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**Title:** Eye movements and behavioural responses to gaze-contingent expressive faces in typically developing infants and infant siblings

**Running title:** Deviant social responsiveness infant siblings

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## Abstract

Studies with infant siblings of children with Autism Spectrum Disorder have attempted to identify early markers for the disorder and suggest that autistic symptoms emerge between 12 and 24 months of age. Yet, a reliable first-year marker remains elusive. We propose that in order to establish first-year manifestations of this inherently social disorder, we need to develop research methods that are sufficiently socially demanding and realistically interactive. Building on Keemink et al. (2019), we employed a gaze-contingent eye-tracking paradigm in which infants could interact with face stimuli. Infants could elicit emotional expressions (happiness, sadness, surprise, fear, disgust, anger) from on-screen faces by engaging in eye contact. We collected eye-tracking data and video-recorded behavioural response data from 122 (64 male, 58 female) typically developing infants and 31 infant siblings (17 male, 14 female) aged 6-, 9- and 12-months old. All infants demonstrated a significant Expression by AOI interaction ( $F(10, 1470) = 10.003, p < .001, \eta_p^2 = .064$ ). Infants' eye movements were 'expression-specific' with infants distributing their fixations to AOIs differently per expression. Whereas eye movements provide no evidence of deviancies, behavioural response data show significant aberrancies in reciprocity for infant siblings. Infant siblings show reduced social responsiveness at the group level ( $F(1, 147) = 4.10, p = .042, \eta_p^2 = .028$ ) and individual level (Fischer's Exact,  $p = .032$ ). We conclude that the gaze-contingency paradigm provides a realistically interactive experience capable of detecting deviancies in social responsiveness early, and we discuss our results in relation to subsequent infant siblings development.

### **Lay summary**

We investigated how infant siblings of children with autism spectrum disorder respond to interactive faces presented on a computer screen. Our study demonstrates that infant siblings are less responsive when interacting with faces on a computer screen (e.g. they smile and imitate less) in comparison to infants without an older sibling with autism.

Reduced responsiveness within social interaction could potentially have implications for how parents and carers interact with these infants.

### **Key Words**

Autistic Disorder, Infant, Endophenotypes, Emotions, Development

A growing body of research has focused on the prospective study of the emergence of Autism Spectrum Disorder (ASD) by studying infant siblings of children with an ASD diagnosis (see Jones et al., 2013 and Szatmari et al., 2016 for reviews). Infant siblings are at elevated familial risk; ASD prevalence within this group is 20% compared to 1.5% in the general population (Ozonoff, 2011; Szatmari et al., 2016). Furthermore, a considerable proportion of non-diagnosed infant siblings present with other developmental issues (Charman et al., 2016; Piven et al., 2018). Uncovering early behavioural, and potentially symptomatic, manifestations of ASD, could lead to earlier diagnosis (Koegel et al., 2013; Zwaigenbaum et al., 2013) and greater opportunity for appropriate interventions that can significantly improve prognosis (Dawson et al., 2010; Dawson et al., 2012; Fernell et al., 2013; MacDonald et al., 2014). Nevertheless, ASD is currently not reliably diagnosed before 24 months of age (Steiner et al., 2011) and the median age of diagnosis in the UK is 55 months (Brett et al., 2016). With only 1 in 5 infant siblings developing ASD, establishing a reliable first-year marker with predictive clinical value is pivotal to enable targeted intervention. Recent studies have demonstrated moderate predictive success at 14 (Bussu et al., 2018) and 18 months (Chawarska et al., 2014). Yet, a reliable first-year marker remains elusive.

In this paper, we argue that in order to reliably identify early manifestations of ASD, we need to carefully consider the appropriateness of the research methods we employ. Fundamentally, ASD is a social-communication disorder (APA, 2013); therefore, in order to capture subtle early deviancies in behaviour, we must develop methods that are sufficiently socially demanding and realistically interactive. Similarly, Bussu et al. (2018) argue that the

lack of reliable predictors could be due to the inability of current methods to capture ASD-related manifestations of social skills at an early age. Consequently, we advocate the utilisation of gaze-contingent (GC) eye-tracking paradigms as a novel interactive method to study infant sibling behaviour. In GC paradigms, responses from a stimulus are contingent on participants' eye movements, enabling participants to 'interact' with stimuli. Recent studies demonstrated the utility of GC paradigms with both typical and atypical populations (Deligianni et al., 2014; Miyazaki et al., 2014; Verneti et al., 2018; Wang et al., 2012, Wilms et al., 2010). We successfully applied a GC paradigm to study face scanning in typically developing (TD) infants and infant siblings (Keemink et al., 2019). In our paradigm infants could 'interact' with on-screen actors by fixating pre-specified face regions. Specifically, fixating the eyes or mouth triggered a socio-communicative response from the actor. GC paradigms are particularly suitable to study socio-communicative behaviour as they allow us to simulate a realistic social interaction whilst retaining empirical rigour. We enhanced the paradigm by video-recording participants during the 'interactions' to obtain a measure of infant socio-communicative responsiveness. Our findings demonstrated that infants are sensitive to differences in engagement from actors, which was visible in their eye movements and their overt behavioural responses. Additionally, preliminary findings from our small infant sibling sample suggested deviant behavioural responsiveness and atypical dwell time as potential early markers of ASD. The current study aims to build on these findings by extending the paradigm with novel, emotionally expressive stimuli and by including a larger sample of infant siblings.



