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S.I. : EMOTION REGULATION AND PSYCHIATRIC COMORBIDITY IN ASD

No Evidence of Emotional Dysregulation or Aversion to Mutual Gaze in Preschoolers with Autism Spectrum Disorder: An Eye-Tracking Pupillometry Study

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Abstract The 'gaze aversion hypothesis', suggests that people with Autism Spectrum Disorder (ASD) avoid mutual gaze because they experience it as hyper-arousing. To test this hypothesis we showed mutual and averted gaze stimuli to 23 mixed-ability preschoolers with ASD (*M* Mullen DQ = 68) and 21 typically-developing preschoolers, aged 2–5 years, using eye-tracking technology to measure visual attention and emotional arousal (i.e., pupil dilation). There were no group differences in attention to the eye region or pupil dilation. Both groups dilated their pupils more to mutual compared to averted gaze. More internalizing symptoms in the children with ASD related to less emotional arousal to mutual gaze. The pattern of results suggests that preschoolers with ASD are not dysregulated in their responses to mutual gaze.

Keywords Mutual gaze · Autism · Gaze aversion hypothesis · Direct eye contact · Eye-tracking pupillometry · Emotional regulation

> The soul that can speak through the eyes can also kiss with a gaze.
>
> —Gustavo Adolfo Bécquer

Introduction

One of the most apparent features of Autism Spectrum Disorder (ASD), a neurodevelopmental disorder defined by reciprocal social-communicative difficulties and behavioural rigidity [American Psychiatric Association (APA), 2013], is problems with responding to and returning other's eye gaze (Kanner 1943; Tonge et al. 1994). When someone gives us direct eye contact, we have an emotional response and our attention becomes captured by their eyes (Senju and Johnson 2009a). Direct eye contact between two people, *mutual* gaze, is an essential component of interpersonal interaction. Moreover, through establishing mutual gaze with another, we may not only initiate, sustain or terminate interpersonal interactions, but also communicate emotional meaning, such as warmth or distrust (Cook 1977; Exline and Winters 1965; Itier and Batty 2009; Mazur et al. 1980; Nielsen 1962). Hence responding to and using mutual gaze are multifaceted social skills.

In typical development, the adult pattern of preferential attention to and enhanced neural response to mutual gaze (George and Conty 2008) emerges during the first months of life (Farroni et al. 2002; Farroni et al. 2004; Striano et al. 2006), though refinement of this phenomena occurs over the course of development (Farran and Kasari 1990; Gliga and Csibra 2007; Johnson et al. 2005; Senju and Johnson 2009a). Abnormalities with eye contact is a defining feature of people with ASD [American Psychiatric Association (APA), 2013] and research shows that they have

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atypical responses to direct eye contact (Lord et al. 2000; Volkmar and Mayes 1990; Willemsen-Swinkels et al. 1998). Reduced engagement in mutual gaze in ASD can be seen over the first 6 months of life (Jones and Klin 2013) and this difficulty commonly persists into adulthood (Senju and Johnson 2009b).

One prominent theory of why people with ASD have such difficulties with mutual gaze is that they find mutual gaze hyper-arousing and/or aversive. We examine this ‘gaze aversion hypothesis’ (Bowman et al. 2004; Tanaka and Sung 2013) by first exploring the findings regarding *visual attention* to mutual gaze, and then by investigating the findings on *emotional arousal* to mutual gaze in ASD.

Visual Attention to Mutual Gaze

If individuals with ASD experience eye contact as an aversive stimulus, they might avert their gaze when people look at them directly. Consistent with this notion, some eye-tracking studies that have examined visual-scanning patterns of neutral/emotional faces with direct eye contact or naturalistic social scenes have found reduced attention to the eye region in ASD (Jones et al. 2008; Klin et al. 2002; Nuske et al. 2014b; Spezio et al. 2007). However, other eye-tracking studies have found normative visual attention to the eye region in ASD (e.g., Elsabbagh et al. 2009; Van der Geest et al. 2002; Young et al. 2009), with some studies suggesting that individuals with ASD, just like TD individuals, do look for a longer duration to the eye region compared to other face regions (e.g., Hernandez et al. 2009).

As most of these studies did not use control conditions showing the face *without* mutual gaze for comparison, it is difficult to ascertain whether these face-scanning patterns are directly related to mutual gaze or rather to general face scanning. To our knowledge, only four studies to date have examined visual attention to mutual versus averted eye gaze or closed eyes in ASD, and the results are mixed (see Table 1; also included are studies on physiological reactivity). Two studies found that both ASD and comparison groups look for a longer duration to mutual gaze than to averted or closed eyes (Louwerse et al. 2013; Vivanti et al. 2011); one study found that both groups looked equally to mutual and averted or closed eyes (Kaartinen et al. 2012) and one study found that children in the ASD group did not look for a longer duration to mutual versus averted gaze while the control did (Vivanti and Dissanayake 2014). Therefore, although reduced use of mutual gaze in ASD is a consistent clinical finding, only a few eye-tracking studies have examined visual attention to mutual gaze with appropriate experimental control conditions, yielding mixed findings.

