Atypical modulation of face-elicited saccades in autism spectrum disorder in a double-step saccade paradigm

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Abstract

Atypical development of face processing is a major characteristic in autism spectrum disorder (ASD), which could be due to atypical interactions between subcortical and cortical face processing. The current study investigated the saccade planning towards faces in ASD. Seventeen children with ASD and 17 typically developing (TD) children observed a pair of upright or inverted face configurations flashed sequentially in two different spatial positions. The reactive saccades of participants were recorded by eye-tracking. The results did not provide evidence of overall impairment of subcortical route in ASD, However, the upright, but not the inverted, face configuration modulated the frequency of vector sum saccades (an index of subcortical control) in TD, but not in ASD. The current results suggests that children with ASD do not have overall impairment of the subcortital route, but the subcortical route may not be specialized to face processing.

Keywords

1. Introduction

Autism spectrum disorder (ASD) is a developmental disorder characterized by an impairment in social interaction and communication, with the presence of restricted and stereotyped behaviour and interests. One of the clearest manifestations of impaired social interaction in ASD is an atypical pattern of eye contact behaviour, which is even used to contribute to diagnosis (American Psychiatric Association, 2000). The development of atypical eye contact may start by around 1-year of age, and has been reported by the retrospective analyses of the home video of infants who later diagnosed as ASD (Elsabbagh & Johnson, 2007; Maestro et al., 2005). Note that atypical patterns of eye contact can occur earlier than the age when reliable diagnosis is possible (around 3 years). Although the mechanism underlying atypical eye contact behaviour is still unclear, it is unlikely to be driven by an active gaze avoidance, at least in early infancy, because neither young toddlers

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with ASD (Chawarska, Volkmar, & Klin, 2010) nor infants at high risk for developing ASD (Elsabbagh et al., 2009) avoid face or gaze in more controlled experimental settings.

Recently, Senju and Johnson(Senju & Johnson, 2009) proposed that atypical eye contact behaviour in ASD could result from the lack of influence of a subcortical face and eye contact detection route. The putative subcortical route consists of superior colliculus (SC), pulvinar and amygdala, and is hypothesized to modulate eye contact processing in typically developing individuals, and guide its emergent specialization during typical development (Johnson, 2005). Several lines of indirect evidence, such as an atypical developmental trajectory of the amygdala (Schumann et al., 2004) and atypical functional connectivity between amygdala and fusiform face area (Kleinhans et al., 2008), support this hypothesis. A recent neuroimaging study with functional magnetic resonance imaging (fMRI) also reported an absence of activation in subcortical route when adults with ASD process briefly presented faces (Kleinhans et al., 2011), which is consistent with the above hypothesis as well.

fMRI is an ideal tool to assess the functioning of subcortical route in adults, but for practical reasons it is difficult to apply the same method to young children and infants. Thus, researchers in developmental cognitive neuroscience have often used neuropsychological "marker tasks", which assess behavioural markers associated with a particular cortical or subcortical circuits. The double-step saccade paradigm is one of the neuropsychological marker tasks which assesses the involvement of the cortical and subcortical route on saccade generation. In a typical double-step saccade task, two identical visual target stimuli are briefly presented in two different spatial locations, one after another, before a participant has time to start their initial saccade. Two features characterize the recruitment of the subcortical route on saccade generation (Figure 1B). Firstly, the subcortical route generates a saccade to the direction of vector summation of two target positions because the summation of retinal position vectors is a hallmark of the SC, a core component of subcortical route (Johnson, Gilmore, Tucker, & Minister, 1996; Mays & Sparks, 1980; Robinson, 1972). Secondly, the subcortical route generates the second saccade to the second target based on the retinotopic representation of its location, because the SC represents space retinotopically (Gilmore & Johnson, 1997a, 1997b; Robinson, 1972). By contrast, cortical parietal circuits generate saccades based on head- or body-centred representations of the location of the second target (Figure 1B). For example, a series of studies has demonstrated that both the vector sum saccades and retinotopic representation become less frequent during the course of development in the first year of life (Gilmore & Johnson, 1997a, 1997b; Kaufman, Gilmore, & Johnson, 2006), suggesting initial dominance of the subcortical route on saccade generation followed developmentally by slower cortical maturation which takes over saccade control at older ages. In addition, Brown et al. (Brown et al., 2003) reported more frequent occurrences of vector sum saccades as well as retinotopic saccades in children with Williams syndrome (WS) compared to both typically developing children and children with Down syndrome, suggesting the greater reliance on subcortical route for saccade generation in WS.

