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Abstract

Attention to social stimuli is associated with language development, and arousal is associated with the increased viewing of stimuli. We investigated whether skin conductance responses (SCRs) are associated with language development in ASD: a population that shows abnormalities in both attention to others and language development. A sample of 32 children with ASD (7 y – 15 y; M =9 y) was divided into two groups, based on language onset histories. A typically developing comparison group consisted of 18 age and IQ matched children. SCRs were taken as the participants viewed faces. SCRs differentiated the ASD group based on language onset and were associated with abnormal attention to gaze in infancy and subsequent language development.

Keywords: language delay, galvanic skin response, language onset, autism spectrum disorder, faces, eye-gaze

Associations between language development and skin conductance responses to faces and eye gaze in children with autism spectrum disorder

1. Introduction

Autism Spectrum Disorder (ASD) is diagnosed on the basis of abnormalities in socialisation, communication, restricted interests and repetitive behaviours (American Psychiatric Association, 2000). Although diagnostic criteria are clearly established, and well validated diagnostic tools are in wide use (Lord et al., 2000), the disorder is nevertheless characterised by a high degree of heterogeneity; a key source of which is language development (DeMyer, Hingtgen, & Jackson, 1981; Tager-Flusberg et al., 2005). Even when individuals with ASD manifest normal intelligence levels, age of language onset and subsequent language development may be delayed (Koyama, Tachimori, Osada, Takeda, & Kurita, 2007). Conversely some children with ASD, who manifest clear deficits in socialisation and communication at later stages, nevertheless acquire words and sentences within normal developmental periods. Attention to others is an important factor in language development and may be modified by arousal levels. In this paper, we investigate whether arousal levels in response to eye gaze and faces, measured by skin conductance responses (SCRs), can differentiate children with high-functioning autism (HFA) based on language onset. We also explore possible associations between language development and SCRs to faces.

The association between language acquisition and preferential attention to others has been well documented in typically developing individuals. Joint attention, a form of co-ordinated

social attention between a child and its caregiver, is strongly implicated in language acquisition (Carpenter, Nagell, & Tomasello, 1998; Mundy et al., 2007) and is positively associated with later social development (Mundy & Newell, 2007; Van Hecke et al., 2007). This signals joint attention as a significant behaviour in those areas of development that are delayed or atypical in ASD. Infants diagnosed with ASD display markedly reduced attention to others (Osterling, Dawson, & Munson, 2002; Swettenham et al., 1998) and are less likely to engage in joint attention behaviours than typically developing children (Dawson et al., 2004; Leekam, López, & Moore, 2000; Warreyn, Roeyers, Oelbrandt, & De Groote, 2005). Atypical attention to eye gaze has been well documented (Jones, Carr, & Klin, 2008; Senju, 2007), and is increasingly considered to be an early behavioural and neurological marker for ASD (Chawarska, Volkmar, & Klin, 2010; Mayada Elsabbagh et al., 2012). Research suggests that joint attention predicts language development in autism (Charman, 2003; Luyster, Kadlec, Carter, & Tager-Flusberg, 2008), and poor eye contact in early infancy has been marked out as a predictor of age of language onset in this population (Eisenmajer et al., 1998). Therefore language onset and subsequent development may be related to attentional preferences for faces.

An important question that has yet to be fully addressed is why attention to faces, and in particular to eye gaze, so strongly differentiates those with autism and typical development. Current explanations include references to an innate Eye Detection Mechanism (EDD) which activates brain regions directly involved in theory of mind computations (Baron-Cohen, 1995). A further explanation is proposed by the First-Track Modulator Model (FMM) which suggests that the cognitive impact of direct gaze is modulated by the subcortical face detection pathway (Senju & Johnson, 2009). An alternative group of theories propose that eye contact activates arousal systems in brain regions and may both direct and sustain attention (Kawashima et al., 1999). This