Emotional Arousal to Mutual Gaze

If mutual gaze is aversive to people with ASD one might also expect emotional dysregulation in response to mutual gaze in this population. Though dysregulation can lead to two overall patterns of emotional arousal, *hyper*-arousal or *hypo*-arousal, hyper-arousal would be predicted if mutual gaze were experienced as ‘threatening’ in ASD. Emotional arousal can be measured by brain activation in sub-cortical emotional brain centres, such as the amygdala (Adolphs 2010). Some neuroimaging studies have found that people with ASD are hyper-aroused (have more amygdala activity) by mutual gaze (Dalton et al. 2005; Kliemann et al. 2012). These findings have been suggested to account for reduced mutual gaze in people with ASD, thought to be an adaptive strategy to regulate arousal during social interactions (Bowman et al. 2004; Dalton et al. 2005; Kliemann et al. 2010; Tanaka and Sung 2013; Tottenham et al. 2013).

Another way to measure emotional arousal is by capturing autonomic nervous system (ANS) or physiological responses, such as skin conductance responses (SCRs), heart rate or pupil dilation (Stern et al. 2001). In typical development, mutual gaze produces higher physiological responses than averted gaze (Emery 2000; Mazur et al. 1980; McBride et al. 1965; Nichols and Champness 1971). In ASD, six studies have measured physiological responses to mutual versus averted gaze or closed eyes to date. As shown in Table 1, between-group differences show that findings are mixed. Some studies have documented the opposite pattern, finding *hypo*-arousal to mutual gaze in ASD relative to comparison groups (Kaartinen et al. 2012; Stagg et al. 2013). These findings have been interpreted in terms of reduced motivational salience of social stimuli in this population (Chevallier et al. 2012; Dawson et al. 1998; Zeeland et al. 2010), such that people with ASD have reduced emotional responses to mutual eye contact, so seek out these experiences less than their TD peers. However, Kaartinen et al. (2012) also found hypo-arousal in ASD relative to a comparison group in response to averted and closed eyes, suggesting a general hypo-responsiveness to faces rather than to mutual gaze. Joseph et al. (2008) found hyper-arousal in ASD relative to a comparison group to mutual and averted gaze, and other studies have found no group differences in physiological arousal to mutual gaze between ASD and non-ASD comparison groups (Kylliäinen et al. 2012; Kylliäinen and Hietanen 2006; Louwerse et al. 2013). Taken together, both the findings of reactivity to mutual gaze and the mechanisms for reduced mutual gaze in ASD remain unclear.

One potential explanation for the contradictory findings is differences in age and/or IQ across studies. However, as

Table 1 Summary of studies on mutual versus averted eye gaze/shut eyes measuring visual attention and/or reactivity in autism

Study (least to most recent)	Age of ASD group (range, or if not provided, M)	Functioning level	Findings: duration of visual attention (VA)/physiological reactivity (PR)	Other findings: correlations with autism symptoms? If not reported, other?	VA within group: Look more to mutual (vs. averted gaze)?	PR between group: In, ASD, hyper-arousal to mutual gaze, hypo-arousal or no difference (ND)?
Kylliäinen and Hietanen (2006)	6–16 years	HF	PR: SCRs of ASD mutual > averted, TD mutual = averted. ASD = TD (across conditions)	ASD = TD on behavioural judgement of eye gaze direction	–	ND
Joseph et al. (2008)	9–16 years	HF	PR: SCRs of ASD > TD on mutual and averted. For ASD and TD, averted = mutual	In ASD (not TD), face recognition accuracy related to SCRs to mutual gaze	–	Hyper (but also for averted eyes)
Vivanti et al. (2011)—Study 4	10–16 years	HF	VA: ASD and TD mutual > averted	Propensity to imitate in ASD not influenced by mutual gaze as is in TD	TD: Yes ASD: Yes	–
Kaartinen et al. (2012)	8–16 years	HF	VA: ASD = TD and for ASD and TD, mutual = averted = eyes closed PR: SCRs of TD > ASD across conditions	In ASD, social impairments correlated with proportion of higher SCRS to mutual versus averted/eyes closed conditions	TD: No ASD: No	Hypo (but also for averted and closed eyes)
Kylliäinen et al. (2012)	10–14 years	HF	PR: SCRs of TD on eyes wide open = eyes open = eyes shut, but for ASD, eyes wide open > eyes open > eyes shut. TD > ASD on eyes shut, but TD = ASD on eyes open and wide open	For both groups familiar faces > unfamiliar faces (across eye gaze conditions)	–	ND
Louwerse et al. (2013)	12–19 years	HF	PR: On HR and SCRs TD = ASD for mutual, averted and closed eyes. On HR, for both groups, closed > mutual eyes	On subjective ratings of arousal, ASD = TD across eye gaze conditions	TD: Yes ASD: Yes	ND (HR and SCRs)
Stagg et al. (2013)	M = 9 years	HF: 2 groups, 1 with a history of language delay (HF–LD), 1 with normal language onset (HF–LN)	PR: SCRs across groups, mutual > eyes closed (averted = mutual, averted = closed). TD = HF–LN > HF–LD (across conditions)	SCRs in ASD (HF groups collapsed) positively related to attention to gaze during infancy and verbal mental age	–	Hypo (HF–LD only, not HF–LN)
Vivanti and Dissanayake (2014)	28–72 months	LF and HF	VA: ASD < TD/DD controls on mutual, ASD = TD/DD controls on averted	Propensity to imitate in ASD not influenced by mutual gaze as is in TD	TD/DD: Yes ASD: No	–

ASD Autism Spectrum Disorder group, *DD* developmentally delayed group, *LF* low functioning, *HF* high functioning, *HR* heart rate, *M* mean, *NR* not reported, *ND* no group difference, *PR* physiological reactivity, *SCR* skin conductance response, *TD* typically-developing group, *VA* visual attention

shown in Table 1, most studies to date have used high-functioning older children–adolescent samples, so these do not appear to map onto the discrepant findings in the literature to date. As differences in physiological reactivity to facial expressions shown live versus on video have been documented (Riby et al. 2012), similar differences across stimuli presentation may be expected for eye gaze stimuli and could also contribute to the variability in findings presented above.