The current study utilized a version of double-step saccade paradigm in order to explore whether children with ASD show atypical functioning of subcortical route, which could be relevant to atypical development of face and eye contact processing. We presented a pair of face configurations (Figure 1A), already thought to recruit the subcortical route in infants (Farroni et al., 2005; Johnson, Dziurawiec, Ellis, & Morton, 1991) and in adults (Tomalski, Csibra, & Johnson, 2009; Tomalski, Johnson, & Csibra, 2009) in its upright orientation. The inverted face configuration served as a visually matched control stimulus, because previous studies demonstrated that it does not recruit subcortical face processing route (Farroni et al., 2005; Johnson et al., 1991; Tomalski, Csibra et al., 2009; Tomalski, Johnson et al., 2009).

As in previous double-saccade paradigms, these pairs of stimuli were presented briefly to different spatial locations, one after another, before participants made initial saccade (Figure 1A). In this exploratory study, we investigated (1) whether children with ASD show atypical patterns of subcortically mediated saccades compared to typically developing children, and (2) whether the subcortically mediated saccades would be modulated by face configuration in each group.

2. Methods

2.1. Participants

Data from 17 children with ASD (5 females and 12 males) and 17 typically developing children (TD, 4 females and 13 males) were included in the analyses. Children with ASD included in the analyses had been diagnosed with Autistic Disorder (9), Asperger Disorder (3), PDD-NOS (2) or Pervasive Developmental Disorder without a specific diagnosis (3) by at least one child psychiatrist or pediatrician. To confirm their clinical manifestation, the Japanese version of the Autism Screening Questionnaire (ASQ-J) (Berument, Rutter, Lord, Pickles, & Bailey, 1999; Dairoku, Senju, Hayashi, Tojo, & Ichikawa, 2004) was administered to all of the children. Verbal and non-verbal intelligence was measured with the Japanese version of the Picture Vocabulary Test (PVT) (Ueno, Nadeo, & Iinaga, 1991) and the Japanese version of Raven's Coloured Progressive Matrices (RCPM) (Raven, 1956; Sugishita & Yamazaki, 1993). Children's scores for each test, as well as their chronological ages and scores of ASQ-J, are summarized in Table 1. All the children were recruited from a local school, and written informed consent was obtained from one of the children's guardians before the study. This study has been approved by the Research Ethics Committee of the Graduate School of Arts and Sciences, University of Tokyo.

2.2. Apparatus and Stimuli

A Tobii (Stockholm, Sweden) 2150 Eye Tracker, integrated with a 20-inch TFT monitor was used to present the stimuli and record eye movements. Stimulus presentation and recording were controlled via a computer with Tobii's ClearView software. Children were seated approximately 50 cm from the monitor. A five-point calibration was completed before the stimulus presentation (For technical details about the apparatus and the calibration procedure, see (von Hofsten, Dahlström, & Fredricksson, 2005).

The target stimuli were a pair of face configurations, each of which were composed of three black circles (1.3×1.1 cm each on the monitor) allocated within a white oval (8.4×5.8 cm). The stimuli were presented against grey background, either in upright or in upside down position (Figure 1A). Colourful cartoon animations (about 5.0×5.0 cm) were also used to attract children's fixation before the onset of target stimuli.