Emotional expressions are inherent to human interactions and essential socio-communicative signals for survival (Bannerman et al., 2009). It is therefore pivotal for social success that infants develop the ability to discriminate, categorize, and comprehend a multitude of different emotions (Izard et al., 2001). Studying how infants process social-communicative expressions is particularly relevant for infant siblings, as older children with ASD show difficulties in emotion processing (Dapretto et al., 2006; Begeer et al., 2008; Rosset et al., 2007). To date, emotion processing in infant siblings has not been studied using interactive faces, although several studies suggest it could be a relevant marker (Blasi et al., 2015; Fox et al., 2013; Mattson et al., 2013; McCleery et al., 2007; Wagner et al., 2016). Studies with TD infants suggest that infants as young as 36 hours show some evidence of emotion discrimination (Addabo et al., 2018; Farroni et al., 2007), which becomes more distinguished over the first few months (Barrera & Maurer, 1981; Nelson & Dolgin, 1985; Schwartz et al., 1985). Emotion categorization develops slightly later (Caron et al., 1988; Cong et al., 2018; Kotsoni et al., 2001; Ludemann, 1991), and some studies suggest that TD infants show expression-specific eye movements, in particular to threat-related expressions (Gredebäck et al., 2011; Hunnius et al., 2011). Few studies have explicitly addressed emotion comprehension in TD infants (Phillips et al., 1990; Soussignan et al., 2017). Several studies conclude an attentional bias towards fearful faces (see review Leppänen & Nelson, 2012), suggesting a robust understanding of its valence, although evidence is mixed. Other studies reason that infants are capable of understanding the valence of emotions, but evidence is either theoretical (Tronick, 1989) or limited to mothers' faces (Sorce et al., 1985; Sroufe, 1979). It is currently unclear if these behaviours develop similarly in infant siblings and therefore we aim to examine if and how these processes deviate in infant siblings by

measuring responses to gaze-contingent face stimuli portraying the six basic emotional expressions (happiness, anger, surprise, fear, disgust and sadness; Ekman, 1973).

Although eye tracking allows us to study cognitive processes in preverbal infants in a non-invasive manner, it is questionable as to whether eye movements alone are most suited to reveal meaningful socio-communicative differences between clinical groups and subgroups. Several eye-tracking studies report differences in fixation patterns (Chawarska et al., 2013; Guiraud et al., 2012; Merin et al., 2007). However, these are not always reliably linked to ASD diagnosis (Young et al., 2009). Moreover, a review by Falck-Ytter et al. (2013) highlights that although eye tracking can be a valuable method in autism research, integration with more naturalistic measures is needed. Interestingly, our 2019 previous findings results (Keemink et al., 2019) suggest that deviant behavioural responsiveness could be a measure of interest. The current study will investigate this further in a larger infant sibling sample by combining eye-tracking and natural behavioural responses. In contrast to previous research, our interactive paradigm enables us to incorporate a measure of infant responsiveness, which will be video-recorded, allowing us to investigate early socio-communicative development in a more meaningful way. Additionally, we will adopt a novel analysis approach by exploring differences between TD infants and infant siblings not only at the group level, but also by investigating individual performance (see Keemink et al., 2019). We propose that infant siblings cannot be categorized as a separate group, as the majority of these infants will develop typically (Ozonoff et al., 2011). Meaningful deviant behaviour could therefore be masked at the group level.

Existing research (Di Giorgio et al., 2013); Keemink et al., 2019) led us to hypothesize that all infants would engage in eye contact with the interactive face stimuli and therefore trigger the expressive responses. In TD infants, we expected to observe moderate to high rates of responsiveness towards the interactive stimuli (Keemink et al. 2019). In line with previous work, subtle differences were expected between TD and ASD in infant participants, characterized by behavioural responses (Fox et al., 2013; Keemink et al., 2019) and by eye movements (Rosset et al., 2007). Lastly, we reasoned that if infants deployed emotion-specific eye-movements, this would support conclusions about emotion categorisation, and if infants demonstrated emotion-specific behavioural responses, we would be able to infer basic emotion comprehension.

## **Methods**

This study was approved by the Ethics Committee of the University of Kent (Ethics ID: 201815168322884850) and the NHS Health Research Authority (IRAS: 239237). All parents signed informed consent for their infant. Data were stored and treated anonymously.

### **Participants**

Typically developing infants (TD) were recruited through the Kent Child Development Unit database including families interested in participating in research. Infants were considered TD if they had not been born prematurely (<6 weeks) and had no family history of Autism Spectrum Disorder (ASD). The final TD sample comprised 122 infants (64 male, 58 female) consisting of 6-, 9- and 12-month-olds. A further 5 infants (2 x 6 months, 2 x 9

months, 1 x 12 months) were excluded due to fussiness. Infants siblings were recruited via The Kent Autistic Trust and Community Child Health, East Kent Hospitals University NHS Foundation Trust. Infants were included if they had at least one older sibling with an ASD diagnosis. All autistic siblings had received a formal diagnosis established by a clinical psychologist. The final infant sibling sample comprised 31 infants (17 male, 14 female) consisting of 6-, 9-, and 12-month-olds. See Table 1 for detailed participant characteristics.

### **The Gaze-Contingent Task**

All infants viewed 18 video-recorded, neutral-looking actors, who would produce expressions representing one of the six basic emotions (happiness, sadness, surprise, disgust, fear and anger) at the moment the infant engaged in eye contact with the actor. The expression produced by the actors was contingent on the infant's first fixation in the eye region (see Figure 1). All six expressions were represented three times and were presented in a random order. If an infant did not fixate the eye region within the trial length, the face would not animate and remain looking neutral. All infants included in the final sample completed a minimum of 15 trials. The trial length of trials where infants did fixate the eye area was 3 seconds (length of the video) plus the time it took infants to fixate the eye area. A trial would be a maximum of five seconds long.

Table 1

*Participant Characteristics per Age and Group*

	<i>Age in Months</i>	<i>N</i>	<i>Mean Age in Days (SD)</i>	<i>Age Range</i>	<i>Gender (M/F)</i>
<i>TD</i>	6	46	191.1 (9.4)	176 – 194	26/20
	9	39	281.3 (11.2)	265 - 290	18/21
	12	37	367 (12.5)	357 - 378	19/18
	Total	122			64/58
<i>HR-ASD</i>	6	6	185 (7.2)	175 - 193	5/1
	9	12	275.7 (7.5)	263 - 282	6/6
	12	13	369.1 (6.8)	364 - 381	6/7
	Total	31			17/14
<b>Total</b>		<b>153</b>			<b>80/73</b>

## **INSERT FIGURE 1 HERE**

### **Stimuli**

Stimuli consisted of 18 colour videos of 18 neutral-looking adults (9 females, 9 males) visible from the shoulders upward standing in front of a green screen (See Figure 2). All stimuli were of Caucasian origin, with the exception of one mixed race stimulus. Race did not affect infant responses. All images subtended a size of 24.77 degrees x 18.25 degrees in visual angle and were presented on a 20-inch monitor with a resolution of 1024 by 768 pixels. Discrete gaze-contingent 'invisible boundaries' for the eye region were defined individually for each face. All eye regions measured 8.3 x 3.4 degrees.