Another explanation for the discrepant findings reviewed above is that it is not ASD per se that produces atypical mutual gaze reactivity, but rather the internalising symptoms/syndromes, such as anxiety or depression (Achenbach 1966; Achenbach and McConaughy 1992), which are common in ASD (Kim et al. 2000; Mazefsky et al. 2008, 2010; White et al. 2009) that account for the atypicality of gaze. Indeed, people with anxiety-related disorders have been found to have heightened physiological responses to mutual eye contact (Wieser et al. 2009), and they tend to avoid or fear mutual eye contact (Roelofs et al. 2010; Schulze et al. 2013). Internalising symptoms, such as anxiety are so prevalent in ASD that Mazefsky and colleagues have argued that a higher risk for anxiety is intrinsic to the disorder, stemming from commonly co-occurring emotion regulation impairments (Mazefsky et al. 2012, 2013; Mazefsky and Herrington 2014; White et al. 2014). Indeed Corden et al. (2008) found that reduced visual attention to the eyes in adults with ASD was related their levels of social anxiety (however, the study did not examine response to mutual vs. non-mutual gaze). Nevertheless, it remains unknown if atypical emotion arousal to mutual gaze in ASD relates to internalising symptoms in affected individuals.

Emotional Arousal to Mutual Gaze in Familiar People

As people typically feel less anxious around familiar people than strangers (Stephan and Stephan 1985), an important research question is whether children with ASD have more normative physiological responses to mutual gaze from familiar versus unfamiliar people. Nuske et al. (2014a) found that typically-developing (TD) children have greater pupil dilation (increased emotional arousal) to emotional facial expressions in unfamiliar people compared to familiar people, but this was not the case for children with ASD. Conversely, in the only published study that has measured emotional arousal to mutual versus averted gaze in familiar and unfamiliar people, Kylliäinen et al. (2012) found that both children with ASD and TD children had greater SCRs to familiar compared to unfamiliar people. Therefore, not only is more research needed to determine whether people with ASD have atypical emotional arousal to mutual gaze, but also more research is needed to determine whether this arousal is affected by person familiarity.

The Current Study

Our main aim was to determine whether young children with ASD show gaze aversion and/or abnormalities in emotional arousal to mutual eye gaze, by measuring visual attention and pupillary reactions using eye-tracking technology to mutual versus averted gaze in familiar and unfamiliar persons. In this study physiological reactivity to mutual versus averted gaze was measured in a sample of mixed-ability children with ASD. To our knowledge this is the first study to examine relationships between mutual gaze reactivity and internalising symptoms in ASD.

We employed eye-tracking pupillometry as it has numerous advantages. First, pupillary responses have been shown to be a reliable marker of emotional arousal (Bradley et al. 2008; Partala and Surakka 2003), and is well established to be functionally linked to the amygdala (Applegate et al. 1983; Graur and Siegle 2013; Urry et al. 2006; Ursin and Kaada 1960; Zbrozyna 1963). Second, whilst movement-related artefacts are common in neurophysiological and physiological data (Patriquin et al. 2013; Tyszka et al. 2013), advanced eye-tracking systems are less prone to this type of artefact (explained further in section “Apparatus”). This issue is particularly relevant to the study of young children with and without ASD, as they often have difficulty staying still and following instructions. Third, eye-tracking pupillometry is non-invasive, and thus circumvents issues surrounding the application of electrodes for measuring ERPs, SCRs or heart-rate which may in itself cause elevated arousal in individuals with ASDs who commonly present with tactile sensitivities (Marco et al. 2011). Fourth, the above-mentioned decrease in movement-related artefacts and the non-invasiveness of this technology together make it well-suited for use with lower functioning children with ASD, who are too often excluded from such research (Vivanti et al. 2013).

We had four main hypotheses. First, based on the gaze aversion theory we expected that, relative to the comparison group, the children with ASD would look less to the eye region during mutual gaze and, second, have hyper-arousal to mutual gaze (greater pupil dilation). Third, following the initial findings of Corden et al. (2008), we expected an association between less visual attention to eye region and more internalising symptoms in the ASD group. Fourth, based on the theoretical model outlined by Mazefsky and colleagues, (Mazefsky et al. 2012, 2013; Mazefsky and Herrington 2014; White et al. 2014), we predicted that emotional arousal to mutual gaze in ASD, a potential measure of emotional dysregulation, would relate to internalising symptoms in this group. Based on the findings presented above, we also expected that children in the TD group would look more and have increased pupil dilation to mutual gaze relative to averted gaze, and greater pupil dilation to unfamiliar compared to familiar people.

Method

Participants

Twenty-seven children with ASD and 21 TD children, aged 2–5 years, participated in the study. However, four children in the ASD group were excluded as they looked for <10 % of the duration of the face stimulus in one or more of the conditions, resulting in a total of 23 children in the ASD group. Participant characteristics are presented in Table 2. Both groups were recruited through the same community childcare centre offering services for children with ASD and TD children. The Mullen Scales of Early Learning (MSEL; Mullen 1995) were administered to all participants to measure cognitive ability. As expected, the ASD group were lower in cognitive ability than the TD group, so cognitive ability was entered as a covariate in the analyses. Following the recommendations of Dykens and Lense (2011), our group of children with ASD included both children who were low- and high-functioning (65.2 % low-functioning, 34.8 % high-functioning, using the cut-off standard score of 70; Minshew et al. 1995).