2.3. Procedure

Children sat in a chair 50 cm from the monitor placed in a sound-proofed room. An experimenter sat behind the children and controlled the experiment. The experiment consisted of one familiarization block and two test blocks. Each block was composed of 64 trials. Each trial started with a fixation stimulus, presented in one of four locations (corresponding to north, south, east and west) for 1 s. Then, a pair of target stimuli was presented on the monitor, one following the other, with no period of overlap. The target pairs were both the upright face configuration in half of the trials, and both the upside down face configurations in the other half. The first target appeared in one of the two diagonally adjacent positions from the fixation, and the second target appeared in the opposite location (Figure 1A). The target stimuli were presented for 80 ms each. Sixteen types of trials, a

combination of eight possible configurations of fixation-target sequences and two stimulus orientations, were presented in pseudorandom order.

2.4. Data reduction

Eye-tracking data was analyzed as follows: After recording, a gaze replay file showing the exact location of each participant's gaze was exported at 25 frames per second with the ClearView program. From the exported data, the point of fixation was coded frame by frame starting from the point when the first stimulus was presented to the end of stimulus presentation.

Trials were excluded from the analyses if the participant (a) did not fixate on the fixation point at the onset of first target stimulus, (b) made no saccade or (c) made a saccade before the offset of second stimulus. Otherwise, the trial was coded valid and included in the analyses. Then, the directions of the first saccade were coded as either to (d) the vector sum of the location of two targets (Figure 1B), (e) the first target, (f) the second target, (g) the centre or (h) other. The main measurement of interest was the frequency of vector sum saccades, which is modulated by the influence of the subcortical route. The ratio of numbers of each saccade type was calculated for each stimulus condition by dividing the number of each saccade by the total number of all saccade.

If the first saccade was to the first target, the direction of the second saccade was coded as either (i) body-centred saccade if it was directed to the body-centred representation (*i.e.* actual location) of the second target or (j) retino-centred saccade if it was directed to the retino-centric representation (*i.e.* the direction of second target relative to the initial fixation) of the second target (Figure 1B), or (k) other directions, following Brown et al. (Brown et al., 2003). The ratio of numbers of each second saccade type was calculated for each stimulus condition by dividing the number of each saccade by the total number of all second saccade.

2.5. Analyses

To analyze the possible modulation of saccades by subcortical route, the relative numbers of vector sum saccades have been analyzed by a three-way mixed-design analysis of variance (ANOVA) with group (ASD or TD) as a between-participant factor and stimulus orientation (upright or inverted) and block (first or second) as within-participant factors. The same ANOVAs were conducted for the other categories of first saccades also. The second saccades were analyzed following Brown et al. (Brown et al., 2003) with a four-way mixed ANOVA, with group (ASD or TD) as a between-participant factor and the type of spatial representation (retino-centred or body-centred) stimulus orientation (upright or inverted) and block (first or second) as within-participant factors.

3. Results

Two groups did not differ significantly in chronological age, verbal mental age or non-verbal abilities (all $t < 1.88$, all $p > .05$). ASD group scored significantly higher in ASQ-J than in TD group, confirming the diagnosis ($t(32) = 8.09$, $p < .001$, $d = 2.77$). The number of excluded trials did not differ between groups or stimulus type (all $F < 2.96$, all $p > .05$). All the participants had at least 5 valid trials for each stimulus type and for each block.

Overall, both groups showed the similar amount of relative frequency of vector sum saccades. The only significant effect was a three-way interaction between the group, face and block ($F(1,32) = 4.54$, $p < .05$, $\eta_p^2 = .124$). Follow-up analyses revealed significant interaction between stimulus orientation and block in TD group ($F(1,16) = 6.28$, $p < .05$, η_p^2