## **INSERT FIGURE 2 HERE**

### **Equipment**

Eye movements were recorded with an Eyelink 1000+ (SR Research, Ontario) at a sampling rate of 500 Hz operated in Remote Mode using a 25mm lens attachment. Under optimal conditions, when operating in Remote Mode the Eyelink has accuracy of 0.5°, a tracking range of 32° (horizontal) x 25° (vertical) and is tolerant to head movements of 22x18x20cm. In order to minimise head movements, infants were securely fastened in an

age-appropriate car seat that was safely attached to a chair. Stimuli were presented using Experiment Builder (SR Research, Ontario) and the raw eye movement data were extracted using Data Viewer (SR Research, Ontario). Fixations and saccades were subsequently parsed in Matlab (The Mathworks, MA, USA) using custom written code. All subsequent data processing was conducted in Matlab. In addition, infants' behavioral responses were recorded with a Logitech webcam. Recordings were analyzed frame-by-frame and coded by one of the researchers and an independent, blind coder.

## **Procedure**

Families were welcomed in a child-friendly area of the Kent Child Development Unit. Parents were asked to sign a consent form before being escorted to the quiet research laboratory with dimmed lighting. Infants were seated in an age-appropriate seat at a viewing distance of 60cm from a monitor. An occluding screen prevented the infant from being distracted by their surroundings. Binocular eye-tracking data and infants' behavioural responses were recorded throughout. A 5-point calibration procedure using custom-made attention-grabbing audio-visual targets was conducted and repeated as necessary. To ensure that all eye movement data was accurate, all infants were calibrated and validated to within 1° and checks for drift were assessed between every single trial. No infant failed to calibrate. Following calibration, the task was initiated. An attention grabber appeared at the side of the screen between each stimulus presentation that ensured the infant's gaze for the beginning of each trial. The study lasted approximately three minutes.

## **Behavioral Coding**

Infants' behavioral responses were video recorded with a webcam. Eye-movement data were time-locked with behavioral data to ensure that infants' behavior occurred in *response* to the triggered animation. Subsequently, recordings were analyzed frame-by-frame to code the infants' responses. Responses could be categorized as approach (e.g. smiling), withdrawal (e.g. averting gaze), ambiguous (e.g. arbitrary head movements), or non-response (no change in facial expression/behavior). Subsequently, behavioural response data was compared to the eye-tracking data to determine the frequency of imitation. All recordings were coded by a researcher and a blind coder. Inter-coder reliability was high ( $r = .89, p < .001$ ).

## **Eye movements**

We used a velocity-based algorithm to identify saccades that has been successfully implemented in several recently published papers (Keemink et al., 2019; Kelly et al., 2019; Prunty et al., 2020). Data was smoothed by applying a 4-sample rolling window that returned a median average. Angular speed was computed based on four samples. Velocity values greater than  $1000^{\circ}/\text{sec}$  were judged to be impossible and removed from analysis. We set a velocity threshold of  $40^{\circ}/\text{sec}$ , with samples falling below this value identified as potential fixation samples. Time and distance between 2 potential fixations were calculated. If inter-fixation values were  $<20\text{ms}$  and  $<.03^{\circ}$  then fixations were merged. All fixations  $<100\text{ms}$  were removed. Following Holmqvist et al. (2012), precision values were calculated as the root mean square (RMS) of sample-to-sample distances within computed fixations.



Precision was calculated separately for each age group and results were as follows: 6 months =  $0.71^\circ$  ( $SD = 0.12^\circ$ ), 9 months =  $0.64^\circ$  ( $SD = 0.08^\circ$ ) and 12 months =  $0.61^\circ$  ( $SD = 0.09^\circ$ ).

In order to identify fixations directed to key face features, AOIs were constructed individually for each face stimulus. The size of AOI regions was identical across all faces (Eyes =  $8.3^\circ \times 3.4^\circ$ ; Nose =  $3.6^\circ \times 2.4^\circ$ ; Mouth =  $6.2^\circ \times 3.4^\circ$ ) but AOI locations differed spatially as dictated by the physiognomic proportions of individual faces.

## Results

### Power analysis

A priori power analyses were based on the effect sizes of Keemink et al. (2019). With our total sample of 122 TD infants and 31 infants siblings, all main and interaction effects adhere to a power of at least .80.

### Analysis plan

First, the results will describe eye movement analyses exploring differences in overall Dwell Time and in looking time towards the distinct Areas of Interest (AOIs). Subsequently, we will analyse infants' behavioural responses investigating differences in overall Responsiveness, Imitation and Smiling. The within-subject variables are Expression (six levels - happiness, surprise, fear, disgust, anger, sadness) and AOI (three levels – eyes, mouth, nose). The between-subject variables are Age (three levels - 6-, 9- and 12-month-olds) and

Group (two levels – typically developing infants and infant siblings). Age has been included to demonstrate consistency of results across ages, no age differences were found. Analyses revealed no effect of participant gender, so this factor was excluded.

The analyses will firstly be discussed at group level using repeated measures ANOVAs. However, since only 1 out of 5 infant siblings will receive an ASD diagnosis (Ozonoff et al., 2011), we argue that group-level analyses might not be sufficient. This may result in meaningful individual differences remaining unnoticed. Similar to Keemink et al. (2019), we will therefore additionally discuss the performance of individual infant siblings relative to TD behavior by investigating the frequency of deviant behavioral responses for each measure. Infants were deemed of interest if their behavior fell +/- 1.5 standard deviations from the sample mean (cf. Kelly et al., 2011). Fisher's exact tests explored the difference in frequency of deviant z-scores between TD infants and infant siblings.

