Eye-tracking Reveals Abnormal Visual Preference for Geometric Images as an Early Biomarker of an Autism Spectrum Disorder Subtype Associated with Increased Symptom Severity

Supplemental Information

This study was approved by the University of California, San Diego Human Subjects Research Protection Program. Legal guardians of all participants gave written informed consent.

Sample Information

Study Time Period and Longitudinal Testing. Eye-tracking data for the independent sample was collected from 2009-2012. The eye-tracking experiment was almost always the first test administered for all toddlers, although there were rare occasions when the test order fluctuated (e.g., due to availability of the eye-tracking technician). As described in the main body of the paper, 424 toddlers attempted participation. All toddlers that participated in eye tracking during this period were included in this paper. No additional toddlers participated during the study period. Only data from the first available eye-tracking session (i.e., youngest age) was included in analyses. Toddlers that participated in eye-tracking at a young age (e.g., 12 months) were diagnostically evaluated at multiple time points until a final diagnosis could be given around age 3 years, a process which extended through 2014. Regarding the ASD sample, while many ASD toddlers were only a year old at the time of testing, all were longitudinally tracked and evaluated across multiple time points and 103 out of the 115 received a final diagnosis at age 32 months or older (mean age of final diagnosis, 40 months). The remaining 12 ASD subjects received a provisional diagnosis at a mean age of 26 months (range 18.7 - 30.7 months, SD 3.52) and were included in the overall ASD sample. As shown in Table 1 in the main body of the paper, ASD toddlers were on average several months older than other toddlers. As such, age was used as a covariate in analyses where appropriate.

Sample Referral Source. The composition of the independent sample included both referrals generated through a general population screening approach called the 1-Year Well-Baby Check-Up Approach (1) as well as community high-risk referrals. Using this latter approach, toddlers at-risk for ASD and other disorders were identified with a broadband screening instrument, the CSBS-DP-IT Checklist, at the 1-year well-baby check-up in pediatric offices and referred to our Center for further evaluation. Regardless of the referral mechanism, all toddlers referred younger than 32 months were re-evaluated every 6-12 months as appropriate until their 3rd birthday when a final diagnosis was given. Within the study sample 266 toddlers enrolled at a prediagnosis age (i.e., between 12-31 months) and 68 toddlers at final diagnosis age or older (i.e., $\geq$ 32 months).

The distribution of general population vs high risk referrals was similar between the current study and our previous study. Specifically, approximately 70% of toddlers were recruited through the 1-Year Well-Baby Check-Up Approach, and 30% were recruited through community referrals which included treatment or other service providers, self referrals based on viewing our website, signing a contact list at an autism race or other related community event, and friend/word of mouth referrals.

Diagnostic Criteria for Study Groups. Toddlers were considered *ASD* if they exceeded a specific cut off score on the ADOS *and* were considered ASD based on clinical judgment and DSM-IV criteria. Specific ADOS cut off scores were determined based on the Module (i.e., T, 1 or 2) and scoring algorithm used (i.e., verbal or non-verbal). Toddlers were considered *ASD-Feat* if they showed signs of autism, but did not receive a final diagnosis at age 3 (e.g., had a previous diagnosis of ASD at young ages but no longer met full criteria at final diagnosis age). Toddlers were determined to be developmentally delayed, *DD,* if they had either a receptive *or* expressive language delay (LD) indexed by >1 standard deviation below expected values on the language subtests on the Mullen, or a global developmental delay as indexed by >1 standard deviation below expected values on 3 or more of the subtests of the Mullen *and* the overall developmental quotient was >1 standard deviation below expected values (i.e., <85). Toddlers were considered *Other* if they did not fit into any of the other diagnostic categories (e.g., motor delay, premature birth). Toddlers were considered *TD* if they fell within the normal range on all standardized assessments during every clinical testing session. A toddler was considered a *Typ Sib*, if their test scores fell within the normal range but they had a sibling with an ASD.

Detailed Information Regarding Developmental Delay Sample. The majority of toddlers (i.e., 48) in the DD group in the independent sample had a language delay and a small number (i.e., 9) had a global developmental delay with IQs ranging from 58-80 (mean 71 $\pm$ 8.6). We first wanted to explore the impact of global developmental delay on % dynamic geometric images (DGI) fixation. *t*-tests were used to compare percent DGI fixation between the global developmental delay toddlers and the other contrast groups. Results revealed no significant difference between this group and any non-ASD contrast group. For example, % DGI fixation in global DD group was 23.5% and in TD toddlers was 22.4%, $t_{71} = .20$, $p = .84$; % DGI fixation in global DD was 23.5% and in LD toddlers was 25.8%, $t_{55} = .334$, $p = .74$. Given the small sample size of the global developmental delay toddlers and the fact there were no significant differences between these toddlers and the language delay toddlers, children from both categories were combined to arrive at the final group of “DD” toddlers.