Clinic-based diagnoses of the children with ASD were confirmed using the Autism Diagnostic Observation Schedule (Lord et al. 1999), by clinicians certified for research purposes on the administration and coding of the ADOS, with 15 children meeting criteria for Autistic Disorder and 8 meeting criteria for ASD; Calibrated Severity Scores (CSS) were used (Gotham et al. 2007). One participant was taking methylphenidate at the time of testing. However, as this participant was not an outlier on any dependent variable, and given that results remained unchanged with the exclusion of his data, he was retained in the sample. All participants, including TD controls, were free from any other medical conditions, and had no visual, hearing or motor impairments. The research was approved by the La Trobe University Human Ethics Committee.

Apparatus

A Tobii 120 binocular eye tracker and Tobii Studio software (version 3.0.3 Tobii, Stockholm, Sweden) were used to present stimuli and record visual attention and pupil diameter. This system presents stimuli on a computer-like monitor and does not require any equipment to be fastened onto the participant. Using multiple sensors, with bright and dark pupil tracking, a 3D model of the pupil, taking into account optical distortions from the cornea and lens, is built, allowing for both pupil diameter and distance from the screen to be measured at a sampling rate of 60 Hz (one sample every 16.67 ms). With this tracking technique, movement-related artefacts are handled in two ways. Firstly, as pupil size is a function of distance from the screen (of participant's head to the monitor), the effect of head movements perpendicular to the monitor are eliminated from the measure of pupil diameter on a sample-to-sample basis, using basic principles of trigonometry. Secondly, other head movements (i.e., those parallel to the monitor) are accurately tracked up to 25 cm/s. The eye-tracking monitor (TFT-LCD; W: 34 cm × H: 27 cm) had a refresh rate of 60 Hz. Brightness was set to 100 %.

Materials

Video Filming

Continuous videos were taken of adults who were familiar and unfamiliar to the children, first looking out to the side of the camera (for the averted gaze condition) and then looking directly at the camera (for the mutual gaze condition), and vice versa. To standardise the averted and mutual gaze frame length across the videos, we digitally

Table 2 Participant characteristics

	ASD group (N = 23)	TD group (N = 21)	Comparison coefficients
Age in years: *M* (*SD*)	4.05 (1.01)	4.27 (0.60)	$t(42) = .85, p = .40$
Gender: M, F	19, 4	18, 3	$\chi^2 = .08, p = .78$
MSEL, SS[a]: *M* (*SD*)	68.48 (22.47)	100.29 (16.41)	$t(42) = 5.32, p < .001$
ADOS-2, C-SevSc[b]: *M* (*SD*)	6.52 (2.76)	–	–
ADOS-2, C-SA[c]: *M* (*SD*)	11.83 (5.08)	–	–
ADOS-2, C-RRB[d]: *M* (*SD*)	4.22 (2.39)	–	–
VABS-II, Internalising[e]	20.68 (1.84)	–	–

[a] Mullen Scales of Early Learning standard score (Early Learning Composite), Autism Diagnostic Observation Schedule-2: [b] Calibrated Severity Score, [c] Calibrated Social Affect Score, [d] Calibrated Restricted and Repetitive Behaviours Score, [e] Vineland Adaptive Behaviour Scales, second edition-Internalising subscale score

edited these to be displayed for exactly 4 s each using iMovie HD 6.0.3 (Apple Computer Inc., Cupertino, CA, USA). Twelve videos in total were taken for each child: three familiar people and three unfamiliar people were in two videos each, i.e., six videos were shown for each familiarity condition, for each child. For the children with ASD, the familiar people were their intervention therapists and centre staff within their childcare playroom, and for the TD children the familiar people comprised the staff within their childcare playroom. The criterion that was set to ensure the childcare staff were familiar to the child participants was that the children had to be enrolled for a minimum of 3 months in the childcare centre.

Video Preparation

As different colours emit different levels of luminosity, the selected videos were first converted to grey scale so that pupil size would not be affected. Also, as the videos were not the same luminosity across participants, the videos were matched on luminosity by analysis of the first still frame of the videos, per familiarity condition and group, using Adobe Photoshop 8.0 (Adobe Systems, San Jose, CA, USA). There were no significant differences in luminosity of familiar and unfamiliar stimuli, and between the stimuli for each group (all $p > .55$). A scrambled image was created from the averted gaze still frame for each video and was also matched on luminosity to this still frame, which served as a buffer for the pupillary light reflex, to ensure that changes in pupil size captured during the presentation of the first gaze image in the videos were not due to pre-stimulus to stimulus luminosity changes. Using iMovie HD 6.0.3 (Apple Computer Inc., Cupertino, CA, USA), the videos were adjusted so that the averted and mutual gaze frames were each shown for 4 s in each video, to standardise the presentation duration of each gaze frame across the videos (see Fig. 1).

Parent-Report of Internalising Symptoms

The Vineland Adaptive Behaviour Scales, second edition (VABS-II; Sparrow et al. 2005) was completed by the parents of children with ASD to measure internalising symptoms, including anxiety, depressive and withdrawal-type behaviours. The VABS-II internalising scale was not administered to the TD group, as our research question regarding this scale was only relevant for the ASD group.