### **Eye movement analyses – Group Level**

**Overall Dwell Time.** The dependent variable for these analyses was total looking time in seconds. A 6 x 3 x 2 repeated measures ANOVA yielded a significant main effect of Expression,  $F(5, 735) = 4.949, p < .001, \eta_p^2 = .033$ . Post-hoc analyses revealed that infants looked significantly longer at surprised expressions compared to happy ( $p < .001$ ), fearful ( $p = .003$ ), disgusted ( $p < .001$ ), angry ( $p = .035$ ) and sad expressions ( $p < .001$ ) (See Table 2 for means) across all ages and regardless of group status.

**AOIs.** The dependent variable for these analyses was percentage of total looking time. A 3 x 6 x 3 x 2 repeated measures ANOVA revealed a significant main effect of AOI,  $F(2,$

294) = 58.331,  $p < .001$ ,  $\eta_p^2 = .284$ . Post-hoc inspection of means confirmed that across expressions eyes were fixated more (31.9%) than nose (13.8%,  $p < .001$ ) and mouth (15.9%,  $p < .001$ ) by infants of all ages and regardless of group status. Additionally, a significant Expression x AOI interaction was found  $F(10, 1470) = 5.592$ ,  $p < .001$ ,  $\eta_p^2 = .037$ , with infants distributing their fixations to AOIs differently per expression (see Table 3).

### Eye movement analyses – Individual Performance

**Dwell Time & AOI.** For overall Dwell Time and AOIs, we computed z-scores and explored the frequency of deviant z-scores for TD infants and infant siblings. Fisher exact tests revealed no significant differences in frequency. Infant siblings and TD infants showed no differences in their eye movements whilst watching expressive stimuli in our paradigm.

### Behavioural analyses – Group Level

**Overall Responsiveness.** Descriptive statistics demonstrated that on average infants showed a behavioral response on 58% of trials. A 6 x 3 x 2 repeated measures ANOVA on percentage of trials yielded a significant main effect of Expression,  $F(5, 735) = 3.301$ ,  $p = .006$ ,  $\eta_p^2 = .022$ . Infants in all age groups responded more towards happiness relative to surprise ( $p = .001$ ), fear ( $p = .009$ ) and sadness ( $p = .003$ ), and more toward disgusted expressions compared to surprised expressions ( $p = 0.12$ ).

**Imitation.** Descriptive statistics demonstrated that on average infants showed imitation on 5.56% of trials. A 6 x 3 x 2 repeated measures ANOVA conducted on percentage of trials revealed a significant main effect of Expression,  $F(1, 147) = 27.734$ ,  $p < .001$ ,  $\eta_p^2 =$

.159. Infants in all age groups imitated happiness significantly more than other expressions (all  $p < .001$ ). Additionally, a significant main effect of Group,  $F(1, 147) = 7.262, p = .008, \eta_p^2 = .047$  demonstrated that infant siblings exhibited less imitation (3.04%) than TD infants (6.21%).

**Smiling.** On average infants smiled on 21.24% of trials. A 6 x 3 x 2 repeated measures ANOVA conducted on percentage of trials revealed a significant main effect of Group,  $F(1, 147) = 4.10, p = .042, \eta_p^2 = .028$ . Infant siblings showed less smiling (12.58%) than TD infants (23.37%).

### **Behavioural analyses – Individual Performance**

We computed z-scores for overall responsiveness, and explored the frequency of deviant z-scores. For imitation and smiling rates, the restricted range of values (resulting in no normalised values falling below -1.5 SDs) required us to take an alternative approach. For these measures, we examined the frequency of absence and presence of the behaviour.

**Responsiveness.** Inspection of z-scores revealed that eight out of 31 infant siblings (25.81%) produced unusually low rates of responsiveness relative to only 12 out of 122 TD infants (9.84%). A Fisher's Exact Test yielded a significant difference in frequency,  $p = .032$ .

**Imitation.** Inspection of z-scores revealed that 19 out of 31 infant siblings (61.29%) did not show any evidence of imitation relative to 43 out of 122 TD infants (35.25%). A Fisher's Exact Test yielded a significant difference in frequency,  $p = .013$ .

**Smiling.** Inspection of z-scores revealed that 17 out of 31 infant siblings (54.84%) did not exhibit any smiling. Conversely, 41 out of 122 TD infants (33.61%) showed similar behavior. A Fisher's Exact Test yielded a significant difference in frequency,  $p = .038$ .

Table 2

*Mean Looking Time (in seconds) for Each Expression*

<i>Expression</i>	<i>Mean (SE)</i>
Happy	3.830 (.093)
Surprise	4.259 (.073)
Fear	3.914 (.098)
Disgust	3.869 (.087)
Anger	4.056 (.075)
Sadness	3.874 (.083)

Table 3

*Mean Proportion of Looking Time per AOI for Each Expression*

<i>Expression</i>	<i>AOI</i>	<i>Mean (SE)</i>
<i>Happy</i>	Eyes	.307 (.020)
	Nose	.144 (.014)
	Mouth	.159 (.016)
<i>Surprise</i>	Eyes	.285 (.021)
	Nose	.137 (.012)
	Mouth	.227 (.018)
<i>Fear</i>	Eyes	.375 (.023)
	Nose	.100 (.012)
	Mouth	.125 (.015)
<i>Disgust</i>	Eyes	.345 (.022)
	Nose	.132 (.014)
	Mouth	.138 (.015)
<i>Anger</i>	Eyes	.301 (.020)
	Nose	.175 (.015)
	Mouth	.161 (.018)

<i>Sadness</i>	Eyes	.299 (.022)
	Nose	.138 (.014)
	Mouth	.146 (.016)

## Discussion

The present study aimed to contribute to the emerging literature on early manifestations of ASD in infant siblings by assessing infants' eye-movements and behavior in response to GC stimuli conveying socio-communicative information. This interactive research paradigm gives us a better understanding of how infants, both typically developing and at risk for atypical development, process expressive socio-communicative faces. Our findings underscore the strengths of the GC paradigm as an interactive and socially demanding research method capable of detecting early manifestations of ASD and highlights the additional value of behavioural responses in an eye-tracking task.