Total Looking Time

The means and standard deviations in total looking time per group within the independent sample were as follows: ASD 50.3 sec (9.01); ASD Features 49.84 sec (9.8); DD 51.92 sec (9.05); Other 46.25 sec (9.69); TD 52.9 sec (8.05); Typ Sib 50.19 sec (9.46). Significant differences in total looking time were found ($F_{5,328} = 3.34$, $p < 0.006$). Follow up *t*-tests revealed that toddlers in the "Other" group had significantly less looking time than ASD ($t_{166} = -2.64$ $p < .009$), TD ($t_{115} = -4.06$, $p < .0001$), DD ($t_{108} = -2.79$, $p < .006$) toddlers. No other significant differences were found.

Excluded Subjects

Ninety subjects (38 ASD, 0 ASD Features, 15 DD, 13 Other, 19 TD, 2 Typ Sib and 3 toddlers with unknown diagnoses) were excluded from analyses due to insufficient looking time, parental interference, poor behavior, technical issues, dropped from study, vision loss or a

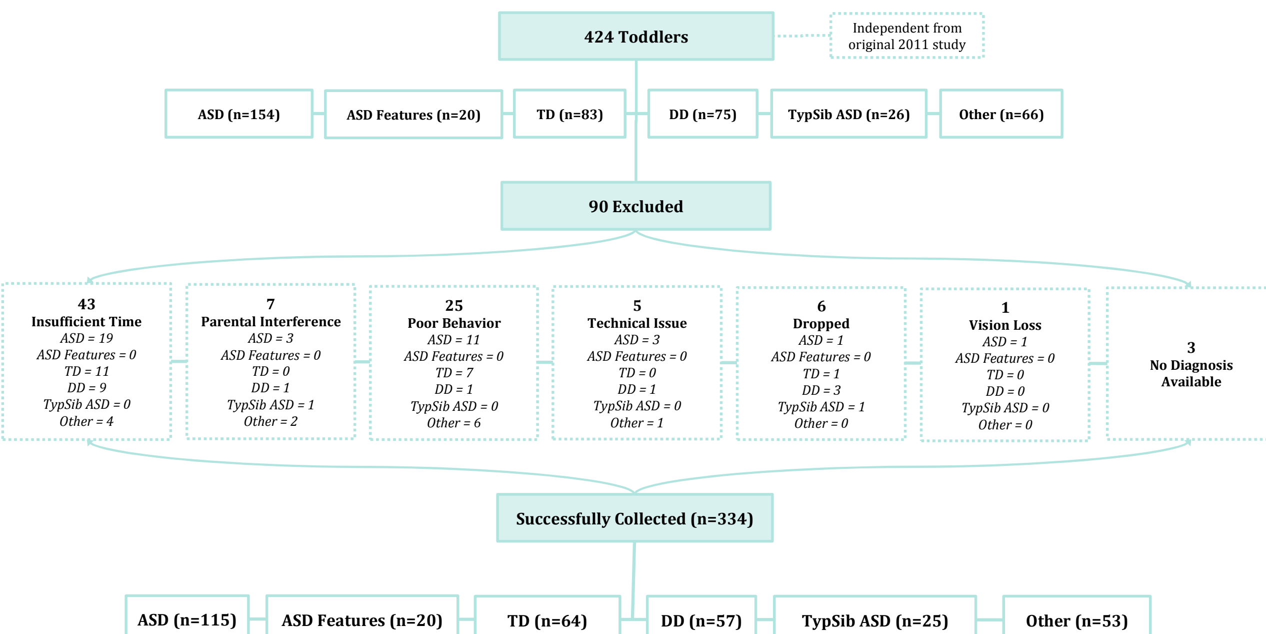


Figure S1. Flowchart of subject inclusion and exclusion for the independent sample.

unavailable diagnosis. This level of dropped data is similar to other toddler eye-tracking studies (2-4) and the clinical characteristics (e.g., age) of the toddlers that were excluded were not different from those that were included. Details regarding subject exclusion categories were as follows:

Insufficient looking time (*n* = 43) which included a failure to attend to at least 50% of the video.

Parental interference (*n* = 7) which included parent cell phone ringing during experiment or a parent orienting child's attention to a particular location on the screen.

Poor behavior (*n* = 25) which included a child crying, saying "no", or moving excessively during the experiment.

Technical issues (*n* = 5) which included computer freeze or the presence of a thin white vertical line on the display monitor.

Drop (*n* = 6) which included children whose parents requested withdrawal from the study.

Vision loss (*n* = 1) which included a child whose vision was later determined to be significantly impaired.

Unknown diagnosis (*n* = 3) which included children who passively dropped from the study by virtue of failing to come in for diagnostic testing. For example, a child may have participated in the eye-tracking test as well as a Mullen on their first visit, but the parents failed to return phone calls and thus never brought their child in for ADOS testing. Without a diagnostic test, the child's eye-tracking data could not be placed in any particular diagnostic category. See **Figure S1**.