Procedure

Testing took place in a well-lit room of the community childcare centre which had no external light. Ambient luminosity was checked prior to each testing session, using a handheld photometer (model PLMX, Quantam Instruments). Ambient luminosity did not differ during testing between the ASD and TD groups, $t(36) = -.09$, $p = .93$. The children were seated in a comfortable chair, approximately 60 cm (36.46° visual angle) from the eye-tracking monitor. The experimenter first calibrated the children's eye movements with the built-in five point Tobii Studio calibration procedure. Following this, each child passively viewed the videos which were counter-balanced for stimuli order and interspersed between the presentation of 'filler' stimuli to maintain attention (Janisse 1977).

Data Reduction

Pupil data, preprocessed to be free of movement-artefacts (see section "Apparatus"), were further processed with a custom-built LabVIEW 2010 (National Instruments, Austin, TX, USA) algorithm (Beaton, unpublished), based on previously published methodology (e.g., Farzin et al. 2009; Hepach et al. 2012). First, samples for which only one eye was tracked were eliminated, to minimise pupil size miscalculation due to head angle or ambient light exposure. Where both eyes were tracked, a mean pupil diameter across eyes was computed. Second, to remove extreme sample-to-sample changes in pupil diameter due to partial eyelid closures, which are common in samples either side of missing data due to blinks, samples outside 2 × standard deviations of the mean rate of change, calculated for each participant, were removed. Third, gaps in data, due to blinks, were only linearly interpolated between stable data points (traces), to a maximum of 350 ms (Chau and Betke 2005; Martineau et al. 2011). A trace was deemed stable if there were a minimum of 50 % of the samples in 2 × total length of the gap, pre- and post-gap. This method allowed for a differential threshold for linear interpolation, based on gap length and the reliability of the pre/post gap data. Finally, a standardised pupillary response variable was computed from the data, controlling for a baseline response to the scrambled face image. The following formula was used:

$$a = (b - c)/c \times 100$$

where a = percentage change from scrambled to face image, b = mean pupil diameter during the face image gaze condition and c = mean pupil diameter during the scrambled image, averaged across trials, per participant. Four standardised pupil percentage change variables were calculated: familiar mutual, familiar averted, unfamiliar mutual and unfamiliar averted. For brevity, these will be referred to as 'pupil dilation' (PD), for each of the four conditions, as follows: PD-Familiar Mutual, PD-Familiar Averted, PD-Unfamiliar Mutual and PD-Unfamiliar Averted.

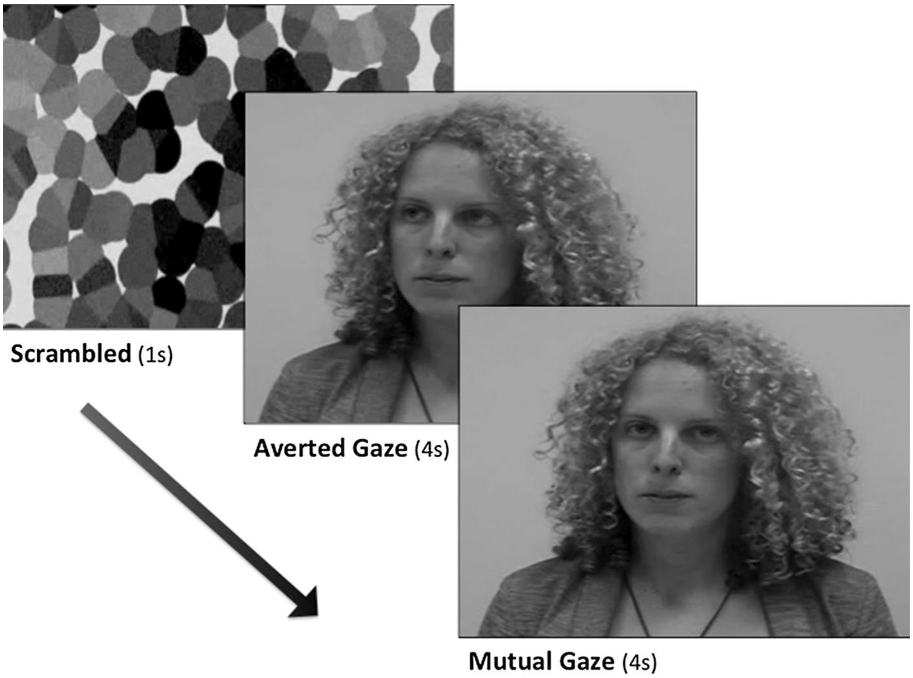

Fig. 1 Video stimuli. The scrambled image was shown first, for 1 s, followed by the averted gaze video frame (digitally edited to 4 s) and then the mutual gaze video frame (digitally edited to 4 s). The starting order of the averted and mutual gaze frames was counterbalanced in the testing block within participant groups

Visual attention data (fixation counts) were extracted from Tobii Studio using a fixation filter (I-VT), using the default pre-sets (maximum gap length: 75 ms, window length: 20 ms, velocity threshold: 30°/s, maximum time between fixations: 75 ms, maximum angle between fixations: 0.5°), with the exception that the minimum fixation duration for the fixation counts was set to 100 ms. This minimum fixation duration was chosen as eye-tracking data of 100 ms or more are not only more reliable than data tracked for shorter durations (Komogortsev et al. 2010), but are also considered to be a reliable index of what elements in a scene are actually captured and processed (Poole and Ball 2006). To examine visual attention to the eye region of faces, eye areas of interest (AOIs) were created on the facial stimuli (see Fig. 2).

