Archival Report

Temporal Profiles of Social Attention Are Different Across Development in Autistic and Neurotypical People

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ABSTRACT

BACKGROUND: Sociocommunicative difficulties, including abnormalities in eye contact, are core diagnostic features of autism spectrum disorder (ASD). Many studies have used eye tracking to measure reduced attention to faces in autistic people; however, most of this work has not taken advantage of eye-tracking temporal resolution to examine temporal profiles of attention.

METHODS: We used growth curve analysis to model attention to static social scenes as a function of time in a large (N = 650) sample of autistic participants and neurotypical participants across a wide age range (6–30 years).

RESULTS: The model yielded distinct temporal profiles of attention to faces in the groups. Initially, both groups showed a relatively high probability of attending to faces, followed by decline after several seconds. The neurotypical participants, however, were significantly more likely to return their attention to faces in the latter part of each 20-second trial, with increasing probability with age. In contrast, the probability of returning to the face in the autistic participants remained low across development. In participants with ASD, more atypical profiles of attention were associated with lower Vineland Adaptive Behavior Scales communication scores and a higher curvature in one data-driven cluster correlated with symptom severity.

CONCLUSIONS: These findings show that social attention not only is reduced in ASD, but also differs in its temporal dynamics. The neurotypical participants became more sophisticated in how they deployed their social attention across age, a pattern that was significantly reduced in the participants with ASD, possibly reflecting delayed acquisition of social expertise.

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Autism spectrum disorder (ASD) is a neurodevelopmental disorder affecting 13.1 to 29.3 of every 1000 children worldwide (1). Core diagnostic criteria include socio-communicative impairments, such as difficulties in nonverbal communication and reduced social interactions (2). Several theoretical frameworks have emphasized the role that reduced social attention may play in the early development of ASD (3–6)—particularly the possibility of cascading effects across development, whereby less attention to faces leads to fewer rewarding social interactions and a reduced acquisition of social expertise (7–10). Indeed, many studies have reported a reduction in attention to social cues, such as faces and eyes (11).

Despite a broad consensus in the literature for reduced social attention in ASD, there is nevertheless significant heterogeneity in findings (11,12). This not only may reflect heterogeneity between people who received a diagnosis of ASD (13), but also may be an artifact of small sample sizes, narrow age ranges, and high variability of stimuli selection and preprocessing choices (12). Furthermore, the majority of studies do not exploit the temporal precision afforded by eye tracking and simply examine averaged looking time over the duration of a stimulus. In this article, we examine social attention in a large and diverse cohort of autistic (AUT) individuals (i.e., with a clinical diagnosis of ASD) and neurotypical (NT) subjects (i.e., without a clinical diagnosis of ASD) 6- to 30-year-olds. We preserved the temporal dimension of social attention by performing a growth curve analysis (GCA) (14) on the time course of social attention within each trial. This allowed us to detect transient changes in social

attention between groups that may be lost in more traditional approaches, in which variables are collapsed over time (4,15–17).[1]

Endogenously driven changes in attention may be best evaluated during static scene viewing, in which exogenous changes in the stimulus do not confound results (18). Major models of attention distinguish orienting and maintenance stages that occur sequentially (19). On presentation of a static social scene, initial fixations to the face are likely driven relatively more by stimulus-driven, perhaps subcortically mediated orienting processes (20,21); as time elapses, attentional selection likely becomes increasingly driven by intrinsic interest and motivation (15,16). A difference in the average looking time at faces in ASD may thus reflect a failure of immediate social orienting at the start of a scene (22) or a reduction in sustained focus to social information after a period of time (17). Distinguishing these possibilities will illuminate the mechanisms underlying atypical social attention in ASD. Indeed, an emerging line of evidence from both infants and adults suggests that subcortically mediated, rapid orienting to faces is intact in ASD (4,23). In contrast, more top-down, cortically driven aspects of social attention may be altered because of reduced social engagement (24), social motivation (25), social reward (10), or altered learnability of social information (26). Distinguishing these stages by examining the temporal profile of social attention within a trial should thus 1) increase separation between group distributions and afford greater statistical power, 2) allow us to identify developmental changes in different components of social attention, and 3) more precisely delineate the mechanisms underlying atypical social attention through separating their temporal dynamics.

In the present study, we tested whether our large cohort of AUT individuals look less at faces, whether this varies over the temporal course of the stimulus presentation, and whether this changes across our wide age range. To strengthen the specification of the fixed effect, we carried out a prespecified stepwise process of selection (27). Furthermore, we combined a categorical group comparison approach with correlation analysis of dimensional data and a clustering analysis to test whether atypicalities in social attention (either absolute measures of temporal trends or degree of atypicality relative to the cohort profile) relate concurrently and/or predict clinical characteristics (28) across the AUT group in general, or within data-driven subtypes.

METHODS AND MATERIALS

Sample

We used the eye-tracking data from the multisite EU-AIMS LEAP (European Autism Interventions Longitudinal European Autism Project) study (29). The LEAP study involved 453 AUT

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[1]Alternative approaches to examining within-trial temporal dynamics exist, such as modeling categorical time bins in a traditional analysis of variance. However, any follow-up tests on individual time bins must be corrected for multiple comparisons, thus imposing a trade-off between temporal resolution and statistical power. The modeling approach used in GCA allows us to represent attentional dynamics using a mathematical function and to test differences in the shape of these dynamics in one model.

participants diagnosed with ASD and 311 NT participants; for the list of the sites, and the inclusion and exclusion criteria, see Supplement sections 1.1 and 1.2. For the full protocol details, see (29).

The main characteristics of the participants included in the analysis are reported in Table 1. Of the total 764 participants, 86.91% (n = 664) had data for the specific task targeted by the current study (see Supplement section 1.3 and Table S1 for details). Five of these participants were excluded for having >75% missing gaze samples in any of the presented trials (see Table S2 for number of excluded trials); 9 others were excluded for not having a record of the Full Scale IQ (FSIQ). The final dataset consisted of 650 participants (age range = 6–30 years; mean FSIQ = 100.46, SD = 19.65). Clinical assessments of AUT traits (Social Responsiveness Scale, Second Edition [SRS-2]) and adaptive communication and socialization (Vineland Adaptive Behavior Scales [VABS]) were collected concurrently with the eye-tracking data (time 1), and at a second visit after 12 to 24 months (time 2).

Eye Trackers, Stimuli, and Procedure

Stimuli were 6 validated photographs of people in natural settings (full description in Supplement section 2.1; original images available for consultation upon request) (29,30). Participants viewed the photographs for 20 seconds each in pseudorandom order while gaze was recorded with Tobii eye trackers (Tobii, Danderyd, Sweden) (Supplement section 2.4). The stimuli were presented full screen on the T120 (17 inches, 1280 × 1024 pixels, aspect ratio 5:4), and with black borders corresponding to a 17-inch, 5:4 display on the TX-300 (23 inches, 1920 × 1080 pixels, aspect ratio 16:9). Participants were approximately 60 cm from the screen; stimuli covered approximately 33 × 18 visual degrees of angles.