= .282), but not in ASD group ($F(1,16)$ =.306, $p > .05$, η_p^2 = .019). In TD group, as can be seen in Figure 2A, the frequency of vector sum saccades dropped significantly between blocks when the stimuli were upright face configuration ($t(16) = 2.49$, $p < .05$, $d = .603$), but not when inverted face configurations were presented ($t(16)$ =.914, $p > .05$, $d = .222$). The frequency of the vector sum saccades between upright and inverted conditions did not differ significantly in the first block ($t(16) = 1.16$, $p > .05$, $d = .282$). However, in the second block, the vector sum saccades occurred less frequently when the upright face configurations were presented than when the inverted face configurations were presented ($t(16) = 2.77$, $p < .05$, $d = .671$). In ASD group, by contrast, the frequency of vector sum saccade remained constant regardless of the orientation of face configuration (Figure 2B). No main effects or interactions reached significance in the relative number of the saccades to the first target, second target or other locations (all $F < 2.33$, all $p > .05$).

Only 14 children (8 in ASD group and 6 in TD group) made second saccades in both face orientation conditions and in both blocks. Among these children, the only significant effect was the type of spatial representation ($F(1,12) = 19.2$, $p < .01$, η_p^2 = .616). This was because most of the second saccades were based on head- or body-centred saccades (Table 2). No other main effects or interactions reached significance (all $F < 2.92$, all $p > .05$).

4. Discussion

The current study explored the functioning of subcortical route in children with ASD, and its sensitivity to face processing. Overall, the results showed similar frequency of subcortically mediated saccade in both TD children and children with ASD. Children with ASD showed similar overall proportion of vector sum saccades as in TD children, suggesting that there is no overall impairment in the subcortical route in ASD. This contrasts with children with WS, who demonstrated overall increase in vector sum saccades, indicating increased reliance on the subcortical route (Brown et al., 2003). Similarly, we did not find the modulation of retinotopic saccade planning by the orientation of face configuration in either the TD or ASD group. Instead, both groups showed significantly more body-centred saccades regardless of the orientation of face configuration. These results suggest that the overall development of subcortical route for saccade generation is similar between children with ASD and TD children.

The current results also demonstrated that upright face configuration modulates the frequency of vector sum saccades in the TD group, but not in the ASD group. In TD group, the modulation was evident as the significant reduction in the ratio of vector sum saccades in response to the upright face configuration only during the course of experiment. This observation is consistent with a known property of the subcortical route, which is prone to adaptation. As a result, one explanation of the changes we observed is that cortical saccadic control takes over following presentation of the upright face configuration during the course of experiment. This transition away from sub-cortical processing in response to upright faces during the course of experimental trials is consistent with previous studies with TD adults(Crouzet, Kirchner, & Thorpe, 2010; Tomalski, Csibra et al., 2009), suggesting that the subcortical route modulates saccade generation to some extent beyond infancy. The majority of face and gaze processing studies in typical and atypical development reported so far have focused on the development of cortical structures such as fusiform gyrus (Itier & Batty, 2009; Taylor, Batty, & Itier, 2004) and superior temporal sulcus (Pelphrey & Carter, 2008). The current results, by contrast, suggest that the contribution of subcortical structures such as SC, pulvinar and amygdala on face and gaze processing exists not only in early infancy, but may persist through to childhood.

Unlike TD children, the frequency of vector sum saccades was not modulated by face configuration in the ASD group. The upright face configuration did not result in the adaptation of the subcortical route and subsequent take over by the cortical route, but constantly elicited equivalent proportion of vector sum saccades. The current results suggest the absence of face-sensitive interaction between subcortical and cortical routes in ASD (Senju & Johnson, 2009), despite the generally intact functioning of the subcortical route on saccade generation. These results are consistent with the theories suggesting the importance of the interaction between the subcortical and the cortical structures on the atypical development of social cognition in ASD (Dawson, Webb, & McPartland, 2005; Schultz, 2005; Senju & Johnson, 2009). Further studies will be required to better understand how such atypical interaction between subcortical and cortical face and gaze processing develops in ASD, and how it relates to the atypical development of social interaction and communication in this population.