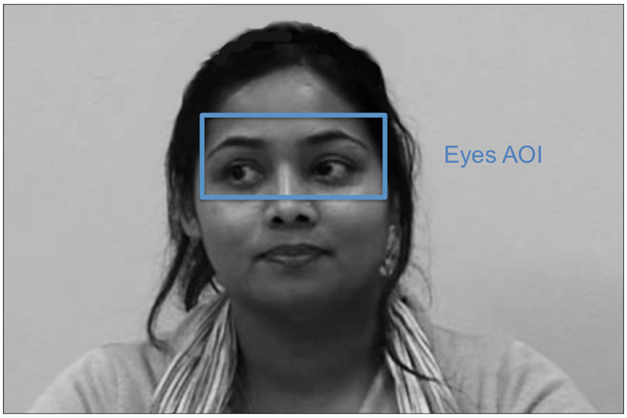

Fig. 2 Eye areas of interest (AOIs)

Statistical Analysis

Data were first analysed for skewness, kurtosis and outliers. As data were normally distributed, parametric tests were used in all analyses. To test our four main hypotheses stated above we conducted two repeated measures (RM) ANOVAs and ran two Pearson correlation analyses.

First, to test whether the children with ASD showed gaze aversion to the eye region of faces compared to the TD children, a 3-way RM ANCOVA was conducted on fixation counts (2 Groups × 2 Familiarity Levels × 2 Gaze Directions), controlling for overall fixation counts to the whole screen (averaged across the four conditions) as the ASD group looked for a shorter duration across the four conditions (all Independent Samples *t* test *ps* $< .025$; TD group $M = 37.988$, $SD = 13.402$; ASD group $M = 27.380$, $SD = 8.448$). Moreover, the effect of the whole-screen fixation counts covariate was significant, $F(1,41) = 9.775$, $p = .003$, $\eta^2 = .193$. Second, to determine whether the children with ASD had hyperarousal to mutual versus averted gaze of familiar/unfamiliar people, as compared to the TD children, a 3-way RM ANOVA (2 Groups × 2 Familiarity Levels × 2 Gaze Directions) was conducted on pupil dilation percentages.

To decide whether cognitive ability should be entered as a covariate in the RM ANOVAs, we checked whether cognitive ability (Mullen standard score) was correlated with visual attention (fixation counts) or pupil dilation in the two groups, in each of the familiarity and eye gaze conditions, by computing Pearson correlations between these variables. For both groups, cognitive ability was not related to visual attention (r range = −.186–.280, p range = .195–.853), nor to pupil dilation (r range = −.138–.283, p range = .213–.983). Furthermore, taking a conservative approach, we initially ran the two RM ANOVAs (described above) as RM ANCOVAs, controlling for cognitive ability. For both the RM ANCOVA on visual attention and pupil dilation, the effect of the cognitive ability covariate was non-significant [$F(1,41) = .931$, $p = .340$, $\eta^2 = .022$ and $F(1,40) = .006$, $p = .937$, $\eta^2 < .001$, respectively]. Therefore the analyses reported below were run without this covariate.

As reacting emotionally to the stimuli presented is necessarily related to visually attending to the stimuli, to determine whether visual attention needed to be partialled out of the analyses for the pupil dilation RM ANOVA, we also initially ran a series of Pearson correlations between fixation counts and the pupil dilation variables. Although visual attention was not related to pupil dilation in the TD group (r range = .209–.335, p range = .137–.363), in the ASD group visual attention was significantly related to each of the pupil dilation conditions (familiar averted: $r = .509$, $p = .013$, familiar mutual: $r = .561$, $p = .005$, unfamiliar averted: $r = .471$, $p = .023$ and unfamiliar mutual: $r = .471$, $p = .023$). Moreover, the effect of the visual attention covariate was significant, $F(1,41) = 8.950$, $p = .005$, $\eta^2 = .179$; thus we retained this covariate in the analysis.

Third, the relationship between internalising symptoms (VABS-II Internalising Scale) and visual attention (fixation counts to the eye AOI), for each of the familiarity and eye gaze conditions was computed with a Pearson correlation analysis. Fourth, the association between internalising symptoms and pupil dilation to mutual versus averted gaze for each of the familiarity and eye gaze conditions was computed with another Pearson correlation analysis.

Results

Between-Group and Within-Group Effects

Visual Attention

Though there was a trend toward both groups looking for more time at the averted versus mutual gaze, across familiarity conditions, the main effect of Gaze Direction was not significant, $F(1,41) = 3.908$, $p = .055$, $\eta^2 = .087$. Adjusted means are shown in Fig. 3, taking into account overall attention to whole screen. Like wise, the other main effects and interaction effects were not significant (p range = .140–.995).