### Eye-tracking responses

In line with Keemink et al. (2019), all infants engaged in eye contact and triggered the expressive responses. Additionally, infants employed expression-specific eye movements, indicating that they are capable of perceiving *visual* differences between expressions, and confirming previous studies on emotion categorisation and discrimination (e.g. Hunnius et al., 2011). Eye-movements analyses revealed no meaningful differences between TD infants and infant siblings at both the group and individual level, suggesting that visual exploration

of interactive faces in infant siblings is typical and other measures are required to reliably observe early deviancies.

### **Behavioural responses**

Our paradigm demonstrated that infants do not show expression-appropriate behavioural responses in the first year of life. While eye-movement patterns differ across expressions, infants' typical behavioural response is smiling regardless of group status. With the exception of 'happiness' to which infants readily respond with a smile, infants are not providing behavioural responses that suggest conceptual understanding at this age. Furthermore, imitation for expressive faces appears to be rare. Although previous research suggest mimicry of emotional and non-emotional facial actions from 4 months of age (de Klerk et al., 2018; Isomura & Nakano, 2016), these studies only presented infants with simple actions, such as 'mouth opening', and not with full, complex expressions.

We argued that group-level analyses might not be sufficient to detect symptomatic behaviour in infant siblings, as they cannot be treated a separate group, which was clearly corroborated by our behavioural findings. Whereas differences in imitation and smiling yielded significance at group level, responsiveness did not. However, looking at individual behaviour, our results revealed that the frequency of deviant behaviour on all three measures is higher in infant siblings when viewing interactive emotional faces. This cannot be explained by a difference in the amount of triggered expressions, as infant siblings and TD infants triggered expressions equally. These findings converge with studies on parent-infant interaction in infant siblings (Wan, et al., 2012) and neuropsychological research on



expression processing in children with ASD (Dapretto et al., 2006), and align with the APA (2013) criteria of ASD. In addition to demonstrating the need for individual analyses, our behavioural findings compellingly underline the value of video recordings during eye-tracking tasks as a measure of early behavioural differences in infant siblings. The behavioural measures offered an in-depth analysis of the interaction and enabled the detection of subtle socio-communicative differences.

A limitation to this study is the lack of infant sibling follow-up data. Evidently, follow-ups with our participants are required to establish the predictive value and specificity of our measures (Piven et al., 2018), for which we have now started the first phase. Future studies should aim to recruit a larger sample of infant siblings and should include follow-up data. Nevertheless, our method has yielded promising results and this study has provided an important first step in establishing deviancies in behavioural responsiveness.

### **Implications for infant sibling development**

Reduced responsiveness to socio-emotional, interactive stimuli has demonstrable implications for further infant sibling development. The infant is part of a social world, in which responses are contingent upon input. Arguably, diminished responsiveness affects the frequency and ways their social world responds to infants (Leezenbaum et al., 2014). Indeed, studies on parent-infant sibling interaction suggest that parents display less infant-sensitive responses and obtain more directive interaction styles (Wan et al, 2012; Yirmiya et al., 2006). Such interaction styles may in-turn affect the infant, as research with typical populations underscores the importance of contingent parental responsiveness for cognitive and social development (Ainsworth et al., 1974; Tamis-LeMonda et al., 2014). Future

longitudinal studies examining how infant sibling and parent interactional behaviours affect each other are required for further understanding of the mechanisms behind this potential developmental trajectory of ASD, which subsequently can inform intervention.

It is important to note that we do acknowledge there may be many different pathways to ASD, which is supported by research (Jones et al., 2014; Landa et al., 2012). Considering the heterogeneity of the disorder, it seems highly unlikely that one behavioural marker will be present in all infants who develop ASD. Nevertheless, our findings contribute to the literature on early markers by demonstrating that behavioural measures within the GC paradigm are capable of detecting early differences.

## **Conclusion**

Despite its potential clinical utility and interactive nature, no studies to date have investigated early socio-communicative deviancies using a GC paradigm. We demonstrated that video recordings during a GC eye-tracking task can detect early deviances in behavioural responsiveness in infant siblings. Additionally, our study contributed to the wider infant literature by confirming that infants perceive *visual* differences between expressions and demonstrating that infants *conceptual* understanding is at its best rudimentary in the first year of life. We advocate for the implementation of GC paradigms within developmental research, as its interactive nature has the potential to study numerous social processes in different populations. Our findings hold important implications for early infant sibling development that need to be investigated further in order to provide adequate support as early as possible.

## References

- Addabbo, M., Longhi, E., Marchis, I. C., Tagliabue, P., & Turati, C. (2018). Dynamic facial expressions of emotions are discriminated at birth. *PLOS One*, *13*, 1-11. doi: 10.1371/journal.pone.0193868
- Ainsworth, M. D. S., Bell, S. M., & Stayton, D. F. (1974). Infant-mother attachment and social development: Socialization as a product of reciprocal responsiveness to signals. In M. P. M. Richards (Eds.). *The Integration of a child into a social world*, 99-135.
- American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5<sup>th</sup> ed.). Washington, DC: American Psychiatric Association.
- Bannerman, R. L., Milders, M., de Gelder, B., & Sahraie, A. (2009). Orienting to threat: faster localization of fearful facial expressions and body postures revealed by saccadic eye movements. *Proceedings of the Royal Society B*, *276*, 1635-1641. doi: 10.1098/rspb.2008.1744
- Barrera, M. E., & Maurer, D. (1981). The perception of facial expressions by the three-month-old. *Child Development*, *52*, 203-206. doi: 10.2307/1129231
- Begeer, S., Koot, H. M., Rieffe, C., Meerum Terwogt, M., & Stegge, H. (2008). Emotional competence in children with autism: Diagnostic criteria and empirical evidence. *Developmental Review*, *28*, 342-369. doi: 10.1016/j.dr.2007.09.001
- Blasi, A., Lloyd-Fox, S., Sethna, V., Brammer, M. J., Mercure, E., Murray, L., ...Johnson, M. H. (2015). Atypical processing of voice sounds in infants at risk for autism spectrum

disorder. *Cortex*, 71, 122-133. doi: 10.1016/j.cortex.2015.06.015

Brett, D., Warnell, F., McConachie, H., & Parr, J. R. (2016). Factors Affecting Age ASD Diagnosis in UK: No Evidence Age has Decreased Between 2004 and 2014. *Journal of Autism and Developmental Disorders*, 46, 1974-1984. doi: 10.1007/s10803-016-2716-6