Of the 90 excluded subjects, we report estimates of % fixation on dynamic geometric images from 32 subjects (15 ASD, 1 ASD-Feat, 6 DD, 6 Other, and 4 TD) that were obtained from the exclusion category "insufficient time." Toddlers from this category had looking times that ranged from 10-29 seconds (mean 21.83 $\pm$ 5.27). Data from subjects that had looking times < 10 seconds, or were from other exclusion categories (e.g., poor behavior, technical problems, parental interference, dropped from study) were not included in the scatterplot. The mean estimates and distribution of percent fixation towards DGI did not significantly differ from the sample used in the main analyses, see **Figure S2**.

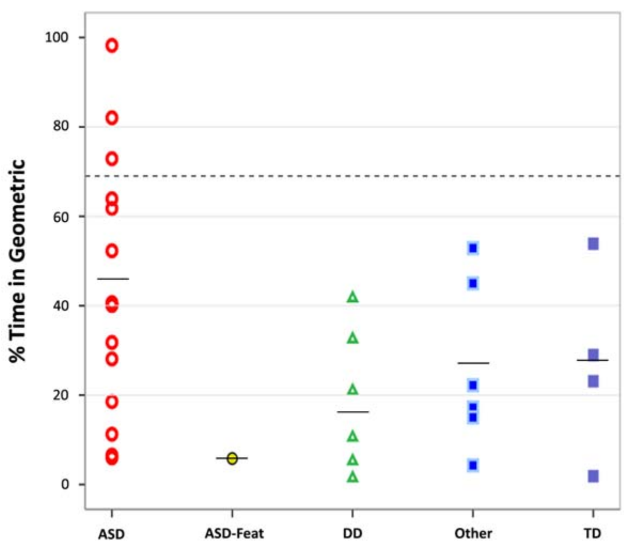


Figure S2. Scatterplot illustrating the percentage of fixation time to dynamic geometric images across each diagnostic group of excluded subjects with available data. Dotted line is at 69% fixation level. Solid lines represent group means.

Calibration

During calibration, images such as a cartoon cat moving within a box appeared paired with a child-friendly sound (a sound a toy might make) in 1 of 5 locations on the screen. Each image was 4.75 cm by 4.75 cm (6.8 degrees visual angle horizontally and vertically) and the image positions were in the center of the monitor plus slightly offset from each of the four corners of the monitor (**Figure S3A & B**). The experimenter was able to judge that the infant was looking at the calibration image based on an estimated gaze display overlaid on the calibration image field (**Figure S3B**). As soon as the child oriented to a calibration image and fixated, the experimenter captured that calibration data and moved rapidly to the calibration image in the next position.

During this procedure the eye tracker measured characteristics of the toddler's eyes (e.g., corneal light reflection) and used them together with a 3D eye model to calculate the gaze data. Immediately following the calibration session which generally lasted 5-10 seconds, quality of calibration was displayed as green lines with varying lengths, with shorter lines indicating better calibration (**Figure S3C**).

The calibration process was repeated if necessary until the error was less than one degree at each of the five calibration points, as indicated by a red circle displayed by the Tobii Studio software where the radius represents .5 degrees error. Screenshots capturing the calibration summary page were immediately taken following the procedure and stored in a database.

Guidelines for good calibration were posted in the eye-tracking room and all

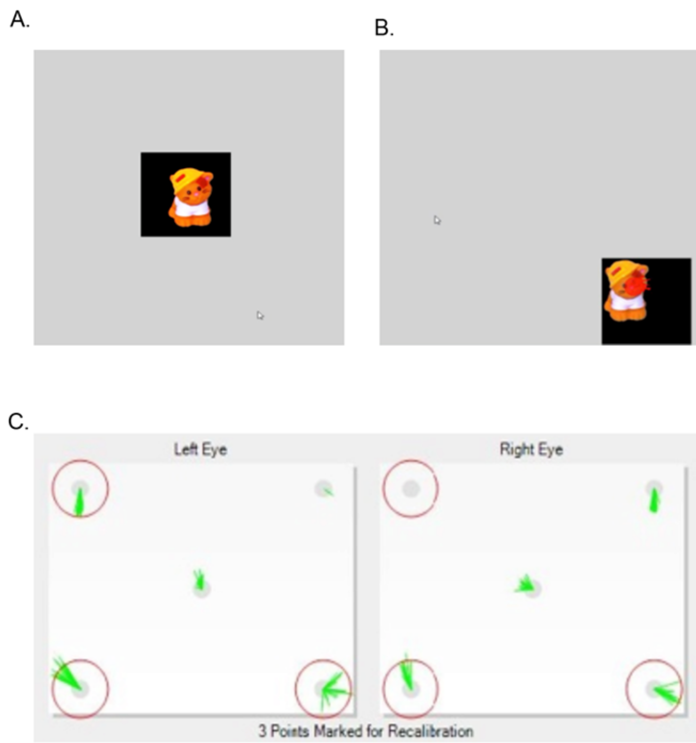


Figure S3. (**A**) Sample image used during calibration. (**B**) Red dot superimposed on the calibration images informed technician in real-time regarding the approximate accuracy of each calibration point. (**C**) Immediately following calibration, a calibration summary page appeared on the monitor. Absent green lines, or lines that extended beyond the circle represented poor calibration and the procedure was repeated. Note: figure not drawn to scale.

