., 2009; Rice et al., 2012). Even when those with SYNGAP1-ID were looking at the face they spent proportionally less time looking at the eyes compared with their typically developing controls. They also demonstrated a smaller percentage of fixations to the eyes. The eye region of the face has been suggested to be important in the expression of social information. Diminished attention to the eyes during social interactions is suggested to have a significant influence on development through its impact on communication (Norbury et al., 2009), theory of mind (von dem Hagen et al., 2014), and language development (Norbury et al., 2009). Evidence from autism studies have previously reported that autistic individuals fixate less on the eyes (Papagiannopoulou et al., 2014), or other nonfeature regions of the face (Pelphrey et al., 2002). Consistent with this, we did find that those with higher SRS SCI spent more time proportionally focused on the mouth region, and, when we analyzed only those individuals with a deviation of less than 2°, a significant relationship between SRS SCI and proportional LT at nonfeature regions emerged (see Data S1).

A similar finding to the face scanning task was also observed in the pop-out task with the SYNGAP1-ID group showing significantly fewer fixations to the face and a near significant reduction in proportional time spent looking toward the face ($p = 0.051$). Again, this is in line with the findings from previous autism studies (e.g., Riby & Hancock, 2009). Interestingly, those with SYNGAP1-ID were also found to look at the phone stimulus significantly less than the typically developing controls. Previously, individuals with autism have been found to show an attentional propensity toward nonsocial items (Gale et al., 2019). This tendency to look less at the social stimulus has often been accompanied with a greater interest and preference for the nonsocial stimuli (Gale et al., 2019), when both social and nonsocial objects are presented together and attributed to social avoidance. However, for our results, this is difficult to elucidate given that those with SYNGAP1-ID did not look more at the nonsocial objects to a greater extent.

For the social preference task, we found that there were no differences in preferential looking, time to first fixate, or percentage of fixations to scenes, with and without children, between those with SYNGAP1-ID and typically developing controls; with both groups showing greater LTs to the social than the nonsocial scenes. These findings initially seem inconsistent with those of the previous two tasks, but have several possible explanations. First, it is important to highlight the differences in how the individuals are presented in the social preference task compared with the other two tasks. Not only did the individuals presented in the tasks differ in age (e.g., the social preference task contained children, while the others contained adults) they also displayed differences in gaze direction. For example, in the social scenes of the social preference task, few of the scenes presented children looking directly toward the camera. In contrast, both the faces presented in isolation and face stimuli presented in an array of objects were pictures of faces with eyes directed outwards toward the participant. A previous study found that in tasks lacking eye contact and speech, autistic individuals did not show a difference in attention to the face of an actress. However, differences emerged when she "engaged" (spoke to/looked at) the participant (Chawarska et al., 2012). It is possible that there is a difference between a face stimulus with seemingly direct eye contact and a person in a complex scene with averted gaze. Second, we analyzed scenes as a whole, and not individual components. It is possible that, within the social scenes, some of the nonsocial objects were capturing attention sufficiently, and the presence of a child within the scene had no impact. Third, and related to the first point, is that this task might be delineating the difference between social preference and social anxiety. In a study of FXS, findings akin to those stated here were reported (Hong et al., 2019). They compared participants with FXS, autism and controls while looking at images of faces with emotional content, and viewing social and nonsocial scenes side-by-side. While both the autism and FXS groups showed reduced fixation to eyes for the face stimuli, only the autism group differed from controls in the side-by-side social scenes (in which the character in the scene had an averted gaze). The authors suggest disentangling social anxiety, which may manifest as gaze avoidance, from social interest in FXS. Indeed, it is not impossible that something similar is present in the SYNGAP1-ID group. Interestingly, SYNGAP1-ID and FXS have been found to show overlaps in synaptic pathophysiology (Barnes et al., 2015).

Although in our SYNGAP1-ID group only eight individuals had a formal ASD diagnosis, the majority showed high levels of autistic traits on the SRS and SCQ measures alongside visual social attention that are similar to those with idiopathic ASD. As such this may suggest that ASD in the SYNGAP1-ID population is currently potentially underdiagnosed. For some, this may represent an unmet need and they may benefit from a formal ASD evaluation and interventions or more tailored support strategies. Although it is worth noting that Mignot et al. (2016) reported an ASD diagnostic rate of 73% in their SYNGAP1 sample and so low ASD diagnostic levels may not be universal. Further to this, it has been reported that the SRS may only have limited diagnostic utility for those who have a significant ID (Gergoudis et al., 2020).

It is also important to highlight that we did not compare performance of our SYNGAP1-ID group against an idiopathic ASD group, matched for ID/developmental level or another genetic disorder. This makes it difficult to determine how specific our findings are to a SYNGAP1-ID population. It would therefore be beneficial for future studies to include these additional groups

with larger samples, potentially matched for developmental level to gain a better understanding of our results and to allow for further significant conclusions to be reached.

We were also interested generally in the feasibility of using a lab-based eye tracker in this population. While many SYNGAP1-ID participants had difficulty with the calibration process, as well as maintaining attention and interest throughout the task, we nevertheless successfully managed to obtain data from these participants. The possibility of remote eye tracking, which could be done via a tablet or remote webcam software in the participants own home, may help in future to improve inclusion numbers (Frazier et al., 2023). In addition, creating more tailored tasks to individual interests, although introducing variability, may allow a greater retention of participants and thus allow for more meaningful conclusions to be extracted about this group. Even so, this study has produced novel findings using a relatively unexplored method in this group, and the outcomes observed should provide fertile ground for future investigations into potential social differences in SYNGAP1-ID.

AUTHOR CONTRIBUTIONS

A.S., A.G.M., and D.W. were involved in the conception and design of the study. A.K. and D.W. drafted the manuscript, collected, and analyzed the data. A.M., S.E., and A.S. were involved in the interpretation of the results. All authors read and approved the final version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

D.W., S.E., and A.K. declare no conflicts interests. A.G.M. has previously received consultancy fees from G.W. Pharma and Shionogi. A.C.S. has received grants and consultancy fees from Novartis, Roche, Shionogi, and Zynerba.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

Ethical approval was received from NHS Scotland A Research Ethics Committee (19/SS/0036).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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