Bussu, G., Jones, E. J. H., Charman, T., Johnson, M. H., Buitelaar, J. K., & the BASIS Team (2018). Prediction of Autism at 3 Years from Behavioural and Developmental Measures in High-Risk Infants: A Longitudinal Cross-Domain Classifier Analysis. *Journal of Autism and Developmental Disorders*, 48, 2418-2433. doi: 10.1007/s10803-018-3509-x

Caron, A. J., Caron, R. F., & MacLean, D. J. (1988). Infant Discrimination of Naturalistic Emotional Expressions: The Role of Face and Voice. *Child Development*, 59, 604-616. doi: 10.2307/1130560

Charman, T., Young, G. S., Brian, J., Carter, A., Carver, L. J., Chawarska, K., ... & Zwaigenbaum, L. (2016). Non-ASD outcomes at 36 months in siblings at familial risk for autism spectrum disorder (ASD): A baby siblings research consortium (BSRC) study. *Autism Research*, 10, 169-178. doi: 10.1002/aur.1669

Chawarska, K., Macari, S., & Shic, F. (2013). Decreased spontaneous attention to social scenes in 6-month-old infants later diagnosed with ASD. *Biological Psychiatry*, 74, 195-203. doi: 10.1016/j.biopsych.2012.11.022

Chawarska, K., Shic, F., Macari, S., Campbell, D. J., Brian, J., Landa, R., & Bryson, S. (2014). 18-month predictors of later outcomes in younger siblings of children with autism spectrum disorder: A Baby Siblings Research Consortium study. *Journal of the American Academy of Child and Adolescent Psychiatry*, 53, 1317-1327. doi:

10.1016/j.jaac.2014.09.015

Cong, Y, Junge, C., Aktar, E., Raijmakers, M., Franklin, A., & Sauter, D. (2018). Pre-verbal infants perceive emotional facial expressions categorically. *Cognition and Emotion*, 33, 391-403. doi: 10.1080/02699931.2018.1455640

Dapretto, M., Davies, M. S., Pfeifer, J. H., Scott, A. A., Sigman, M., Bookheimer, S. Y., & Iacoboni, M. (2006). Understanding emotions in others: mirror neuron dysfunction in children with autism spectrum disorder. *Nature Neuroscience*, 9, 28-30. doi: 10.1038/nn1611

Dawson, G., Jones, E. J. H., Merkle, K., Venema, K., Lowy, R., Faja, S., ...& Webb, S. J. (2012). Early Behavioral Intervention is Associated With Normalized Brain Activity in Young Children With Autism. *Journal of American Academy of Child & Adolescent Psychiatry*, 51, 1150-1159. doi: 10.1016/j.jaac.2012.08.018

Dawson, G., Rogers, S., Munson, J., Smith, M., Winter, J., Greenson, J., ...& Varley, J. (2010). Randomized, Controlled Trial of an Intervention for Toddlers With Autism: The Early Start Denver Model. *Pediatrics*, 125, 17-23. doi: 10.1542/peds.2009-0958

De Klerk, C. C. J. M., Hamilton, A. F. de C., & Southgate, V. (2018). Eye contact modulates facial mimicry in 4-month-old infants: An EMG and fNIRS study. *Cortex*, 106, 93-103. doi: 10.1016/j.cortex.2018.05.002

Deligianni, F., Senju, A., Gergely, G., & Csibra, G. (2011). Automated Gaze-Contingent Object Elicit Orientation Following in 8-months-old Infants. *Developmental Psychology*, 47, 1499-1503. doi: 10.1037/a0025659

Di Giorgio, E., Méary, D., Pascalis, O., & Simion, F. (2013). The Face Perception System Becomes Species-Specific at 3 Months: An Eye-Tracking Study. *International Journal of Behavioral Development*, 37, 95-99. doi: 10.1177/0165025412465362

Ekman, P. (1973). Universal facial expressions in emotion. *Studia Psychologica*, 15, 140-147.

Farroni, T., Menon, E., Rigato, S., & Johnson, M. H. (2007). The perception of facial expressions in newborns. *European Journal of Developmental Psychology*, 4, 2-13.

doi: 10.1080/17405620601046832

Falck-Ytter, T., Bölte, S., & Gredebäck, G. (2013). Eye tracking in early autism research. *Journal of Neurodevelopmental Disorders*, 5.

Fernell, E., Eriksson, M. A., & Gillberg, C. (2013). Early diagnosis of autism and impact on prognosis: a narrative review. *Clinical Epidemiology*, 5, 33-43. doi:

10.2147/CLEP.S41714

Fox, S. E., Wagner, J. B., Shrock, C. L., Tager-Flusberg, H., Nelson, C. A. (2013). Neural processing of facial identity and emotion in infants at high-risk for autism spectrum disorders. *Frontiers in Human Neuroscience*, 7, 1-18. doi:

10.3389/fnhum.2013.00089

Gredebäck, G., Eriksson, M., Schmitow, C., Laeng, B., & Stenberg, G. (2011). Individual Differences in Face Processing: Infants' Scanning Patterns and Pupil Dilations are Influenced by the Distribution of Parental Leave. *Infancy*, 17, 79-101. doi:

10.1111/j.1532-7078.2011.00091.x

Guiraud, J. A., Tomalski, P., Kushnerenko, E., Ribeiro, H., Davies, K., Charman, T., ...the BASIS Team. (2012). Atypical Audiovisual Speech Integration in Infants at Risk for Autism.