technicians were trained to accept a calibration once green bars were present in all 5 circles for each eye, and no green line extended beyond the .5 degree radius red circle. For more information regarding calibration accuracy, see the Tobii manual and a recent accuracy and precision white paper:

Tobii Manual:

http://www.tobii.com/Global/Analysis/Downloads/User_Manuals_and_Guides/Tobii_T60_T120_EyeTracker_UserManual.pdf?epslanguage=en

Accuracy and Precision White Paper:

http://www.tobii.com/Global/Analysis/Training/Metrics/Tobii_Test_Specifications_Accuracy_and_PrecisionTestMethod_version%202_1_1_.pdf

Areas of Interest (AOIs), Eye-Tracking Procedure and Real Time Eye-Tracking Monitoring

AOIs. DGI and dynamic social image AOIs were identical in size (13.75 cm horizontal x 9.5 cm vertical; visual angles 12.91° horizontal and 9.05° vertical).

Procedure. Prior to entering the eye-tracking room, parents were read a series of standardized instructions describing the eye-tracking procedure and were asked not to look directly at the images or to direct their child's attention. Toddlers were seated on their parent's lap or in a car seat 60 cm in front of the eye-tracking monitor, separated from the experimenter by a partition. Calibration data was first collected and re-done if quality did not meet acceptable standards.

Using corneal reflection techniques, the Tobii eye-tracker records the X and Y coordinates of toddlers' eye position at a frequency of 120 Hz (i.e., 7200 data collections per minute). An additional camera was placed on top of the eye-tracking monitor in order to obtain video of the toddlers' behavior during the entire experiment. This additional camera was separate from the "live tracker" described below.

Eye-Tracking Monitoring. Using a "live tracker" which superimposes the toddlers' eye-tracking data on the test image in real time, the operator observed the infants' gaze position and head position on a secondary monitor during the experimental procedure. If an infant's eyes were no longer picked up by the live tracker, or if an infant attempted to get out of his mother's lap as indicated by the video recording, then the process was repeated including pre-trial calibration.

Filter

The 35-pixel Tobii fixation filter (.88 degrees) is the standard default setting and is based on the gaze point averaged from the gaze data of both eyes. The algorithm interpolates missing data for gaps of less than 100 ms. Then for each subset of the data greater than 100 ms duration, it calculates a vector difference between the adjacent 5 data point windows, for each data point, using a sliding window. It then looks for peak differences, indicating a shift from fixation point to fixation point, that exceed a threshold that we set to 35 pixels per window. Because we are sampling at 120 Hz (one data point collected every .0083 sec), the 35 pixel window corresponds to a velocity threshold of 35/(8.33*5)=.84 pixels/ms.

Differences in Visual Preference Patterns towards DGI between Diagnostic Groups in the Combined Sample (*N* = 444)

As reported in the main body of the paper, within the combined sample, the exact same pattern was observed in differences to DGI fixation percentages controlling for the age of participants ($F_{6,437} = 20.23$, $p < 0.001$, partial $\eta^2 = 0.22$) as was found in the independent sample. Planned contrasts revealed that the ASD group had significantly greater fixation on DGI than all other diagnostic groups (ASD vs. DD, $p < 0.001$, CI: 10.97-22.93% fixation, Cohen's d = 0.76; ASD vs. Other, $p = 0.002$, CI: 3.75-16.71% fixation, Cohen's d = 0.45; ASD vs. TD, $p < 0.001$, CI: 15.38-25.36% fixation, Cohen's d = 0.99; ASD vs. Typ Sib, $p < 0.001$, CI: 15.00-25.36% fixation, Cohen's d = 0.78), except the ASD-Feat Group (ASD vs. ASD-Feat, $p = 0.28$, CI: -4.33-14.79% fixation, Cohen's d = 0.19).

Test-Retest Reliability

If a toddler was part of the test-retest cohort, the data collected during his first eye-tracking test was always used in the main analyses. Data from the second test session was only used for test-retest analyses. Toddlers were divided into 4 test-retest categories depending on the time interval between the 1st and 2nd eye-tracking test: immediate, short term, long term and very long term. Paired samples *t*-tests and intraclass correlations (ICCs) were used to determine if significant differences in percent fixation towards dynamic geometric images occurred between visits. The number of toddlers that changed their preference across test sessions using the 69% fixation towards DGI as the diagnostic cut-off threshold was also calculated.