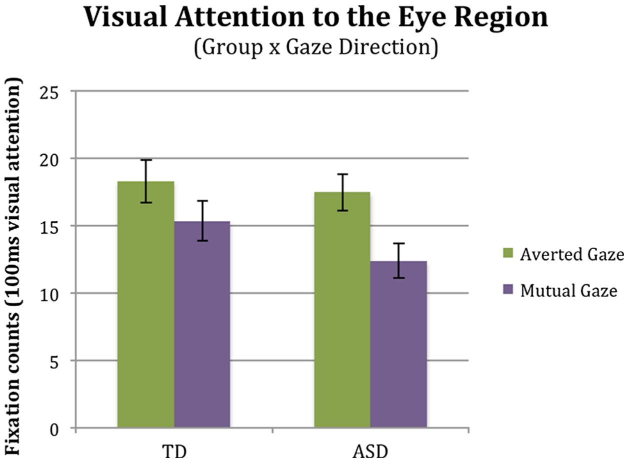

Fig. 3 Visual attention (fixation counts) to the eye area of interest (AOI) is shown above, by group, averaged across familiarity conditions (adjusted means, taking into account overall attention to whole screen). No main effects or interaction effects were significant ($p > .05$). *Error bars* represent standard error of the mean

Pupil Dilation

The main effect of Gaze Direction was significant, $F(1,41) = 4.511$, $p = .040$, $\eta^2 = .099$, showing that both groups dilated their pupils more to mutual than averted eye gaze, across the familiarity conditions. The Group x Familiarity interaction effect was also significant, $F(1,41) = 14.605$, $p < .001$, $\eta^2 = .263$. Between-group pairwise comparisons showed no group differences on the familiar or unfamiliar conditions, across gaze directions ($ps > .200$). However, within-group pairwise comparisons showed more pupil dilation to unfamiliar compared to familiar faces in the ASD group ($p < .001$, $\eta^2 = .367$). The TD group did not

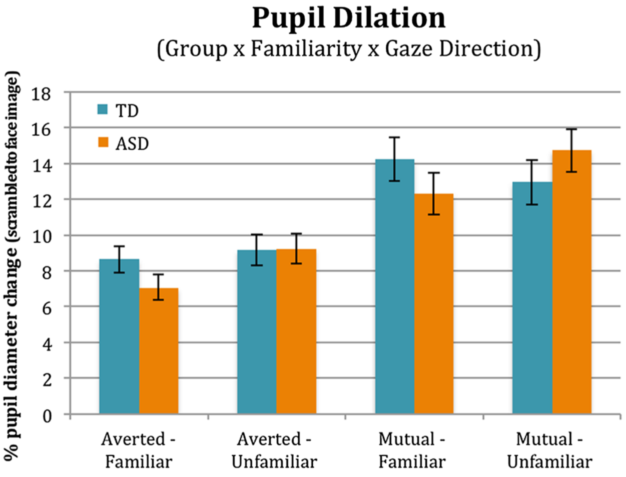

Fig. 4 Mean percentage change in pupil diameter from scrambled to face image, with averted versus mutual eyes, by group and familiarity condition (adjusted means). *Error bars* represent standard error of the mean

show this difference ($p = .434$, $\eta^2 = .015$). Adjusted means are presented in Figs. 4 and 5. No other main effects or interaction effects were significant.

Individual Differences Analyses

Is less visual attention to mutual gaze related to more internalising symptoms in ASD? There were no significant correlations between visual attention and internalising symptoms (r range $= -.110$–$.281$, p range $= .103$–$.313$).

Is emotional arousal to mutual gaze related to internalising symptoms in ASD? Correlations showed that greater pupil dilation to unfamiliar people and marginally also to familiar people with mutual eye gaze correlating with *less* internalising symptoms ($r = -.377$, $p = .042$ and $r = -.301$, $p = .087$, respectively). For unfamiliar people with averted gaze, no significant correlation of pupil dilation with internalising symptoms was found ($r = -.273$, $p = .109$), which suggests that for unfamiliar people this relationship is specific to mutual eye gaze. However, for familiar people, the same direction and strength of correlation was also found in the averted gaze condition ($r = -.362$, $p = .049$). This pattern of results suggests less internalising symptoms in ASD is related to a greater response to familiar people, rather than to their eye gaze direction.

Discussion

Our main objective was to determine whether gaze aversion and/or abnormalities in emotional arousal to mutual eye gaze are present in young mixed-ability children with ASD. We found no evidence of aversion to mutual gaze in these children. Rather, when taking into account the children's general attention to the screen, there were no group differences in attention to the averted or mutual gaze stimuli. Moreover, we found no evidence of physiological dysregulation in response to mutual gaze in this group; children with ASD, like TD children, responded more (had greater pupil dilation) to mutual versus averted gaze, irrespective of whether the person was familiar or unfamiliar. There were also no between-group differences in pupil dilation on any of the familiarity or gaze direction conditions. This pattern of results speaks against the notion that children with ASD have hyper-arousal in response to mutual gaze as suggested in the gaze aversion hypothesis (Bowman et al. 2004; Tanaka and Sung 2013). These findings also suggest that children with ASD do not experience hypo-arousal during mutual gaze. This suggests that reduced engagement in mutual gaze commonly seen in ASD might not be explained by less physiological reactivity to mutual gaze (Lord et al. 2000; Volkmar and Mayes 1990; Willemsen-Swinkels et al. 1998).