*Plos One*, 7, e36428. doi: 10.1371/journal.pone.0036428

Holmqvist, K., Nyström, M., & Mulvey, F. (2012). Eye tracker data quality: What it is and how to measure it. *Proceedings of the Symposium on Eye Tracking Research and Applications*, 45-52. doi: 10.1145/2168556.2168563

Hunnius, S. De Wit, T. C. J., Vrinns, S., & Von Hofsten, C. (2011). Facing threat: Infants' and

- adults' visual scanning of faces with neutral, happy, sad, angry and fearful emotional expressions. *Cognition and Emotion*, 25, 193-205. doi: 10.1080/15298861003771189
- Isomura, T., & Nakano, T. (2016). Automatic facial mimicry in response to dynamic emotional stimuli in five-month-old infants. *Proceedings of the Royal Society B*, 283. doi: 10.1098/rspb.2016.1948
- Izard, C., Fine, S., Schultz, D., Mostow, A., Ackerman, B., & Youngstrom, E. (2001). Emotion knowledge as a predictor of social behaviour and academic competence in children at risk. *Psychological Science*, 12, 18-23. doi: 10.1111/1467-9280.00304
- Jones, E. J. H., Gliga, T., Bedford, R., Charman, T., & Johnson, M. H. (2014). Developmental pathways to autism: A review of prospective studies of infants at risk. *Neuroscience and Biobehavioral Reviews*, 39, 1-33. doi: 10.1016/j.neubiorev.2013.12.001.
- Keemink, J. R., Keshavarzi-Pour, M. J., & Kelly, D. J. (2019). Infants' Responses to Interactive Gaze-Contingent Faces in a Novel and Naturalistic Eye-Tracking Paradigm. *Developmental Psychology*, 55, 1362-1371. doi: 10.1037/dev0000736
- Kelly, D. J., Duarte, S., Meary, D., Bindeman, M., & Pascalis, O. (2019). Infants rapidly detect human faces in complex naturalistic visual scenes. *Developmental Science*, 22. doi: 10.1111/desc.12829
- Kelly, D. J., Liu, S., Rodger, H., Miellet, S., Ge, L., Caldara, R. (2011). Developmental Cultural Differences in Face Processing. *Developmental Science*, 14, 1176-1184.
- Koegel, L. K., Koegel, R. L., Ashbaugh, K., & Bradshaw, J. (2013). The importance of early identification and intervention for children with or at risk for autism spectrum disorders. *International Journal of Speech-Language Pathology*, 16, 50-56. doi: 10.3109/17549507.2013.861511
- Kotsoni, E., De Haan, M., & Johnson, M. (2001). Categorical Perception of Facial Expressions

- by 7-Month-Old Infants. *Perception*, *30*, 1115-1125. doi: 10.1068/p3155
- Landa, R. J., & Garrett-Mayer, E. L. (2006). Development in infants with autism spectrum disorders: a prospective study. *Journal of child psychology and psychiatry*, *47*, 629-638. doi: 10.1111/j.1469-7610.2006.01531.x
- Leezenbaum, N. B., Campbell, S. B., Butler, D., & Iverson, J. (2014). Maternal verbal responses to communication of infants at low and heightened risk of autism. *Autism*, *18*, 694-703. doi: 10.1177/1362361313491327
- Leppänen, J. M., & Nelson, C. A. (2012). Early Development of Fear Processing. *Current Directions in Psychological Science*, *21*, 200-204. doi: 10.1177/0963721411435841
- Ludemann, P.M. (1991). Generalised discrimination of positive facial expressions by seven- and ten-month-old infants. *Child Development*, *62*, 55-67. doi: 10.1111/j.1467-8624.1991.tb01514.x
- Ludemann, P. M., & Nelson, C. A. (1988). Generalised discrimination of positive and negative facial expressions. Paper presented at the International Conference on Infant Studies, Washington, DC.
- MacDonald, R., Parry-Cruwys, D., Dupere, S., & Ahearn, W. (2014). Assessing progress and outcome of early intensive behavioral intervention for toddlers with autism. *Research in Developmental Disabilities*, *35*, 3632-3644. doi: 10.1016/j.ridd.2014.08.036
- Mattson, W. I., Ekas, N. V., Lambert, B., Tronick, E., Lester, B. M., & Messinger, D. S. (2013). Emotional Expression and Heart Rate in High-Risk Infants during the Face-To-Face/Still-Face. *Infant Behavior and Development*, *36*, 776-785. doi: 10.1016/j.infbeh.2012.11.009
- McCleery, J.P., Allman, E., Carver, L. J., & Dobkins, K. R. (2007). Abnormal Magnocellular