approach predicts that lack of interest in faces may result from abnormal levels of arousal (Hutt & Ounsted, 1966; Rogers & Ozonoff, 2005). Whilst early work suggested hyperarousal may be associated with a withdrawal response (Palkovitz & Wiesenfeld, 1980), recent work suggests that arousing stimuli are attended to for longer (Vogt, De Houwer, Koster, Van Damme, & Crombez, 2008). Although in complex interaction with others over stimulation may lead to withdrawal in order to marshal cognitive resources (Doherty-Sneddon, Riby, & Whittle, 2012). In infancy arousal has been viewed as a regulator of attention in infant-caregiver interactions; modulating the amount of time the infant spends in active engagement with others (Field, 1981). When considered as a basic mechanism for directing attention, arousal theory is not incompatible with either the EDD or FMM and may underlie early and subsequent language development. For example, the amygdala is strongly involved in the arousal response (Dalton et al., 2005; Ortiz-Mantilla, Choe, Flax, Grant, & Benasich, 2010), and Munson et al. (2006) reported an association between larger left amygdala volumes and language ability in individual with ASD. The arousal responses may act to attach a 'sense of value' to different precepts (Hirstein, Iversen, & Ramachandran, 2001) and in early infancy may engender emotional significance to the actions and vocalisations of caregivers during play acts or joint attention behaviour. Following this reasoning, arousal may be one factor, among others, influencing joint attention behaviour and subsequent language development.

In relation to ASD, research has tended to report hyposensitive skin conductance responses in individuals with ASD to visual stimuli in general (Hirstein et al., 2001) and to faces in particular; although there is some evidence suggesting hypersensitivity to direct eye gaze (looking directly into the eyes of another) when comparisons are made using gaze direction as an independent variable (Blair, 1999; Kylliäinen & Hietanen, 2006; Van Engeland, Roelofs,

Verbaten, & Slangen, 1991). For example, Kylliäinen and Hietanen (2006) recorded skin conductance responses to faces displaying either direct or averted eye gaze in children with autism. The authors noted significantly higher skin conductance responses to the direct gaze condition in their autism group, but not in their typically developing comparison group, when comparing gaze conditions. These results may suggest hyper-arousal to direct gaze in autism; however, an alternative explanation is hypo- arousal in the averted eye-gaze condition and normal arousal responses in the direct gaze condition. The stimuli employed were unable to address questions concerning direction of effect. The authors also reported lower (but not significant) SCRs to faces in general in their ASD group. In contrast to hypo-sensitivity theories of arousal to faces, Joseph, Ehrman, McNally and Keehn (2008) observed increased SCRs to photographs of faces in a group of children with ASD (compared to TD children), during a face recognition task. However, the direction of eyes gaze displayed by the faces did not differentiate arousal responses in either their TD or ASD groups. This contradiction may be down to the specific samples used in each study. (Dalton et al., 2005) demonstrated that the arousal response in individual with autism is best understood on a continuum for low to high rather than as a categorical division.

A possible association between arousal and eye contact in ASD is important because eye contact has been linked to the age of language onset in infants with ASD (Eisenmajer et al., 1998). If, as studies suggest (Dalton et al., 2005; Vogt et al., 2008), an increased arousal response is associated with increased viewing of a stimuli, then those individual with ASD showing increased arousal responses to faces may be expected to have better language skills than those showing decreased arousal responses to social stimuli. The present study has two main aims. The first is to replicate the study conducted by Kylliäinen and Hietanen (2006) within a

paradigm that can draw a firm conclusion about whether the direct eye-gaze of another produces hyper-or hypo responses of arousal in children with ASD. The second aim is to determine whether arousal in response to social stimuli (in this cases faces) is associated with language onset and development. In order to do this we constituted two groups of individuals with ASD. One group had experienced delayed language onset and the other group had gained language within the normative time scale: for simplicity the groups are referred to as high-functioning autism- language normal (HFA-LN) and high-functioning autism-language delay (HFA-LD)

In line with current findings (Joseph et al., 2008; Kylliäinen & Hietanen, 2006), we hypothesised that the magnitude of arousal response would not differ statistically between gaze conditions for the TD group. As research studies into arousal and eye gaze in ASD have produced equivocal findings, we did not formulate a directional hypothesis for the HFA-LD and HFA-LN groups. In relation to faces, we predicted that the HFA-LN group would show higher levels of arousal responses to faces when compared with the HFA-LD group. Further we predicted that current arousal in response to faces would be associated with language onset, normative attention to gaze in infancy and current language levels in children with ASD.