Areas of interest (AOIs) were manually drawn on each image (see Figure 1). Given our focus on social attention, analyses were focused on the proportion of looking on the "head"—encompassing hair, upper, and lower face (31)—relative to the whole scene.

The eye-tracking session began with online feedback as to the participant's position in front of the eye tracker. The experimenter positioned the participant in the center of the eye tracker headbox (32). A 5-point calibration sequence was run (see Supplement section 2.2), followed by the task battery; the progression between stimuli was gaze-contingent (see Supplement section 2.3).

Data Aggregation and Analysis

As a sanity check on the distribution of data quality, we tested for group and age differences in the percentage of missing values with a mixed model including the trial time course with a GCA approach; additionally, we tested differences in accuracy and the number of AOIs sampled by trial with multiple linear regression (see Supplement section 3.3 for details).

Trials and time bins with >75% missing data were excluded (see Table S2 for sample size before/after exclusion); the proportional looking time (PLT) (equal to samples in AOI/total valid samples) on the head was calculated in 1-second bins for each stimulus (see Supplement section 3.2 for details).

Table 1. Descriptive Statistics of the Sample

Group	Time	NT Group	AUT Group	Between-Group χ^2 (*df*), *p*	Group Difference (Cohen's *d* Effect Size)[a]
Total Participants, *n*	1	273	377		
	2	243	346		
Female, *n*; Male/Female Ratio	1	94; 1.90	105; 2.5	2.92 (1,650), .09	
	2	88; 1.76	99; 2.49	3.46 (1,589), .06	
Age, Years, Mean (SD)	1	17.35 (5.89)	16.75 (5.68)		0.03
	2	16.78 (5.71)	16.26 (5.44)		0.03
Full Scale IQ, Mean (SD)[b]	1	104.28 (18.79)	97.64 (19.81)		0.28
Proportional Looking Time on Screen, Mean (SD)	1	0.84 (0.16)	0.80 (0.18)		0.002
SRS-2 T-Score, Mean (SD)	1	48.38 (9.45)	72.25 (11.78)		1.29
	2	46.12 (8.15)	73.11 (10.86)		1.58
VABS					
Communication score, Mean (SD)	1	89.75 (25.79)	74.64 (17.37)		0.55
	2	80.49 (35.58)	73.74 (17.22)		0.20
Socialization score, Mean (SD)	1	95.37 (25.08)	69.90 (16.56)		0.94
	2	90.82 (31.60)	74.19 (16.79)		0.54
DAWBA ADHD Score, Mean (SD)[c]	1	0.46 (1.08)	2.00 (1.60)		0.09

ADHD, attention-deficit/hyperactivity disorder; AUT, autistic; DAWBA, Development and Well-Being Assessment; NT, neurotypical; SRS-2, Social Responsiveness Scale, Second Edition; VABS, Vineland Adaptive Behavior Scales.

[a]Formula: $\frac{m_1 - m_2}{s}$ with m = group mean, and s = pooled SD $= \sqrt{\frac{(n_1 - 1)s_1^2 + (n_2 - 1)s_2^2}{(n_1 - n_2) - 2}}$. Effect sizes <0.2, between 0.5 and 0.8, >0.8 correspond to small, medium, and big effects, respectively.

[b]The Full Scale IQ was standardized across countries (see Supplement section 1.2.1 for additional information).

[c]The DAWBA was used to screen for comorbidities in the current sample and is reported in terms of effect size given the possible influence of attention (but it is not otherwise mentioned elsewhere in this work).

To present the findings of a traditional analytical approach for comparability to other literature, we first conducted an analysis of variance by age and group to examine group differences in head looking (see Supplement section 3.4). Then, we used mixed GCA to investigate temporal profiles of attention (see Supplement section 3.5). Briefly, our base model included linear, quadratic, and cubic terms as fixed effects, and varying intercepts and slopes per participant; we then tested the progressive increase in fit of other models (see Supplement section 3.5.1) and selected the model with a significant decrease in Akaike information criterion but no increase in Bayesian information criterion for the rest of the analyses with the likelihood ratio test (see Supplement section 3.5.1.3). The final model included group in interaction with continuous age, and with sex and FSIQ as covariates.

Second, we examined dimensional relations to concurrent and future clinical traits measured with the SRS-2 and the VABS (see Supplement section 3.9). Specifically, we extracted measures of both individual temporal profiles (beta coefficients) and their degree of deviance from the overall temporal profile of their group (standard deviations of the random effect) from the base model. We associated those beta coefficients with both concurrent and future symptoms, and standard deviations with concurrent symptoms (given the lack of directionality of the standard deviation).

Finally, to examine whether there were discrete subgroups within the AUT group, we conducted a hierarchical cluster
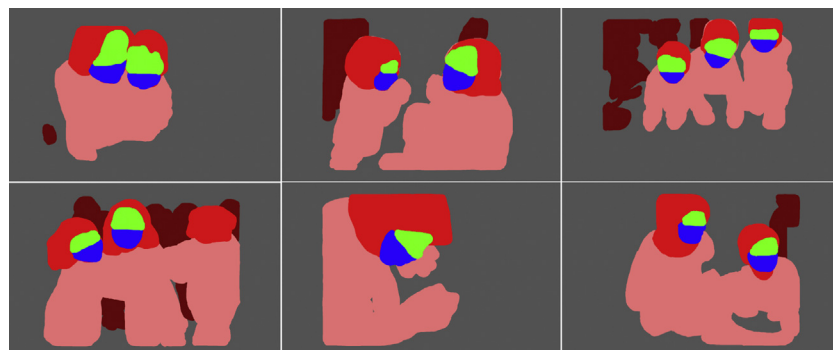

Figure 1. Areas of interest drawn on the elements of the stimulus (red = hair, green = upper face, blue = lower face, pink = body, maroon = background people). The red, green, and blue areas form the head.

Table 2. Results from the Analysis of Variance of the Proportional Looking Time on the Head by Group and Age

Variable	Sum of Squares	Mean Squared	F (df)	p Value	Adjusted p Value	Cohen's F
Group	0.13	0.11	11.17 (1)	<.001	.001	0.13
Age	0.10	0.10	9.70 (1)	.001	.005	0.12
Sex	0.05	0.05	4.99 (1)	.02	.05	0.10
Full Scale IQ (Scaled)	0.06	0.06	6.18 (1)	.01	–	0.10
Group × Age	0.04	0.04	4.15 (1)	.04	.08	0.08
Residuals	6.51	0.01	(644)			

analysis (see Supplement section 3.10). We compared phenotypic data across clusters. We ran a parallel analysis in the NT group to see whether the clusters were ASD specific. Within the AUT clusters, we reran concurrent and predictive correlations with temporal profiles and degree of deviance from the overall temporal profile. We assumed a significance threshold of p values $< .05$ (adjusted with the Bonferroni correction where appropriate)[2] throughout.