- Pathway Visual Processing in Infants at Risk for Autism. *Biological Psychiatry*, *62*, 1007-1014. doi: 10.1016/j.biopsych.2007.02.009
- Merin, N., Young, G. S., Ozonoff, S., & Rogers, S. J. (2007). Visual Fixation Patterns during Reciprocal Social Interaction Distinguish a Subgroup of 6-Month-Old Infants At-Risk for Autism from Comparison Infants. *Journal of Autism and Developmental Disorders*, *37*, 108-121. doi: 10.1007/s10803-006-0342-4
- Miyazaki, M., Takahashi, H., Rolf, M., Okada, H., & Omori, T. (2014). The image-scratch paradigm: a new paradigm for evaluating infants' motivated gaze control. *Scientific Reports*, *4*, 5498. doi: 10.1038/srep05498
- Nelson, C. A., & Dolgin, K. (1985). The generalised discrimination of facial expressions by 7-month-old infants. *Child Development*, *56*, 58-61. doi: 10.2307/1130173
- Ozonoff, S., Young, G. S., Carter, A., Messinger, D., Yirmiya, N., Zwaigenbaum, L. ... Stone, W. L. (2011). Recurrence risk for autism spectrum disorders: a Baby Siblings Research Consortium Study. *Pediatrics*, *128*, 488-495. doi: 10.1542/peds/2010-2825.
- Philips, R. D., Wagner, S. H., Fells, C. A., & Lynch, M. (1990). Do Infants Recognize Emotion in Facial Expressions?: Categorical and 'Metaphorical' Evidence. *Infant Behavior and Development*, *13*, 71-84. doi: 10.1016/0163-6383(90)90006-T
- Piven, J., Elison, J. T., & Zylka, M. J. (2018). Toward a conceptual framework for early brain and behavior development in autism. *Molecular Psychiatry*, *23*, 165. doi: 10.1038/mp.2017.212
- Prunty, J. E., Jackson, K. C., Keemink, J. R., & Kelly, D. J. (2020). Caucasian infants' attentional orienting to own- and other-race faces. *Brain sciences*. doi: 10.3390/brainsci10010053
- Rosset, D. B., Rondan, C., Da Fonseca, D. D., Santos, A., Assouline, B., & Deruelle, C. (2007).

- Typical Emotion Processing for Cartoon but not for Real Faces in Children with Autistic Spectrum Disorders. *Journal of Autism and Developmental Disorders*, 38, 919-925. doi: 10.1007/s10803-007-0465-2
- Schwartz, G., Izard, C., & Ansul, S. (1985). The 5-month-olds' ability to discriminate facial expressions of emotions. *Infant Behavior and Development*, 8, 65-77. doi: 10.1016/S0163-6383(85)80017-5
- Sorce, J. F., Emde, R. N., Campos, J., & Klinnert, M. D. (1985). Maternal Emotional Signaling: Its Effect on the Visual Cliff Behavior of 1-Year-Olds. *Developmental Psychology*, 21, 195-200.
- Soussignan, R., Dollion, N., Schaal, B., Durand, K., Reissland, N., & Baudouin, J. (2017). Mimicking emotion: how 3-12-month-old infants use the facial expressions and eyes of a model. *Cognition and Emotion*, 32, 827-842. doi: 10.1080/02699931.2017.1359015
- Sroufe, L. A. (1979). The coherence of individual development: Early care, attachment, and subsequent developmental issues. *American Psychologist*, 34, 834-841.
- Steiner, A. M., Goldsmith, T. R., Snow, A. V., & Chawarska, K. (2011). Practitioner's Guide to Assessment of Autism Spectrum Disorders in Infants and Toddlers. *Journal of Autism and Developmental Disorders*, 42, 1183-1196. doi: 10.1177/1098300713482977
- Szatmari, P., Chawarska, K., Dawson, G., Georgiades, S., Landa, R., Lord, C. ... Halladay, A. (2016). Prospective longitudinal studies of infant siblings of children with autism: lessons learned and future directions. *Journal of the American Academy of Child & Adolescent Psychiatry*, 55, 179-187. doi: 10.1016/j.jaac.2015.12.014
- Tamis-LeMonda, C. S., Kuchirko, Y., & Song, L. (2014). Why is infant language learning facilitated by parental responsiveness? *Current Directions in Psychological Science*,

23. doi: 10.1177/0963721414522813

Tronick, E. (1989). Emotions and Emotional Communication in Infants (1989). *American Psychologist*, *44*, 112-119.

Vernetti, A., Senju, A., Charman, T., Johnson, M. H., Gliga, T., & the BASIS team (2018). Simulating interaction: Using gaze-contingent eye-tracking to measure the reward value of social signals in toddlers with and without autism. *Developmental Cognitive Neuroscience*, *29*, 21-29. doi: 10.1016/j.dcn.2017.08.004

Wagner, J. B., Luyster, R. J., Tager-Flusberg, H., & Nelson, C. A. (2016). Greater Pupil Size Response to Emotional Faces as an Early Marker of Social-Communicative Difficulties in Infants at High Risk for Autism. *Infancy*, *21*, 560-581. doi: 10.1111/inf.12128

Wan, M. W., Green, J., Elsabbagh, M., Johnson, M., Charman, T., & Plummer, F. (2012). Quality of interaction between at-risk infants and caregiver at 12-15 months is associated with 3-year autism outcome. *Journal of Child Psychology and Psychiatry*, *54*, 763-771. Doi: 10.1111/jcpp.12032

Wang, Q., Bolhuis, J., Rothkopf, C. A., Kolling, T., Knopf, M., Triesch, J. (2012). Infants in Control: Rapid Anticipation of Action Outcomes in a Gaze-Contingent Paradigm. *PLoS ONE*, *7*, e30884. doi: 10.1371/journal.pone.0030884

Wilms, M., Schilbach, L., Pfeiffer, U., Bente, G., Fink, G. R., & Vogely, K. (2010). It's in your Eyes – Using Gaze-contingent Stimuli to Create Truly Interactive Paradigms for Social Cognitive and Affective Neuroscience. *Social Cognitive and Affective Neuroscience*, *5*, 98-107. doi: 10.1093/scan/nsq024

Yirmiya, N., Gamliel, I., Pilowsky, T., Feldman, R., Baron-Cohen, S., & Sigman, M. (2006). The development of siblings of children with autism at 4 and 14 months: social engagement, communication, and cognition. *Journal of Child Psychology and*

*Psychiatry*, 47, 511-523. doi: 10.1111/j.1469-7610.2005.01528.x

Young, G. S., Merin, N., Rogers, S. J., & Ozonoff S. (2009). Gaze Behavior and Affect at 6-Months: Predicting Clinical Outcomes and Language Development in Typically Developing Infants and Infants At-Risk for Autism. *Developmental Science*, 12, 798-814. doi: 10.1111/j.1469-7610.2009.01833.x

Zwaigenbaum, L., Bryson, S., & Garon, N. (2013). Early identification of autism spectrum disorders. *Behavioural Brain Research*, 251, 133-146. doi: 10.1016/j.bbr.2013.04.004