2. Methods

2.1 Participants

The ASD group consisted of 32 children recruited from local autism self-help groups. All children had previously been diagnosed as having autism by a trained clinician, and diagnosis was confirmed at the point of entry to the study using the 3di (described below). The term high-functioning is used here to refer to individuals with IQ scores that fall within the normative range. IQ was tested using the Raven's Standard Progressive Matrices and British Picture Vocabulary test (see below).

The ASD group was sub-divided into a HFA-LD (male = 16, female = 2) and HFA-LN group (male = 14). The HFA-LN group met criteria for normal language onset. Following from the DSM-IV-TR (American Psychiatric Association, 2000) stipulation that 'there is no clinically significant general delay in language', this was operationalized according to guidelines set out in the ICD-10 (WHO, 1992) as single words at 24 months and phrase speech at 36 months. This criterion has been adopted in a number of studies carried out with Asperger Syndrome groups (Ghaziuddin, 2008; Saalasti et al., 2008). Parents were asked to verify language onset with reference to baby books in which this information had been recorded. We did not ask for written evidence and accepted the information communicated by parents.

The typically developing group (TD) consisted of 18 children from local schools (male = 16, female = 2). The study was approved by the ethics committee at Goldsmiths, University of London. Consent for participation was gained from both the parents and the children. The three groups were matched on age, performance IQ measured with the Raven's Standard Progressive Matrices and on verbal IQ measured using the British Picture Vocabulary

Scale. The two clinical groups were also matched on symptom severity using the 3di.

Information concerning age and matching criteria is displayed in Table 1.

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2.2 Measures

The developmental, dimensional and diagnostic interview (3di). The 3di (Skuse, et al., 2004) is a computer based diagnostic tool, developed by the Institute of Child Health, increasingly used to diagnose cases of ASD. Outcome measures on the 3di correlate highly with the Autism Diagnostic Interview (Lord, Rutter, & Le Couteur, 1994) equivalent scores. It achieves an inter-rater reliability of 0.9 and a test-retest reliability of 0.9. The 3di was used to confirm the diagnosis of the ASD participants and to record parental reports of their child's eye-contact in infancy. The question 'Did you ever get the impression during the first year or so of your son/daughter's life that they avoided eye contact with you' could be answered by the responses 'no', 'possibly' or 'definitely'.

The British Vocabulary Picture Scale-II (BPVS). The BPVS-II (Dunn, Dunn, Whetton, & Burley, 1997) assesses receptive vocabulary through verbal comprehension and provides a measure of verbal mental age. It is a commonly used tool to determine intelligence in autism research (Mottron, 2004). Scores on the BPVS-II are highly correlated with mental age and IQ derived from the Wechsler Intelligence Scale (BPVS-II manual, p. 35-36; Dunn, Dunn, Whetton, & Burley, 1997).

The Raven's Standard Progressive Matrices (Raven, 1998). The RPM assess non-verbal cognitive ability through a set of tasks in which the participant completes the missing part of a

puzzle. The RPM is commonly used to test nonverbal cognitive ability in autism (Mottron, 2004).

2.3 Stimuli

Male faces have been shown to induce greater skin conductance responses than female faces (Donovan & Leavitt, 1980) therefore only male faces were used in the study. It was important that the face stimuli would only vary on the critical manipulations made in the different conditions; therefore, simulated faces were used. Six male faces were initially created using the Poser 7 software package, and from these three experimental conditions, (direct gaze, averted gaze and eyes-closed) were constructed and these were displayed in colour in the study (Fig.1). It may be argued that the simulated faces would not be processed in a similar manner to photographs of faces. Previous studies examining gaze have used artificial faces (Kuhn et al., 2010; Ruffman, Garnham, & Rideout, 2001) and schematic representations of eyes (Bonato, Priftis, Marenzi, & Zorzi, 2009; Ristic et al., 2005). Neurobiological evidence also suggests schematic faces activate the fusiform gyrus in a manner similar to photographs of faces (Britton, Shin, Barrett, Rauch, & Wright, 2008; Miall, Gowen, & Tchalenko, 2009).