RESULTS

Quality Check

In the uncleaned dataset, the percentage of missing data diminished more with age in the NT group than the AUT group ($\chi^2_2 = 45.55$, $p < .001$) (see Table S3a and Supplement section 3.3.1 for the full list of coefficients); both groups developed a curved and descending trend with age (quadratic component), with a higher curvature in the NT group compared with the AUT group ($\chi^2_2 = 30.34$, $p < .001$) (see Table S3b). The groups did not differ in terms of slope or cubic component, configuring a similar ascending trend over the time of the trial (see Figure S1).

Group and age did not influence accuracy throughout the session and the average number of AOIs sampled by trial. The full list of coefficients and p values is available in Supplement sections 3.3.2 and 3.3.3.

The process of preparation with the threshold of 75% determined the exclusion of 228 individual trials (5.73% of total completed trials) and 5 AUT participants (see Table S2 for the full report). In order to account for the group and age differences and possible effects introduced by thresholding data of differential missingness, we tested the contribution of the covariate overall looking time to the screen to the final model, which did not result in significantly influencing temporal profiles (beta coefficient = 0.03, SE = 0.02, $p = .09$) (see Supplement section 3.5.1.3). The robustness of this finding echoes the small effect size of the group difference in overall time looking at the screen (Cohen's $d = 0.002$) (see Table 1).

Case-Control Comparison

Raw data per AOI are visualized in Figure S1. The analysis of variance showed greater looking at the head in the NT versus AUT groups ($F_1 = 11.17$, $p < .001$, adjusted $p = .001$) and greater looking at the head with older age overall ($F_1 = 9.70$, $p = .001$, adjusted $p = .005$). An age × group interaction, indicating

a developmental change in the NT group that was diminished in the AUT group just below the significance level ($F_1 = 4.15$, $p = .04$), did not resist correction for multiple comparisons (adjusted $p = .08$) (Table 2 and Figure 2).

Temporal and Developmental Profiles (GCA)

Model Selection. With the likelihood ratio test, we selected a final model with group modulated by age as fixed effect, and sex and the FSIQ as covariates (Akaike information criterion = 46331.83, Bayesian information criterion = 46588.43, degree of deviance = 46275.83; $\chi^2 = 5.91$, $p < .001$). The formula of the final model is reported in equation 1. For a full list of the outputs, see Tables S6–S10.

$$\text{Equation 1: } y_{i,j,s} = \beta_0 + \beta_1 x_{ij} + \beta_1 x_{ij} z_i + k_1 + k_2 + \beta_{0ij} + \beta_{0i|j} + \beta_{0j}$$
$$+ \beta_{0s} + \beta_{1i} x_{ij} + \beta_{1i} x_{i|j} + \beta_{1j} x_j + \varepsilon_{ij} + \varepsilon_{i|j} + \varepsilon_j + \varepsilon_s$$

where $y_{i,j,s}$ = proportional looking time on the head of the ith participant (i) nested in the jth site (j) for the sth stimulus (s), β_0 = fixed intercept, β_1 = fixed group slope, x_{ij} = polynomials up to degree 3 at site j for the ith participant, z_i = age of the ith participant, k_1; k_2 = covariates (sex and FSIQ), β_{0ij} = random intercept for the ith participant at site j, $\beta_{0i|j}$ = random intercept for the ith participant within one site j, β_{0j} = random intercept at site j, β_{0s} = random intercept for the sth stimulus, $\beta_{1i} x_{ij}$ = random slope at site j for the ith participant, $\beta_{1i} x_{i|j}$ = random slope for the ith participant within one site j, $\beta_{1j} x_j$ = random slope at site j, ε_{ij} = overall variability, $\varepsilon_{i|j}$ = variability within one site j, ε_j = site variability, and ε_s = stimulus variability.

Growth Curve Analysis. The overall PLT on the head was significantly above zero ($\sim 34\%$ on average, SE = 5.71, $p < .001$; 95% confidence interval [CI], 23.48 to 45.86) (see Table S12). The significant, negative slope indicated that the average PLT decreased across the trial (beta coefficient = −16.16, SE = 3.06, $p < .001$; 95% CI, −22.17 to −10.16). The significant and positive quadratic component indicated a U shape, with attention on the head being high initially (beta coefficient = 6.94, SE = 2.79, $p = .02$; 95% CI, 1.47 to 12.41).

The average height of PLT (i.e., the intercept) varied by group and age ($\chi^2_2 = 20.98$, $p < .01$); there was a greater increase in the NT intercept (overall looking) with age (beta coefficient = 0.33, SE = 0.07, $p < .001$; 95% CI, 0.18 to 0.48) than in the AUT intercept (beta coefficient = 0.19, SE = 0.07, $p = .01$; 95% CI, 0.04 to 0.33). The slope and quadratic components did not significantly vary with group or age

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[2]Adjusted p value = p value/number of comparisons (12 = 4 terms × 3 variables for each of the 3 independent hypotheses, as specified in Supplement section 3.9).

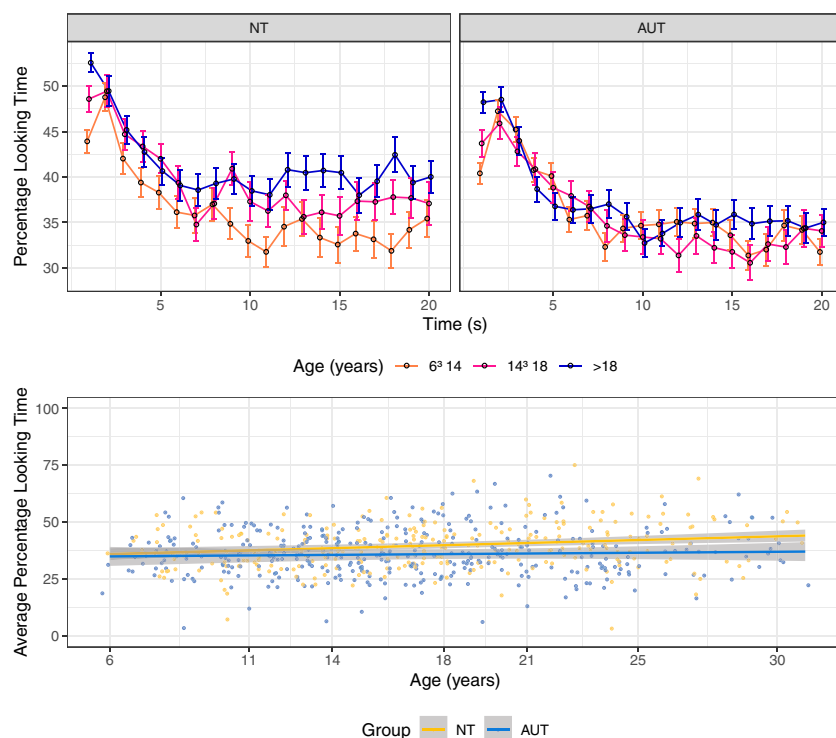Temporal and Developmental Profiles of Social Attention

Figure 2. **(A)** Group-level averages and 95% confidence intervals of the observed proportional looking time on the head over the course of the trial by group and putative age group. **(B)** Change in linear slope by group and age (interaction term) with 95% confidence intervals (line). AUT, autistic; NT, neurotypical.