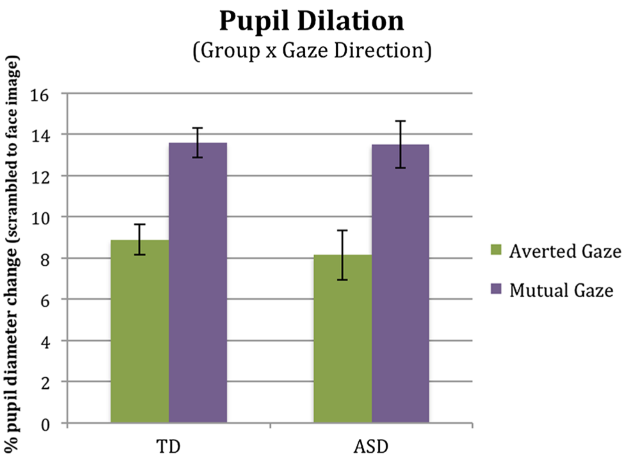

Fig. 5 Mean percentage change from scrambled to face image, with averted versus mutual eyes, by group, across familiarity conditions (adjusted means). *Error bars* represent standard error of the mean

As mentioned above, pupil dilation is functionally connected with amygdala activity (Applegate et al. 1983; Graur and Siegle 2013; Urry et al. 2006; Ursin and Kaada 1960; Zbrozyna 1963). Some neuroimaging and neurophysiological studies have found atypical (hyper- and hypo-) responsiveness in cortical brain regions in ASD whilst participants watched mutual gaze stimuli (Davies et al. 2011; Elsabbagh et al. 2012; Georgescu et al. 2013; Pelphrey et al. 2005; Pitskel et al. 2011; Senju et al. 2005) and have indicated that mutual gaze has a specific role in strengthening functional connectivity between the amygdala and other cortical processing areas involved in social information processing (George et al. 2001; Kleinhans et al. 2008; Von dem Hagen et al. 2014). It is therefore possible that our finding of no difference in pupil dilation may be understood in terms of a normative emotional arousal response to mutual gaze in ASD, in the presence of possible reduced activity in cortical social information processing areas. However, our study was not equipped to directly test this hypothesis. In keeping with this suggestion, a recent study by von dem Hagen et al. (2014) found reduced functional connectivity between the amygdala and the medial prefrontal cortex, temporoparietal junction and the posterior superior temporal sulcus region during mutual gaze processing in adults with ASD.

We also examined individual differences within the ASD group in gaze reactivity and internalising symptoms. We found that more pupil dilation to mutual gaze and averted gaze in familiar people and more pupil dilation to mutual gaze in unfamiliar people was related to less internalising symptoms in the ASD. This pattern of findings also speaks against the notion of the gaze aversion hypothesis, as the 'more typical' response to mutual gaze in terms of less mental health difficulties is a larger, rather than a reduced response. The pattern of findings also suggests that less internalising symptoms in ASD is associated with a greater response to familiar people, rather than to their eye gaze direction, which is indicative of the protective nature of human relationships, but this point requires further investigation.

Although the TD children were expected to have greater pupil dilation to unfamiliar compared to familiar people based on previous findings (Nuske et al. 2014a; Stephan and Stephan 1985), we did not confirm this hypothesis. The children with ASD, however, did show greater pupil dilation to unfamiliar people than familiar people, across gaze conditions, which is consistent with the idea that unfamiliar people create more anxiety than familiar people in some groups of people (Stephan and Stephan 1985). However, this finding is not consistent with previous data of larger SCRs in ASD and TD children to familiar compared to unfamiliar people (Kylliäinen et al. 2012). Thus further work on this issue is needed to clarify these inconsistent findings. A related issue which is yet to be explored in the literature is whether children with ASD have typical responses to their same-age peers. In the current study, the familiar people in the videos were adults, therefore we cannot rule out the possibility that children with ASD may have atypical response to mutual gaze from their same-age peers. Future research should aim to include different groups of familiar people who differ on interpersonal closeness (e.g., same-age peers vs. family members) to further understand this issue.

As most of the studies on attention and response to mutual gaze in ASD have included both older children and adolescents, it is not yet understood if important developmental changes occur in these skills within this age range or throughout the lifespan from infancy to adulthood. For example, findings from the current and previous studies cannot rule out the possibility that adolescents or adults with ASD may have atypical attention and physiological response to mutual gaze. Therefore future studies should aim to compare attention and response to mutual gaze across different age groups. Moreover, the current findings did not investigate other potential causal factors for the clinical phenomenon of reduced engagement in mutual gaze, such as the perception of eye gaze cues and motivational saliency of engagement in mutual gaze in ASD. Thus, future work should aim to investigate these factors.

Limitations

Firstly, whilst the inclusion of an age-matched TD group afforded an understanding of normative reactivity to mutual and averted gaze in familiar and unfamiliar people, the TD and ASD groups were not matched on cognitive ability. The inclusion of a chronological- and mental-age matched group would have been ideal, and further research should seek to incorporate such a control group. Nonetheless, it should be noted that cognitive ability was not a significant covariate in either RM ANCOVA.

Secondly, following the recommendations of Nakagawa (2004) and Perneger (1998), due to our small sample sizes, we did not correct for multiple correlations as we wanted to avoid inflating the probability of Type-II errors. Nevertheless, this must be taken into account when considering the correlations reported herein.

Thirdly, whilst use of the Internalizing scale of the Vineland Adaptive Behavior Scales afforded a crude investigation of the relationship between internalising symptoms and attention to and response to mutual gaze, more sensitive measures of internalising symptoms are available and should therefore be included in future research in this area.

Conclusions

The pattern of results from the current study suggests that the response of children with ASD to mutual gaze is not dysregulated. Rather they respond more to mutual versus averted gaze just like TD children. Likewise, they do not avert their gaze in response to direct eye gaze. These findings contradict the notion that children with ASD experience mutual gaze as aversive.

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