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2.4 Apparatus

Data were collected using purpose built SCR recoding equipment. The SCR device had a sample rate of 100 Hz, with an analogue to digital converter (ADC) resolution of 12 bits. It used a DC excitation of 0.5 volts. Connection to the subject was made via disposable pre-gelled

electrodes (BioLogic 101603) attached to the palmer surface of the distal phalanxes of the index and middle fingers on the participant's left hand (Scerbo, Freedman, Raine, Dawson, & Venables, 1992). The stimuli were presented on a 21-inch computer CRT monitor with a display size of 800 by 600 pixels. In order to ensure that the participants were looking at the stimuli, a web cam was used to monitor their gaze during the experiment.

2.5 Procedure

Participants sat 80 cm from the display monitor at a height that brought their eyes level to the centre of the monitor. The children were asked to keep still and not talk during presentation of the stimuli. Participants were told that they would view images of faces and they were to identify if the face was looking at them, away from them or had its eyes closed. Presentation of the stimuli was randomized. Each stimulus was presented for a period of six seconds. Each participant viewed six faces showing each of the gaze conditions resulting in 18 trials. The inter-stimulus-interval (ISI) varied from 20 to 30 seconds. After each stimulus presentation the participant was asked whether the face was looking at them, away from them or had its eyes closed. The experimental procedure lasted approximately 12-18 minutes.

2.6 Measurement

At stimulus onset for each of the stimuli a baseline measure was taken. The skin conductance response is defined as the maximum change in amplitude over a five-second period commencing one second after the stimulus onset. The skin conductance response is thought to measure arousal to a specific stimuli (Boucsein, 1992), in our study this represents the presentation of the face stimuli. All recordings that were contaminated by body movement,

outside noise, or the participant talking during stimulus presentation, were disregarded. For the control group no trial was disregarded and for the total ASD group six trials (1%) were disregarded across the autism group. As in Kylliainen and Hietanen (2006), mean SCRs were calculated based on all trials including those with a zero response.

3. Results

3.1 Comparison of the TD and HFA-LN and HFA-LD Groups

All participants correctly reported on whether the gaze of the faces was directed towards them, away from them or if the eyes were closed. The data were analysed using repeated measures ANOVA with eye gaze as the within factor and group as the between factor. The data were not normally distributed and this was rectified by transforming the data using a logarithmic transformation. Means are reported for the untransformed data.

The main effect of gaze was significant $F(2, 45) = 5.24, p = .009$. Simple comparison (applying Bonferroni corrections) showed that there was a significant difference between the direct and closed eyes conditions ($p = .02$), but there was no significant difference between either the direct and averted conditions ($p = .16$) or the averted and closed eye conditions ($p = .83$).

The main effect of group was also significant $F(1,2) = 13.88, p < .001$. Simple comparison (applying Bonferroni corrections) revealed that the TD group displayed significantly higher SCRs than the HFA-LD group ($p < .001$), the HFA-LN group also displayed significantly higher SCRs than the HFA-LD ($p < .01$), there was no significant difference between SCRs for the TD and HFA-LN groups ($p = .83$). There was no significant group x gaze direction interaction $F(2,45) = .73, p = .57$.

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3.2 Correlational analysis

We explored correlations between the SCRs to the direct gaze condition and measures of language and gaze in infancy. The small sample size and the number of correlations conducted meant that separate analysis of the HFA-LD and HFA-LN would be of little statistical benefit. We worked from the premise that the two groups represent a continuum of language development rather than two distinct subgroups of ASD. All results are reported as one-tailed tests.

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Whilst some of the results narrowly failed to reach significance, the pattern of correlations observed demonstrated a possible association between SCRs and language development and were all in the predicted direction. As far as we know, no similar analysis has been reported in previous papers, and so we report the non-significant results with 95% confidence intervals (Table 2) for reference. A Pearson's correlation analyses suggested that onset of first word and SCRs to faces were not significantly correlated ($r = -.25, p = .11$). The association between SCRs and the language and the social communication measure of the 3di ($r = -.31, p = .06$) missed significance. There was a positive correlation between BPVS-VMA and arousal responses ($r = .45, p = < .01$).