(slope [$\chi^2_2 = 3.56$, $p = .16$], quadratic component [$\chi^2_2 = 1.11$, $p = .57$]), indicating a similar early orienting response to the face and following rate of decay. The groups did differ by age in the cubic component ($\chi^2_2 = 9.76$, $p = .007$). The negative beta coefficient for the effect of age in the cubic component in the NT group (beta coefficient = -0.36, SE = 0.12, $p < .001$; 95% CI, -0.60 to -0.12) indicated an age-related increase in the late-trial rise in social looking (see Figure 3A). The beta coefficient for the effect of age in the AUT group was less negative, and nonsignificant (beta coefficient = -0.23, SE = 0.12, $p = .06$; 95% CI, -0.47 to 0.01). Note that, on the one hand, the standard error of the effect of age in the Cubic component in the NT group (0.12) was not close to the beta coefficient (-0.36), suggesting a robust and consistent effect; on the other hand, the SE of the effect of age in the cubic component in the AUT group (0.12) was half the beta coefficient (-0.23). This means that with increasing/older age, the cubic component did not increase as consistently in the AUT vs NT group, resulting in overall diminished social attention at the end of the trial (see Figure 3A).

Association Between Interindividual Differences in Temporal Profiles and Symptoms

We found no significant correlations in the NT group (see Table 3 and 4). Three significant correlations of moderate size remained in the AUT group after Bonferroni correction for multiple comparisons within each hypothesis (see Supplement section 3.9 for details). Specifically, estimates

of conditional standard deviations (degree of atypicality) in the quadratic and cubic components of the dynamic temporal profile of attention correlated negatively with the VABS communication score (quadratic [$r = -.17$, adjusted $p = .03$], cubic [$r = -.17$, adjusted $p = .03$]) (see Table 4 and hypothesis 2 in Supplement section 3.9). For higher scores in the VABS communication domain, the degree of atypicality for each component was smaller, i.e., more consistent with the average looking behavior of the overall sample. Conversely, lower-scoring individuals tended to have larger standard deviations, thus showing more dispersed temporal profiles (see Figures 3B and 4). However, the lack of a significant relation to the beta coefficients (hypothesis 1 in Supplement section 3.9) indicated that this correlation was not specific to low or high levels of social attention; rather, it is the degree of deviation from the overall sample that is most informative. We found no significant correlations with the change in the VABS communication and socialization scores between time 2 and time 1, nor with the beta coefficient and the conditional standard deviations (Table 5 and hypothesis 3 in Supplement section 3.9).

Cluster Analysis and Partial Correlations Within the Clusters

The separation score between clusters (silhouette width) justified 2 clusters with maximum separation across all four components (Figure 5A and Table S14). In terms of temporal profiles of social attention, cluster 1 (92% of the AUT group)
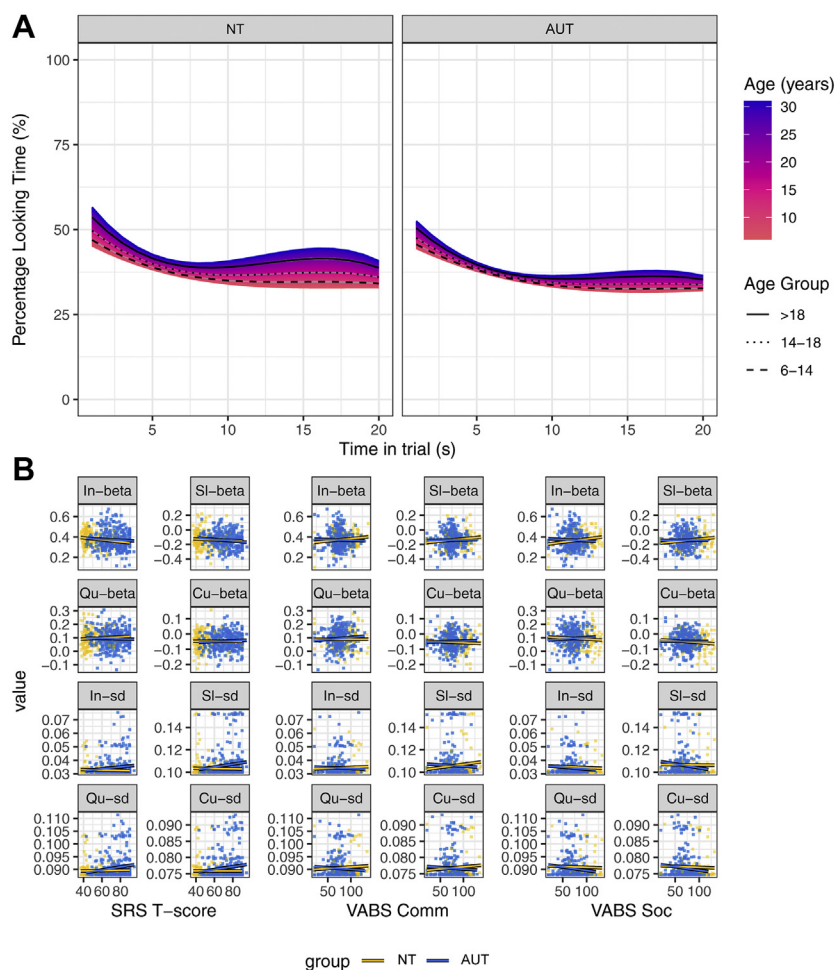
A

Figure 3. **(A)** Fitted curves representing the relationship between proportional looking time, group, and age; changes of the curve represent changes of the probability to fixate the head over the course of the trial at each unit of change of age (1 year, 6–30 years). The curves are estimated through a bootstrapped distribution for the fixed effects (1000 simulations). The superimposed lines represent the predicted intervals averaged across three putative age groups with 95% confidence intervals. **(B)** Scatterplots and concurrent linear relationships between beta coefficients and clinical variables at time 1 and conditional standard deviations (sd) and clinical variables at time 1. AUT, autistic; Comm, communication; Cu, cubic; In, intercept; NT, neurotypical; Qu, quadratic; Soc, socialization; Sl, slope; SRS-2, Social Responsiveness Scale, Second Edition; VABS, Vineland Adaptive Behavior Scales.

showed a slight U-shaped profile (Figure 5B). In contrast, cluster 2 (8% of the AUT group) showed a markedly steep decrease in head looking as a function of time (Figure 5B). The average age, FSIQ, SRS-2 T-score, VABS scores, and proportion of valid trials largely overlapped between clusters (see Table S15). Performing the same steps in the NT subset did not identify a cluster that resembled cluster 2 (see Figure 5C).