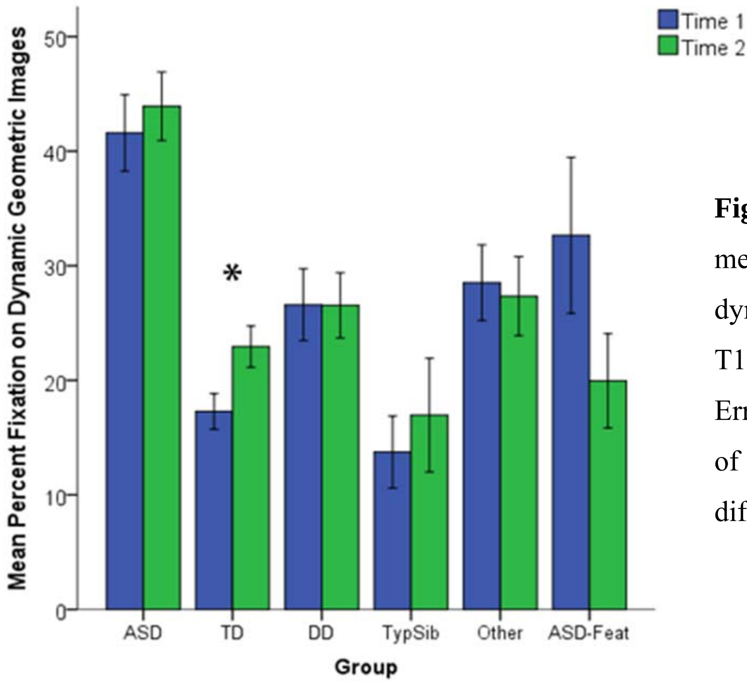


Figure S4. Bar graph illustrating mean overall change in fixation on dynamic geometric images between T1 and T2 for each diagnostic group. Error bars represent the standard error of the mean. *Represents significant differences.

First, test-retest data was considered at an overall level by comparing percent fixation towards dynamic geometric images between Test 1 and Test 2 time points. As shown in **Figure S4,** there was no significant difference in percent fixation towards DGI for any of the groups, except for TD toddlers who slightly increased their preference for geometric images during the 2nd test visit (%fixation towards DGI at T1 = 17.2 vs. T2 = 22.3, $t_{62} = -2.99$, $p = .004$).

Next, test-retest scores were examined based on the time interval between test visits. **Table S1** shows that the distribution of toddlers from each diagnostic category that fell into one of the four test-retest intervals was relatively equal. For example, 48 toddlers participated in their 2nd test within 1 month of the original test and 46 toddlers participated within 24 months. Results from a one-way within subjects ANOVA across time (i.e., the 4 time bins) demonstrated that while absolute change scores in fixation towards DGI did increase across time, this difference was not significant $F_{(3,204)} = 1.39$, $p > 0.05$. Likewise, while all intraclass correlations between fixation towards DGI at T1 and T2 were significant, the correlations were highest for toddlers in the shorter retest intervals and lowest for toddlers in the very long term interval suggesting that the GeoPref test is more consistent when given close in time as one would expect given the dynamic aging effects of toddlers in this age range. Finally, paired *t*-tests between T1 & T2 showed no significant difference in % fixation towards DGI for toddlers in any of the retest intervals. Although differences in DGI fixation were not significant between test intervals, trends suggest that test scores are more likely to be similar with immediate testing, and less so long term. Interestingly, as noted in **Table S2**, % fixation towards Geo became stronger for ASD toddlers with 6 additional toddlers exceeding the 69% threshold on their 2nd test visit.

Table S1. Distribution of Toddlers in 4 Test-Retest Intervals

	Test-Retest Interval				
	0–1 mo. Immediate	**2-6 mo. Short term**	**7-12 mo. Long term**	**13-24 mo. Very long term**	**Total *n***
Diagnostic Group (*n*)					
ASD	12	14	19	16	61
ASD Features	2	3	2	2	9
DD	11	13	7	6	37
Other	10	8	3	7	28
TD	10	20	20	13	63
TypSib	3	3	2	2	10
Total	48	61	53	46	208
Test-Retest Statistics					
Absolute change score, % geo fixation between T1 & T2	12.3%	13.04%	17.48%	17.35%	
Intraclass correlation % geo fixation between T1 & T2	.838***	.768***	.634***	.522**	
Paired *t*-test between T1 & T2	$t_{47} = .136$, *ns*	$t_{60} = .551$, *ns*	$t_{52} = -1.74$, *ns*	$t_{45} = -1.15$, *ns*	

**$p < 0.01$; ***$p < 0.001$.

As a final note regarding test-retest reliability, a small number of test-retest subjects received the protocol 3-5 times. This high-frequency test-retest data was not included in the current manuscript because the sample size was very small in most diagnostic categories (e.g., ≥ 3 test re-test sessions was available for only 2 Typ Sibs, 3 ASD Features toddlers), thus preventing meaningful conclusions that could be drawn. Future studies will examine high-frequency test-retest.