Using a Spearman's rank-order correlation, we also investigated a possible association between arousal responses and the amount of eye-contact reported by parents when considering the first year of their child's life, and the association was positive and significant ($r = .49, p = .002$). These data are shown in Figure 3. Levels of SCR were not significantly associated with any of the other diagnostic measure which formulate the 3di.

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4. Discussion

The aim of this study was to investigate skin conductance responses to faces and gaze direction. The study provided evidence that the magnitude of the arousal response to faces differentiated children with ASD from typically developing children. Our results further suggested that SCRs differentiate late and normal language onset, within the ASD sample. Differential patterns of SCRs to eye-gaze were detected between direct gaze and the closed eyes condition for the three groups as a whole: Figure 2 suggested that this result was largely explained by the viewing pattern of the HFA-LN group. Tentative evidence for an association between SCRs to faces and current levels of language development in the ASD group was also obtained. Based on pre-existing literature (Eisenmajer et al., 1998), we suggest that there is an association between arousal response and the quality of eye-contact in early infancy which leads to language advantages throughout early development in children with ASD.

The results of this study augment previous work showing hypoarousal to faces in individuals with ASD (Dalton et al., 2005; Kylliäinen & Hietanen, 2006). Our study provided converging evidence for hypo-arousal, measured by skin conductance responses, in children with autism when viewing faces. Our study further suggests that that hypo-arousal was more apparent in individuals with autism who had experienced language delay and researchers may wish to consider this when constituting ASD groups for similar studies. It is noted that the lack of a non-face stimulus as a control in both our study and that conducted by Kylliäinen & Hietanen (2006) warrants caution in this interpretation. An alternative explanation is that children with ASD show decreased arousal levels to all forms of stimuli and not specifically to faces.

In line with findings by Joseph et al. (2008) we failed to observe differences in arousal responses to direct and averted gaze, but SCRs were significantly reduced when viewing the faces with eyes closed in comparison to the direct gaze condition. The pattern of data reported by Kylliäinen and Hietanen (2006) and Dalton, et al., (2005) of heightened arousal to direct eye-gaze was observed in the HFA-LN group, although a non-significant interaction precludes the analysing of these data. The HFA-LN group showed a decrease in arousal across the three conditions from direct gaze to eyes closed. The same effect was not observed in the TD group. Previous research suggests that eye gaze modulates arousal in typically developing individuals but only when the stimuli consists of actual people rather than pictures of people (Hietanen, Leppänen, Peltola, Linna-aho, & Ruuhiala, 2008). The fact that the HFA-LN group did display this discrimination suggests that individuals with ASD, are not delayed with respect to language onset, may have an attentional system that manages to overcompensate for their inherent deficits. Such overcompensation has also been noted in siblings of children with ASD (Belmonte, Gomot, & Baron-Cohen, 2010), and overcompensation may be the result of a compensatory measure to approximate normative patterns of behaviour.

A significant aim of our study was to determine whether the level of the arousal response to faces would be associated with language onset and current language levels in children with ASD. It was clear that the HFA-LN displayed both a qualitative and quantitative difference in results from the HFA-LD group. Correlational analysis provided cautious evidence for an association between SCRs to faces and language development in ASD, but evidence for an associating between SCRs and language onset was inconclusive. We noted a significant correlation between SCRs and parental reports of eye contact within the first year after birth, and this may play a role in joint attention behaviour. Although caution is warranted when using

retrospective accounts of behaviour, this finding is important and concurs with the current view that attentional abnormalities commonly reported in ASD are present in early infancy and before the age a diagnosis is commonly made (Elsabbagh et al., in press). Atypical eye contact in early childhood has been shown to reliably differentiate late and normal language onset in ASD (Eisenmajer et al., 1998) and the possibility that eye contact is modulated by levels of arousal provides an interesting topic for further investigation.