We also performed within-cluster age-corrected partial correlations in the AUT group between the beta coefficients of each component and concurrent and prospective SRS-2 and VABS scores (see Figure 5D for SRS-2). We found no significant correlation in cluster 1 for either concurrent or prospective clinical scores (see Table S16). In cluster 2, the SRS-2 scores at time 1 were positively correlated with the quadratic component ($r = .71$, adjusted $p = .01$), indicating a higher curvature in the likelihood of fixating the head as a function of symptom severity.

DISCUSSION

In the present study, we investigated how the temporal profile of social attention varies in typical and atypical development

across a wide age range in a large group of individuals with and without a diagnosis of ASD. The analysis of overall looking time indicated the expected pattern of less looking to social content (faces) in the AUT group as a whole, with a developmental increase in the NT group that was just below the significance level but did not resist correction.

By applying a GCA to spontaneous looking, we were able to tie this change in overall looking to two aspects of the temporal profile that emerged over developmental time in the NT group but not in the AUT group, enhancing the separation between the groups. The GCA confirmed greater overall looking that increased with age in the NT group relative to the AUT group (effect of intercept, and interaction with age).

Further, it indicated that transient orienting to the face (the quadratic component) did not differ between the groups. Finally, older NT participants were more likely to return to looking at the head after the decay of the initial attention-grabbing effect (represented by the cubic component), possibly reflecting successive components of social attention. This effect was substantially diminished in AUT adults, indicating the involvement of different attentional components separated by distinct temporal dynamics. We exclude that this

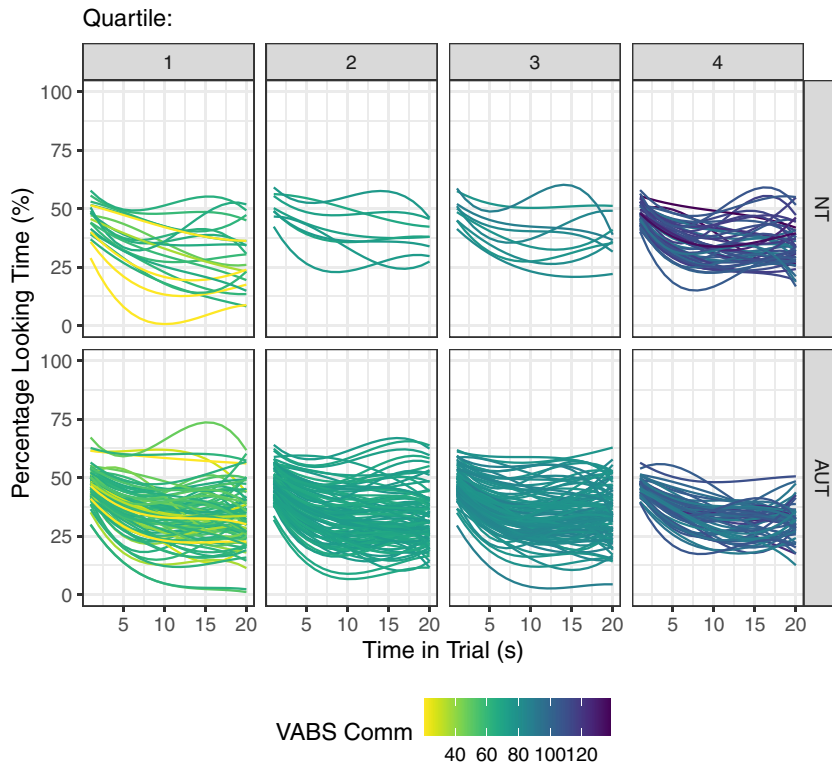Temporal and Developmental Profiles of Social Attention

Figure 4. The curves represent the individual predicted values for each autistic participant (bootstrapped distribution for the random and fixed effects with 1000 simulations), divided and sorted by the quartile proportions of the Vineland Adaptive Behavior Scales (VABS) communication (Comm) scores. The color codes indicate higher/lower VABS Comm scores. AUT, autistic; NT, neurotypical.
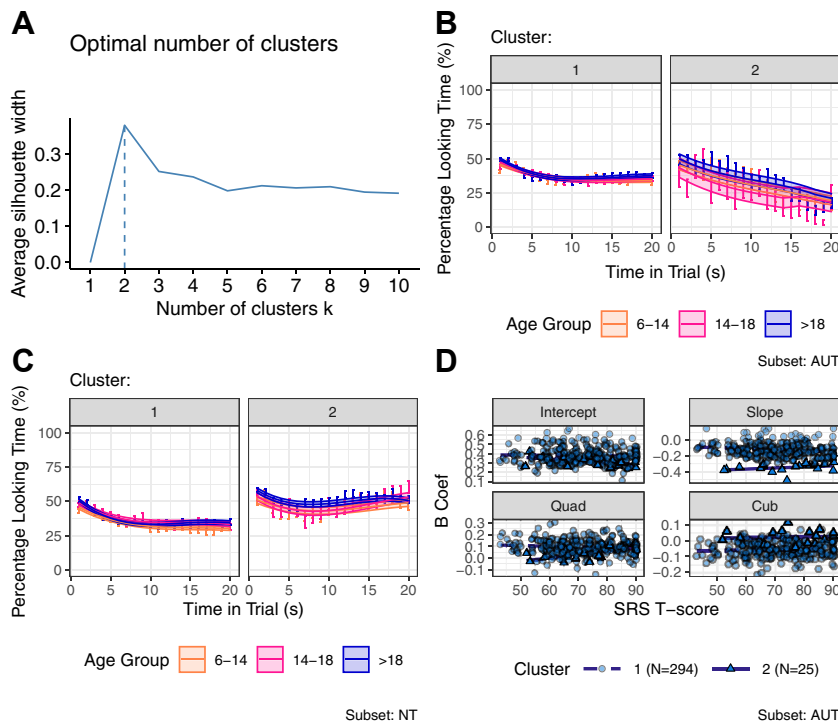

Figure 5. **(A)** Silhouette plot and **(B)** fitted curves and prediction intervals (bootstrapped distribution for the random and the fixed effects with 1000 simulations) of percentage looking within the two clusters and by age across the duration of the trial for the autistic (AUT) group. **(C)** Fitted curves and prediction intervals (bootstrapped distribution for the random and the fixed effects with 1000 simulations) of percentage looking within the two clusters and by age across the duration of the trial for the neurotypical (NT) group. **(D)** Scatterplots and concurrent linear relationships between the beta coefficients and the Social Responsiveness Scale, Second Edition (SRS) within the clusters. B Coef, beta coefficient; Cub, cubic; Quad, quadratic.