Acknowledgments

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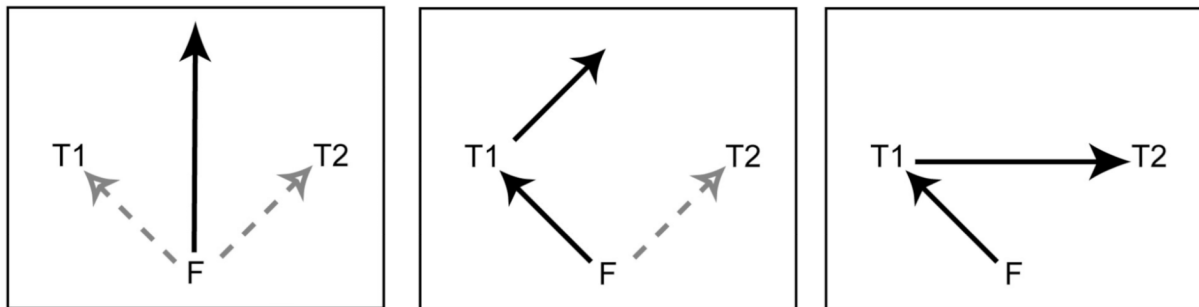
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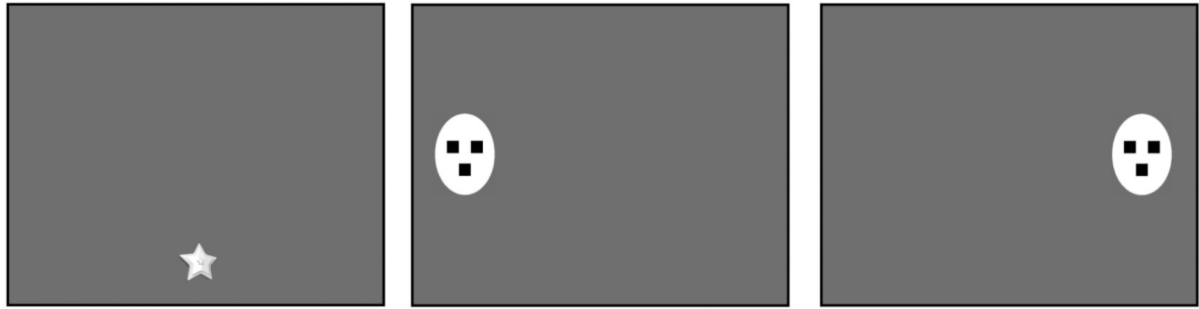
(A) Fixation Target 1 Target 2