Table S2. Number of toddlers that changed their preference to prefer geometric images at the 2nd tests visit defined as >69% fixation on dynamic geometric images.

Diagnostic Group	# Changed to GeoPref at T2	Total # New Cases Detected
ASD	6	6 True Positives
TD	1	1 False Positive
DD	0	0
TypSib	0	0
Other	0	0
ASD-Feat	0	0

Validation Statistics Within Narrow Age Bins (Exploratory)

As illustrated in the age correlation figure in the main body of the paper, the age distributions within each diagnostic group were somewhat different with a greater number of younger TD and contrast subjects and slightly older ASD subjects. Given this shortcoming, and the reduction in power that occurs from reducing sample size, we consider validation statistics within narrow age bins as exploratory. In this exploratory age analysis, data from the combined sample was partitioned using mainly 6-month age intervals (i.e., 12-18 months n = 151; 19-24 months n = 87; 25-30 months n = 97; 31-36 months n = 67) except given the very small number of participants greater than 3 years in age, all subjects >3 years were placed a single age bin (i.e., 37-49 months n = 42). Validation statistics for each age bin are shown in **Table S3** and summarized in **Figure S5** showing the fluctuations in sensitivity and specificity across various age bins depending on the threshold used (50% or 69%). As illustrated, sensitivity fluctuates considerably, likely due to the heterogeneous timescale of symptom onset, and/or due to small sample sizes, whereas specificity is highly stable across age ranges (95% - 100%).

12-18 mo	**Using 50% Geo Fixation Cutoff (ASD only as True Pos)**	**Using 69% Geo Fixation Cutoff (ASD only as True Pos)**
Validation Statistics	*N*	*N*
True Positives (TP)	6	5
True Negatives (TN)	113	127
False Positives (FP)	15	1
False Negatives (FN)	17	18
Total Sample Size	151	151
Sensitivity	26%	22%
Specificity	88%	99%
PPV	29%	83%
NPV	87%	88%

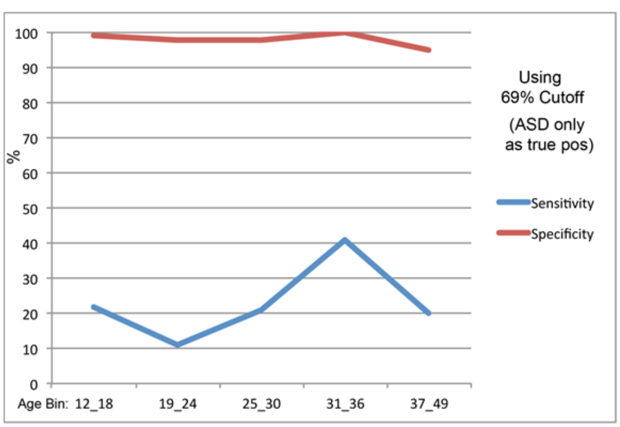
19-24 mo	**Using 50% Geo Fixation Cutoff (ASD only as True Pos)**	**Using 69% Geo Fixation Cutoff (ASD only as True Pos)**
Validation Statistics	*N*	*N*
True Positives (TP)	8	4
True Negatives (TN)	49	51
False Positives (FP)	3	1
False Negatives (FN)	27	31
Total Sample Size	87	87
Sensitivity	23%	11%
Specificity	94%	98%
PPV	73%	80%
NPV	64%	62%

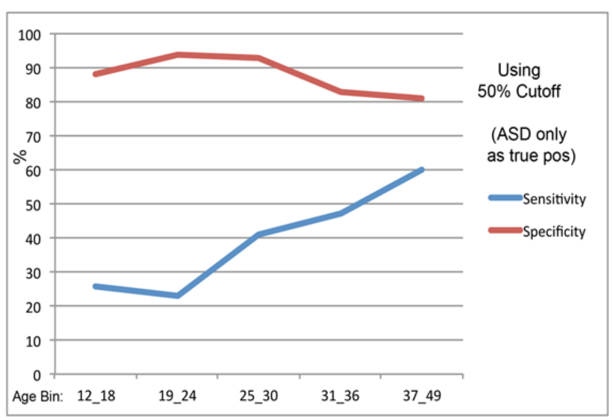
25-30 mo	**Using 50% Geo Fixation Cutoff (ASD only as True Pos)**	**Using 69% Geo Fixation Cutoff (ASD only as True Pos)**
Validation Statistics	*N*	*N*
True Positives (TP)	17	9
True Negatives (TN)	51	54
False Positives (FP)	4	1
False Negatives (FN)	25	33
Total Sample Size	97	97
Sensitivity	41%	21%
Specificity	93%	98%
PPV	81%	90%
NPV	67%	62%