Table 3. Available Data Points, Spearman Correlation Coefficients, and Nominal and Bonferroni-Adjusted *p* Values Between the Beta Coefficients and the Clinical Variables at Time 1

Variable	Group	Component	n	Spearman's ρ	p Value	Adjusted p Value
SRS-2 T-Score (Time 1)	NT	Intercept	146	−.12	.14	1.00
		Slope	146	−.07	.41	1.00
		Quadratic	146	.07	.44	1.00
		Cubic	146	<.001	.96	1.00
	AUT	Intercept	313	−.02	.70	1.00
		Slope	313	−.09	.10	1.00
		Quadratic	313	−.02	.71	1.00
		Cubic	313	.05	.41	1.00
VABS Communication (Time 1)	NT	Intercept	87	.11	.31	1.00
		Slope	87	.10	.36	1.00
		Quadratic	87	−.07	.54	1.00
		Cubic	87	−.05	.67	1.00
	AUT	Intercept	325	−.01	.91	1.00
		Slope	325	.06	.25	1.00
		Quadratic	325	.09	.13	1.00
		Cubic	325	.01	.87	1.00
VABS Socialization (Time 1)	NT	Intercept	86	.05	.64	1.00
		Slope	86	.05	.62	1.00
		Quadratic	86	−.11	.33	1.00
		Cubic	86	−.08	.45	1.00
	AUT	Intercept	321	−.03	.62	1.00
		Slope	321	.03	.58	1.00
		Quadratic	321	.03	.58	1.00
		Cubic	321	−.02	.77	1.00

For hypothesis 1, see Supplement section 3.9.

AUT, autistic; NT, neurotypical; SRS-2, Social Responsiveness Scale, Second Edition; VABS, Vineland Adaptive Behavior Scales.

may be explained by data missingness, given its nonsignificant contribution as covariate and its pattern of variation over time, nonoverlapping with the main model (age × group interaction with the quadratic component in the former, age × group interaction with the cubic component in the latter). Rather, this pattern is consistent with the view that stimulus-driven social orienting is intact (33) but endogenous deployment of attention to social features is diminished in ASD (34). In a dimensional analysis, the degree to which AUT individuals were more divergent in their profile of social attention correlated with poorer skills in adaptive communication. Further, the cluster analysis identified a smaller subgroup of AUT participants who showed particularly atypical social attention and a strong correlation with symptom severity. Taken together, our results provide mechanistic insights into the nature of social visual attention alterations in ASD and indicate methodologies that can improve our ability to detect meaningful links with core symptomatology.

Early Orienting to Faces

The initial high proportion of orienting to the head in both the AUT and NT groups is likely to be related to the transient effect of a stimulus-driven shift of attention. This rapid orienting to social stimuli could be mediated by both domain-specific and domain-general mechanisms. Specifically, initial fixations to a static scene can be driven by bottom-up regulation guided by salience, i.e., the distribution of local feature differences

(13,35). The head is naturally rich in high-contrast features (i.e., zones of differential luminance and color) and elements of different orientation (e.g., nose and mouth) (36). Alternatively, initial face orienting may be driven by domain-specific innate biases that channel emerging specialization under the evolutionary pressure of orienting toward conspecifics/facelike stimuli (20). In line with previous studies, our finding points in the direction of a preserved rapid orienting to faces in ASD (37).

Later Trial Dynamics

Later in a trial, fixations are more heavily influenced by factors such as motivation, relevance, and experience (38). For example, Hedger *et al.* (17) found that prolonged observation of social information was associated with a higher load of empathic traits in a typical population. Within our study, the developmental pattern observed in the NT group may thus reflect motivation to reengage with faces. The lag of this developmental progression in the AUT group may reflect altered motivation to engage with social stimuli (3) and may relate to ASD-specific alterations in a wider spectrum of social behaviors, e.g., gaze cueing and joint attention (39). Indeed, we observed concurrent relations with communication skills (see below). Alternatively, our results may reflect more general difficulties with the control of oculomotor function (40) or other domain-general features of attention (41). Habituation or boredom is less likely to explain the pattern of results, as there were no group differences in overall looking times to the stimuli. Also, the average PLT at the body, the background people, and

Table 4. Available Data Points, Spearman Correlation Coefficients, and Nominal and Bonferroni-Adjusted *p* Values Between the Conditional Standard Deviations and the Clinical Variables at Time 1

Variable	Group	Component	*n*	Spearman's ρ	*p* Value	Adjusted *p* Value
SRS-2 T-Score (Time 1)	NT	Intercept	146	.05	.54	1.00
		Slope	146	.10	.21	1.00
		Quadratic	146	.12	.14	1.00
		Cubic	146	.12	.14	1.00
	AUT	Intercept	313	.04	.51	1.00
		Slope	313	.05	.35	1.00
		Quadratic	313	.08	.15	1.00
		Cubic	313	.05	.34	1.00
VABS Communication (Time 1)	NT	Intercept	87	−.08	.44	1.00
		Slope	87	−.10	.37	1.00
		Quadratic	87	−.10	.36	1.00
		Cubic	87	−.09	.42	1.00
	AUT	Intercept	325	−.12	.03	.30
		Slope	325	−.16	<.001	.05
		Quadratic	325	−.17	<.001	.03[a]
		Cubic	325	−.17	<.001	.03[a]
VABS Socialization (Time 1)	NT	Intercept	86	−.08	.44	1.00
		Slope	86	−.11	.34	1.00
		Quadratic	86	−.15	.17	1.00
		Cubic	86	−.11	.31	1.00
	AUT	Intercept	321	−.07	.22	1.00
		Slope	321	−.11	.06	.68
		Quadratic	321	−.13	.02	.29
		Cubic	321	−.10	.07	.85

For hypothesis 2, see Supplement section 3.9.
AUT, autistic; NT, neurotypical; SRS-2, Social Responsiveness Scale, Second Edition; VABS, Vineland Adaptive Behavior Scales.
[a]Significant correlation.

the non-AOIs was mostly flat in both groups (see Figure S1), probably due to inconsistent exploration that flattens out with averaging. Independent replications will be required to dissect these possibilities.