Response Patterns

(B) Vector Sum Retinotopic Body-centred

Figure 1.
Design of double-step saccade paradigm. (A) A trial began with a presentation of a fixation stimulus consisting of a colourful and animating cartoon, which was followed by the brief presentation of two identical targets that flashed sequentially (80 ms each, with no overlap). Fixation positions varied in a pseudo-random order, between four possible locations: centre bottom (as shown), centre top, centre left and centre right. Targets were either upright (as shown) or upside-down face configurations. (B) Three types of responses were of critical concern: a vector sum saccade, the direction of which is equivalent to the vector summation of two target locations relative to the fovea; a retinotopic saccade consisting of two saccades, each equivalent to the positions of the targets at the time of presentation relative to the fovea; and a body-centred saccade, on to each target location. The black continuous lines represents the direction of exerted saccades, and the gray dashed lines represent the direction vector of each target at the time of presentation relative to fovea.
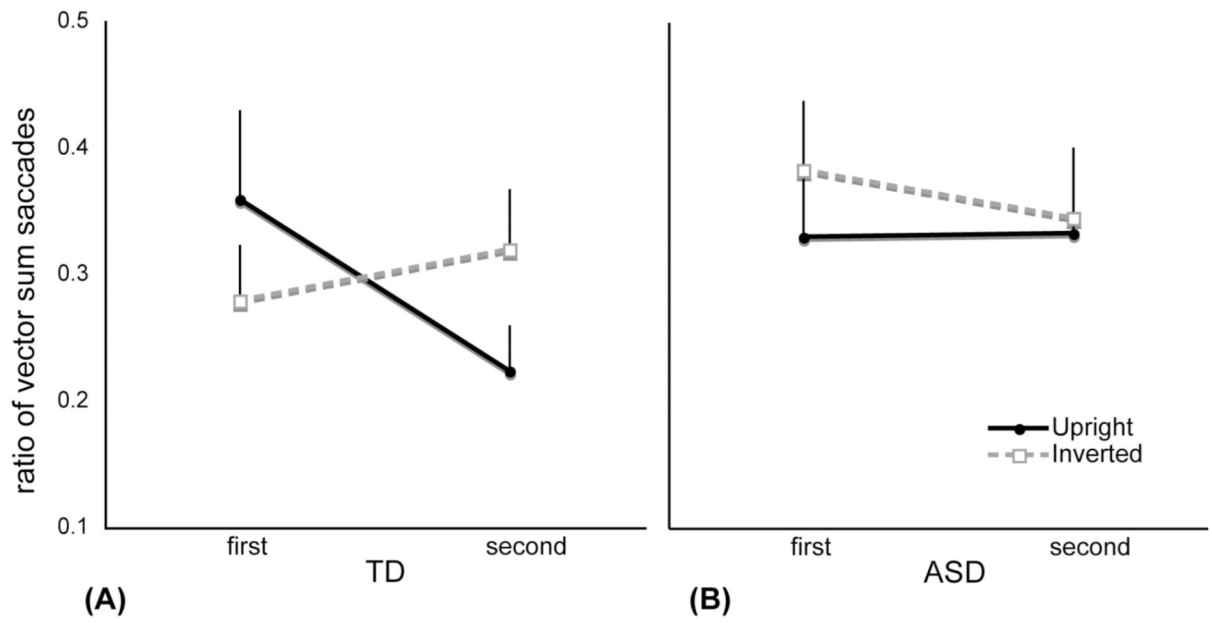
Figure 2.
The change in mean ratio of vector sum saccades from first to second blocks for upright (black continuous lines) and inverted (grey dotted lines) face configurations for (A) typically developing children (TD) and (B) children with Autism Spectrum Disorder (ASD). error bar: standard error.

Table 1

Mean Chronological Age (CA), Verbal Mental Age (VMA), scores of Raven's Coloured Progressive Matrices (RCPM) and scores of Japanese version of Autism Screening Questionnaire (ASQ-J) for children with Autism Spectrum Disorder (ASD) and typically developing children (TD).

	ASD (n = 17)		TD (n= 17)		Group difference
	M (SD)	**range**	**M (SD)**	**range**	
CA	8.8 (1.7)	6.5 – 12.1	8.1 (1.2)	6.35 – 10.0	n.s.
VMA	8.1 (2.2)	5.1 – 12.3	9.0 (2.2)	5.5 – 12.0	n.s.
RCPM	27.9 (5.3)	14 - 35	30.8 (3.4)	25 - 36	n.s.
ASQ-J	20.0 (8.3)	5 - 34	3.1 (2.4)	0 - 8	**

M: average, SD: Standard Deviation,

**
  $p < .01$, n.s.: not significant.

Table 2

Mean and standard deviations (in parentheses) of the ratio of retinotopic and body-centred saccades for children with Autism Spectrum Disorder (ASD) and typically developing children (TD).

orientation	block	ASD (n=8)		TD (n=6)	
		retinotopic	body-centred	retinotopic	body-centred
Upright	first	0.38 (0.42)	0.62 (0.42)	0.10 (0.15)	0.90 (0.15)
	second	0.13 (0.24)	0.83 (0.33)	0.36 (0.43)	0.64 (0.43)
Inverted	first	0.31 (0.37)	0.69 (0.37)	0.39 (0.38)	0.61 (0.38)
	second	0.15 (0.21)	0.81 (0.27)	0.31 (0.43)	0.69 (0.43)