31-36 mo	**Using 50% Geo Fixation Cutoff (ASD only as True Pos)**	**Using 69% Geo Fixation Cutoff (ASD only as True Pos)**
Validation Statistics	*N*	*N*
True Positives (TP)	15	13
True Negatives (TN)	29	35
False Positives (FP)	6	0
False Negatives (FN)	17	19
Total Sample Size	67	67
Sensitivity	47%	41%
Specificity	83%	100%
PPV	71%	100%
NPV	63%	65%

37-49 mo	**Using 50% Geo Fixation Cutoff (ASD only as True Pos)**	**Using 69% Geo Fixation Cutoff (ASD only as True Pos)**
Validation Statistics	*N*	*N*
True Positives (TP)	12	4
True Negatives (TN)	18	21
False Positives (FP)	4	1
False Negatives (FN)	8	16
Total Sample Size	42	42
Sensitivity	60%	20%
Specificity	81%	95%
PPV	75%	80%
NPV	69%	57%

Table S3 and Figure S5. Tables represent validation statistics for 5 separate age bins (e.g., 12-18 months). The line graphs summarize sensitivity and specificity across the different age bins. The left graph used the 69% cut off threshold to define a true positive and the right graph used the 50% cut off threshold to define a true positive. Note that specificity remains high across all age bins, but sensitivity has greater fluctuation. It is unclear if these fluctuations have meaning given the relatively small samples sizes per age bin, uneven distribution of diagnostic groups and clinical characteristics of subjects in each age bin.





Fixation Patterns Between Sibling Pairs (Exploratory)

Data was available from 36 sibling pairs (11 concordant for ASD, 12 discordant for ASD and 13 typical sibling pairs). An ICC was used as an exploratory analysis to determine the degree to which sibling pairs resembled each other in terms of their preference for DGI. A mixed effects model was then used to test the assumption that an additional variance component is needed to account for sibling group code (ASD concordant and TD concordant), with a fixed effect for diagnosis. Significant findings were followed up with a likelihood ratio test statistic.

Results indicated that patterns of visual fixation were significantly correlated in siblings concordant for ASD but not in other sibling groups (see **Table S4**). A follow-up likelihood ratio test statistic showed that differences between ASD concordant vs. TD concordant correlations was 10.91, with a p-value <0.001, suggesting that the similarities observed in patterns of visual fixations between ASD siblings are different than between TD siblings. The degree to which this reflects genetic mechanisms specific to ASD is unknown but raises this as a possibility.

Table S4. Correlations in percent fixation towards geometric images within different sibling groups. Fisher's intraclass correlation (ICC) was used for ASD and TD concordant pairs, and Pearson's correlation (ρ) for ASD discordant.

Group	# Pairs	ICC / ρ	p-value
ASD Concordant	11	0.557	$\leq$ 0.001***
ASD Discordant	12	0.140	0.664
TD Concordant	13	0.086	0.270

Supplemental Video Examples

(*Note: Parents of the toddlers illustrated in the videos signed a full consent form, allowing UCSD researchers to post, and use videos associated with their child's testing performance for educational purposes. The posted videos should remain on the *Biological Psychiatry* website and should not be shared by outside parties. Researchers or educators interested in using the videos for educational purposes should contact the study authors to obtain permission.)

Video 1 – ASD 14 months. Visual fixation patterns during the GeoPref Test of a 14-month old male toddler later diagnosed with ASD. The red dot indicates the location of visual fixation with the size of the dot indexing duration fixation within a single location. For example, a larger dot indicates prolonged staring. As evidenced by total fixation time, this toddler preferred to fixate on dynamic geometric images.

Video 2 – ASD 24 months. Visual fixation patterns during the GeoPref Test of a 24-month old male toddler later diagnosed with ASD. The red dot indicates the location of visual fixation with the size of the dot indexing duration fixation within a single location. For example, a larger dot indicates prolonged staring. As evidenced by total fixation time, this toddler preferred to fixate on dynamic geometric images.

Video 3 – TD 12 months. Visual fixation patterns during the GeoPref Test of a 12-month old male typically developing toddler. The red dot indicates the location of visual fixation with the size of the dot indexing duration fixation within a single location. For example, a larger dot indicates prolonged staring. As evidenced by total fixation time, this toddler preferred to fixate on dynamic social images, and became quite animated and delighted by the sight of the children.