Individual Differences and Stratification

When we examined individual differences within the AUT cohort, progressively greater atypicality of social attention within a trial was associated with poorer VABS communication scores. In terms of fixation behavior, this means that individuals who tend to be more consistent with the average looking behavior of the overall sample possess more adaptive communication skills. The VABS communication domain focuses on skills that involve verbal communication (e.g., "Says both the month and day of his birthday," "Gives complex directions with three or more steps"). Therefore, higher scores in the communication domain imply that the individual is verbal and uses language for everyday communication. Previous research has highlighted that AUT people with stronger language skills have better outcomes, including better social adaptive skills (42), providing a possible link to social attention. Significant relations between communication skills and degree of atypicality in social attention are difficult to mechanistically interpret because atypicality can reflect both less and more looking at faces, and eye tracking measures did not predict

change in communication scores over time. However, they may hold promise for the use of refined temporally resolved measures of social attention to help with symptom tracking in observational or intervention studies.

The characterization of the data-driven clusters may help to understand whether heterogeneity in the nature of atypicality is meaningfully related to symptom variation. This revealed a distinct subgroup of AUT individuals who consistently showed a steeper decline of the fixation probability to the head; within this group, a higher curvature strongly correlated with a dimensional measure of social symptom severity, the SRS-2. The SRS-2 measures a wide range of symptoms (e.g., reduced eye contact, poor coordination, lacking self-confidence) that may significantly impact social functioning. These characteristics may make social encounters difficult and sporadic, providing less experience with others (and their faces). The attentive pattern toward the face observed in this subgroup could reflect social withdrawal (15) or a more pronounced reduction self-directed experiences; dissecting these possibilities deserves further investigation.

Limitations

The use of static images enables the temporal profile of attention to be driven by intrinsic motivation rather than extrinsic cues, a valuable approach given our findings.

Table 5. Available Data Points, Spearman Correlation Coefficients, and Nominal and Bonferroni-Adjusted *p* Values Between the Beta Coefficients and the Conditional Standard Deviations and the Difference in the Clinical Variable Scores Between Time 2 and Time 1 for the AUT Group

Variable	Group	Term	n	Spearman's ρ	p Value	Adjusted p Value
VABS Communication (Time 2 – Time 1)	AUT	Beta Intercept	227	−.08	.26	1.00
		Beta Slope	227	.08	.24	1.00
		Beta Quadratic	227	.15	.03	.34
		Beta Cubic	227	.02	.76	1.00
VABS Socialization (Time 2 – Time 1)	AUT	Beta Intercept	220	−.04	.55	1.00
		Beta Slope	220	−.04	.59	1.00
		Beta Quadratic	220	.05	.43	1.00
		Beta Cubic	220	.08	.22	1.00
VABS Communication (Time 2 – Time 1)	AUT	Intercept SD	227	.11	.09	.27
		Slope SD	227	.08	.24	.72
		Quadratic SD	227	.08	.21	.63
		Cubic SD	227	.09	.20	.60
VABS Socialization (Time 2 – Time 1)	AUT	Intercept SD	220	−.04	.56	1.00
		Slope SD	220	−.03	.66	1.00
		Quad SD	220	−.02	.79	1.00
		Cubic SD	220	−.03	.62	1.00

For hypothesis 3, see Supplement section 3.9.
AUT, autistic; VABS, Vineland Adaptive Behavior Scales.

However, static images do not necessarily capture highly dynamic, everyday social encounters. Furthermore, it has been reported that dynamic scenes produce larger group differences when studying typical and atypical development (43). Future research could use GCA to examine the effect of specific events (e.g., verbal and gaze cues) that have been found to influence looking behavior in ASD (44) and define time windows of influence in terms of latency, duration, and synchrony. Another limitation was that our sample size was not large enough to model variable slopes for each stimulus within the random effect in addition to our inclusion of variable intercepts; this choice implies the assumption that the designed AOI, presented in a slightly different context, would elicit similar trends of visual attention over time. This assumption should be tested in future research with larger samples. Another notable limitation is that while measures of visual attention were related to concurrent aspects of communication skill and AUT symptoms, we did not identify any predictive relations to change in clinical symptomatology. It may be more likely that atypicalities in social attention track behavioral symptomatology, rather than mechanistically contributing to its emergence or consolidation. Furthermore, a promising future avenue of research resides in determining the combined and/or specific contribution of comorbidities, such as attention-deficit/hyperactivity disorder, to social attention in ASD (45). However, there was no evidence that general attentiveness or the presence of attention-deficit/hyperactivity disorder group differences confounded the present results. Finally, sex differences will be important to pursue in future work; here, sex proved to be a significant covariate, but the interaction with factors such as age and pubertal status should be examined across multiple settings. Addressing this question fully requires longitudinal research earlier in development.

Conclusions

This study tested the application of GCA to understand temporal profiles of social attention in autism over a wide age range, uncovering a pattern of a late-occurring return of attention to the face emerging over developmental time in NT adults but not the AUT group. Variations in motivated social attention were related to adaptive communicative skills in the wider AUT group and were correlated with symptom severity within a data-derived subgroup. These results resonate with a model of ASD that implicates altered exploration of the social environment, but they are less consistent with the proposal that early-emerging differences in social attention contribute to later behavioral trajectories (10,46). The results raise the possibility that temporally sensitive eye tracking–based measures have the potential to provide objective measures of symptom profiles in clinical contexts.

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REFERENCES

1. Baio J, Wiggins L, Christensen DL, Maenner MJ, Daniels J, Warren Z, et al. (2018): Prevalence of autism spectrum disorder among children aged 8 Years - Autism and developmental disabilities monitoring network, 11 Sites, United States, 2014. MMWR Surveill Summ 67:1–23.

2. American Psychiatric Association (2013): Diagnostic and Statistical Manual of Mental Disorders, 5th ed. Washington, DC: American Psychiatric Press.

3. Dawson G, Webb SJ, McPartland J (2005): Understanding the nature of face processing impairment in autism: Insights from behavioral and electrophysiological studies. Dev Neuropsychol 27:403–424.

4. Jones W, Klin A (2013): Attention to eyes is present but in decline in 2-6-month-old infants later diagnosed with autism. Nature 504:427–431.

5. Chawarska K, Volkmar F, Klin A (2010): Limited attentional bias for faces in toddlers with autism spectrum disorders. Arch Gen Psychiatry 67:178–185.

6. Pelphrey KA, Sasson NJ, Reznick JS, Paul G, Goldman BD, Piven J (2002): Visual scanning of faces in autism. J Autism Dev Disord 32:249–261.

7. Grossmann T, Johnson MH, Lloyd-Fox S, Blasi A, Deligianni F, Elwell C, Csibra G (2008): Early cortical specialization for face-to-face communication in human infants. Proc Biol Sci 275:2803–2811.

8. Meltzoff AN, Kuhl PK, Movellan J, Sejnowski TJ (2009): Foundations for a new science of learning. Science 325:284–288.

9. Gliga T, Jones EJH, Bedford R, Charman T, Johnson MH (2014): From early markers to neuro-developmental mechanisms of autism. Dev Rev 34:189–207.

10. Chevallier C, Kohls G, Troiani V, Brodkin ES, Schultz RT (2012): The social motivation theory of autism. Trends Cogn Sci 16:231–239.

11. Chita-Tegmark M (2016): Social attention in ASD: A review and meta-analysis of eye-tracking studies. Res Dev Disabil 48:79–93.

12. Frazier TW, Strauss M, Klingemier EW, Zetzer EE, Hardan AY, Eng C, Youngstrom EA (2017): A meta-analysis of gaze differences to social and nonsocial information between individuals with and without autism. J Am Acad Child Adolesc Psychiatry 56:546–555.

13. Amso D, Haas S, Tenenbaum E, Markant J, Sheinkopf SJ (2014): Bottom-up attention orienting in young children with autism. J Autism Dev Disord 44:664–673.

14. Mirman D, Dixon JA, Magnuson JS (2008): Statistical and computational models of the visual world paradigm: Growth curves and individual differences. J Mem Lang 59:475–494.

15. Schofield CA, Inhoff AW, Coles ME (2013): Time-course of attention biases in social phobia. J Anxiety Disord 27:661–669.

16. Shimojo S, Simion C, Shimojo E, Scheier C (2003): Gaze bias both reflects and influences preference. Nat Neurosci 6:1317–1322.

17. Hedger N, Haffey A, McSorley E, Chakrabarti B (2018): Empathy modulates the temporal structure of social attention. Proc Biol Sci 285:20181716.

18. Smith TJ, Mital PK (2013): Attentional synchrony and the influence of viewing task on gaze behavior in static and dynamic scenes. J Vis 13:16.

19. Posner MI (1980): Orienting of attention. Q J Exp Psychol 32:3–25.

20. Johnson MH, Senju A, Tomalski P (2015): The two-process theory of face processing: Modifications based on two decades of data from infants and adults. Neurosci Biobehav Rev 50:169–179.

21. Langton SRH, Law AS, Burton AM, Schweinberger SR (2008): Attention capture by faces. Cognition 107:330–342.

22. Falck-Ytter T, Von Hofsten C, Gillberg C, Fernell E (2013): Visualization and analysis of eye movement data from children with typical and atypical development. J Autism Dev Disord 43:2249–2258.

23. Johnson MH (2014): Autism: Demise of the innate social orienting hypothesis. Curr Biol 24:R30–R31.

24. Klin A, Jones W, Schultz RT, Volkmar FD (2005): The enactive mind, or from actions to cognitions: Lessons from autism. Philos Trans R Soc Lond B Biol Sci 358:345–360.

25. Pelphrey KA, Shultz S, Hudac CM, Vander Wyk BC (2011): Research review: Constraining heterogeneity: The social brain and its development in autism spectrum disorder. J Child Psychol Psychiatry 52:631–644.

26. Johnson MH (2017): Autism as an adaptive common variant pathway for human brain development. Dev Cogn Neurosci 25:5–11.

27. Harrell FE Jr (2015): Regression Modeling Strategies: With Applications to Linear Models, Logistic and Ordinal Regression, and Survival Analysis. Berlin, Germany: Springer.

28. Pickles A, Angold A (2003): Natural categories or fundamental dimensions: On carving nature at the joints and the rearticulation of psychopathology. Dev Psychopathol 15:529–551.

29. Loth E, Charman T, Mason L, Tillmann J, Jones EJH, Wooldridge C, et al. (2017): The EU-AIMS Longitudinal European

Autism Project (LEAP): Design and methodologies to identify and validate stratification biomarkers for autism spectrum disorders. Mol Autism 8:24.

30. Webb SJ, Shic F, Murias M, Sugar CA, Naples AJ, Barney E, *et al.* (2020): Biomarker acquisition and quality control for multi-site studies: The Autism Biomarkers Consortium for Clinical Trials. Front Integr Neurosci 13:71.

31. Amso D, Haas S, Markant J (2014): An eye tracking investigation of developmental change in bottom-up attention orienting to faces in cluttered natural scenes. PLoS One 9:e85701.

32. Niehorster DC, Cornelissen THW, Holmqvist K, Hooge ITC, Hessels RS (2018): What to expect from your remote eye-tracker when participants are unrestrained. Behav Res Methods 50:213–227.

33. Guillon Q, Hadjikhani N, Baduel S, Rogé B (2014): Visual social attention in autism spectrum disorder: Insights from eye tracking studies. Neurosci Biobehav Rev 42:279–297.

34. Joens EJH, Gliga T, Bedford R, Charman T, Johnson MH (2014): Developmental pathways to autism: A review of prospective studies of infants at risk. Neurosci Biobehav Rev 39:1–33.

35. Freeth M, Foulsham T, Chapman P (2011): The influence of visual saliency on fixation patterns in individuals with autism spectrum disorders. Neuropsychologia 49:156–160.

36. Simion F, Di Giorgio E (2015): Face perception and processing in early infancy: Inborn predispositions and developmental changes. Front Psychol 6:969.

37. Del Bianco T, Mazzoni N, Bentenuto A, Venuti P (2018): An investigation of attention to faces and eyes: Looking time is task-dependent in autism spectrum disorder. Front Psychol 9:2629.

38. Orquin JL, Bagger MP, Mueller Loose S (2013): Learning affects top down and bottom up modulation of eye movements in decision making. Judgm Decis Mak 8:700–716.

39. Vivanti G, Fanning PAJ, Hocking DR, Sievers S, Dissanayake C (2017): Social attention, joint attention and sustained attention in autism spectrum disorder and Williams syndrome: Convergences and divergences. J Autism Dev Disord 47:1866–1877.

40. Falck-Ytter T, Bölte S, Gredebäck G (2013): Eye tracking in early autism research. J Neurodev Disord 5:28.

41. Elsabbagh M, Volein A, Holmboe K, Tucker L, Csibra G, Baron-Cohen S, *et al.* (2009): Visual orienting in the early broader autism phenotype: Disengagement and facilitation. J Child Psychol Psychiatry 50:637–642.

42. Suh J, Eigsti IM, Canfield A, Irvine C, Kelley E, Naigles LR, Fein D (2016): Language representation and language use in children with optimal outcomes from ASD. In: Naigles LR, editor. Innovative Investigations of Language in Autism Spectrum Disorder. Washington, DC: American Psychological Association, 225–244.

43. Harrop C, Jones D, Zheng S, Nowell S, Schultz R, Parish-Morris J (2019): Visual attention to faces in children with autism spectrum disorder: Are there sex differences? Mol Autism 10:28.

44. Chawarska K, Macari S, Shic F (2012): Context modulates attention to social scenes in toddlers with autism. J Child Psychol Psychiatry 53:903–913.

45. Johnson MH, Gliga T, Jones E, Charman T (2015): Annual research review: Infant development, autism, and ADHD - Early pathways to emerging disorders. J Child Psychol Psychiatry 56:228–247.

46. Salley B, Colombo J (2016): Conceptualizing social attention in developmental research. Soc Dev 25:687–703.