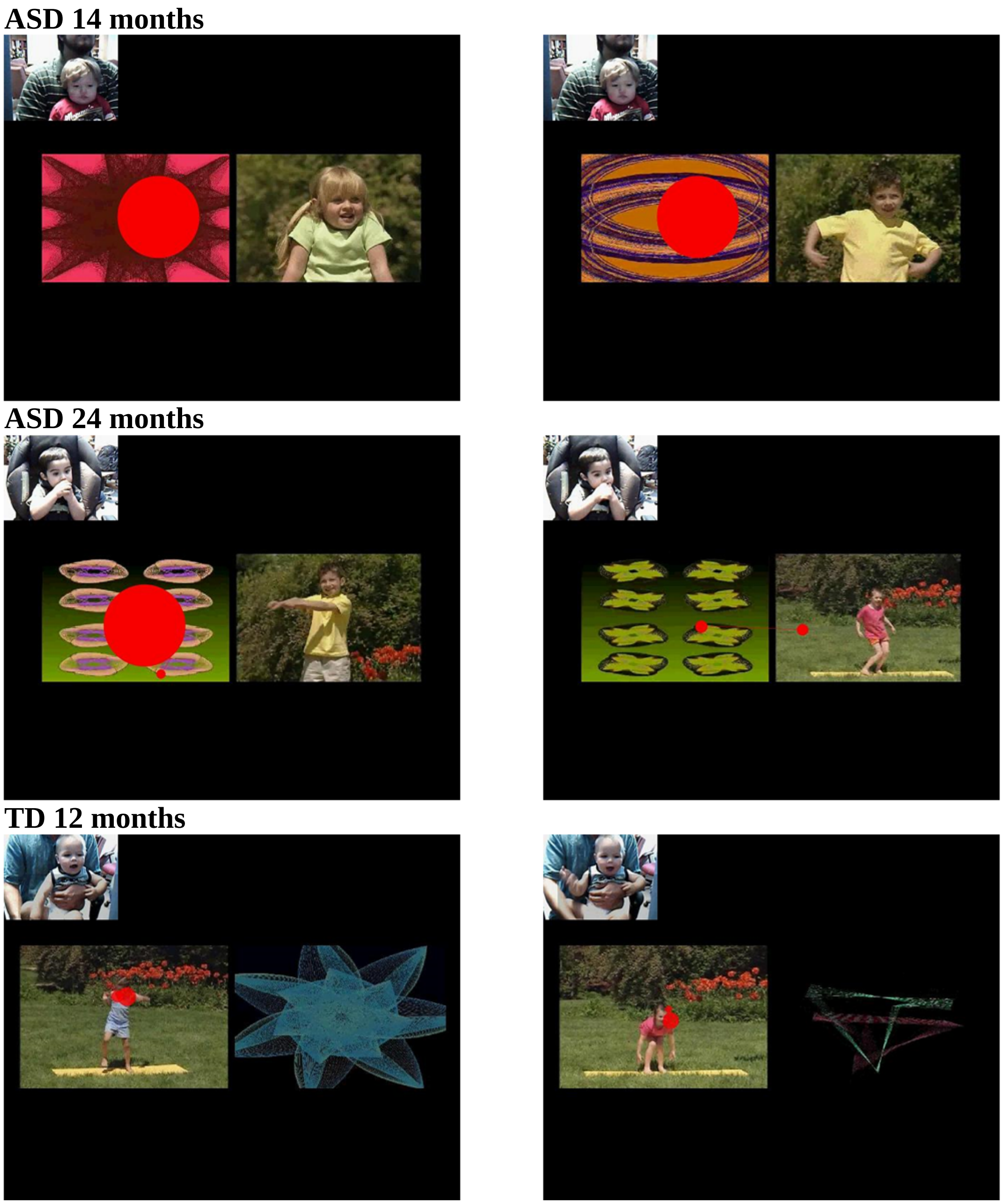


Figure S6. Still images captured from the eye-tracking videos from 2 ASD toddlers and 1 TD toddler. The red dot illustrates where the toddler is looking. The diameter of the red dot illustrates duration fixation within a specific location, with a larger red associated with longer looking times. (See associated videos).

Supplemental References

1. Pierce K, Carter C, Weinfeld M, Desmond J, Hazin R, Bjork R, *et al.* (2011): Detecting, studying, and treating autism early: The one-year well-baby check-up approach. *J Pediatrics*. 159:458-465.

2. Tummeltshammer KS, Wu R, Sobel DM, Kirkham NZ (2014): Infants track the reliability of potential informants. *Psychol Sci*. 25:1730-1738.

3. Shic F, Bradshaw J, Klin A, Scassellati B, Chawarska K (2011): Limited activity monitoring in toddlers with autism spectrum disorder. *Brain Res*. 1380:246-254.

4. Jones W, Carr K, Klin A (2008): Absence of preferential looking to the eyes of approaching adults predicts level of social disability in 2-year-old toddlers with autism spectrum disorder. *Arch Gen Psychiatry*. 65:946-954.