Atypical arousal to stimuli has long been implicated in an explanation for some of the cognitive deficits observed in individual with ASD. The amygdala is thought to be a key region involved in moderating arousal (Baron-Cohen et al., 2000), plays a role in the interpretation of gaze direction (Kawashima et al., 1999) and participates in skin conductance responses (Critchley, Mathias, & Dolan, 2002). Our findings, along with recent studies, suggest a further role for the amygdala in language acquisition and development. Enhanced arousal during child-parent interactions in infancy may focus both attention and memory systems and thus facilitate the acquisition of early language (Ortiz-Mantilla et al., 2010). Munson et al. (2006) reported a positive association between larger left amygdala volumes and language ability in individual with ASD. Given the evidence above and the outcome of our study it would be expected that the volumes for the left amygdala in ASD individuals with language delay would be smaller than for those with typical language onset. Haznedar et al. (2000) reported such an association in a study which measured amygdala volumes in individual with ASD diagnosed with Asperger Syndrome or autistic disorder. Those individual with Asperger Syndrome (normal language onset) showed greater left amygdala volumes when compared to the autism group.

Limitations

The retrospective accounts of language onset and attention to eye gaze potentially introduce a level of error to our study. Whilst parents reported first words from baby books, it is unlikely that they would have kept records of eye contact in early infancy. Our study suggests SCRs to faces differentiates children with autism based on early language development. However, we cannot rule out other experiences in the intervening years which may have influenced these results. We nevertheless believe this small scale study offers evidence to support further study into the relationship between SCRs to faces and language ability in ASD.

Whilst our study demonstrates differential SCRs to faces in ASD it is a necessarily limited account of a particular response to social stimuli. In real life situations, people with ASD have more with which to contend: The flow of a speech needs to be followed, individual words need to be understood, and ideas need to be linked together. This complex task will necessarily have an impact on the allocation of attention. Research shows that attention to faces increases cognitive load (Riby, Doherty-Sneddon, & Whittle, 2012) and averting gaze may be a means by which individuals with ASD cope with increased demands on processing resources (Doherty-Sneddon et al., 2012). Future work also needs to examine the time individuals with autism spend viewing social stimuli and how this relates to the arousal provoked by the stimuli.

Conclusion

The study reported here demonstrated an overall difference between HFA-LN and HFA-LD children in their levels of arousal response to faces. Importantly the study also implicates the involvement of arousal to faces in language development and early social attention. The role arousal plays in social attention and the direction of effect are likely to be complex. Questions

about how levels of response are categorised as hypo- and hyper-arousal are also difficult to address. It is probable that extremes of this continuum, whilst having different aetiologies, result in similar behaviours, for example, avoidance of eye contact. For infants with ASD early over- or under-arousal may be reflected in upstream difficulties in joint-attention and language acquisition. This pattern of results, along with previously reported data (Norbury et al., 2009) suggests that language ability and language onset history are important factors to consider when constituting ASD groups for studies using social stimuli.

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Appendices

[Insert appendices here]

Footnotes

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Table 1

Matching criteria for the TD, HFA-LN and HFA-LD. Means are reported with standard deviation in brackets.

	TD N=18	HFA-LN N=14	HFA-LD N=18	<i>p</i>
Age	114 m (27)	116 m (22)	122 m (27)	.73
Raven's Percentiles	61 (30)	57 (27)	51 (29)	.55
BPVS Verbal Mental Age	132 m (37)	130 m (37)	122 m (31)	.63
3di Scores				
Reciprocal Social Interaction		15.77 (3.98)	18.12 (4.70)	.19
Language and Social Communication		16.57 (3.50)	16.93 (3.24)	.79
Repetitive and Stereotyped Behaviours		4.65 (2.41)	4.72 (2.10)	.97
Age of first word		9 m (5)	16 m (8)	.001
Age of phrase speech		17 m (8)	37 m (12)	<.001
Age at which parents expressed concern		37 m (18)	14 m (19)	.006
Age of formal diagnosis		79 m (24)	53 m (27)	.01

Table 2

Correlational results with 95% confidence intervals in brackets

	Attention to gaze in infancy	BPVS- VMA	First word	Reciprocal social interaction	Language and social communication	Repetitive and stereotyped behaviours
Direct	.49**	.45**	-.25	-.18	-.31	-.11
Gaze	[.12, .72]	[.12, .69]	[-.55, .11]	[-.50, .18]	[-.59, .04]	[-.44, .25]

* $p < .05$, ** $p < .01$



A



B



C

Figure 1 Sets of three male faces were used as stimuli. Set A (direct eye gaze), set B (averted eye gaze), set C (eyes closed).

Figure Captions

[Insert Figure Legends here]

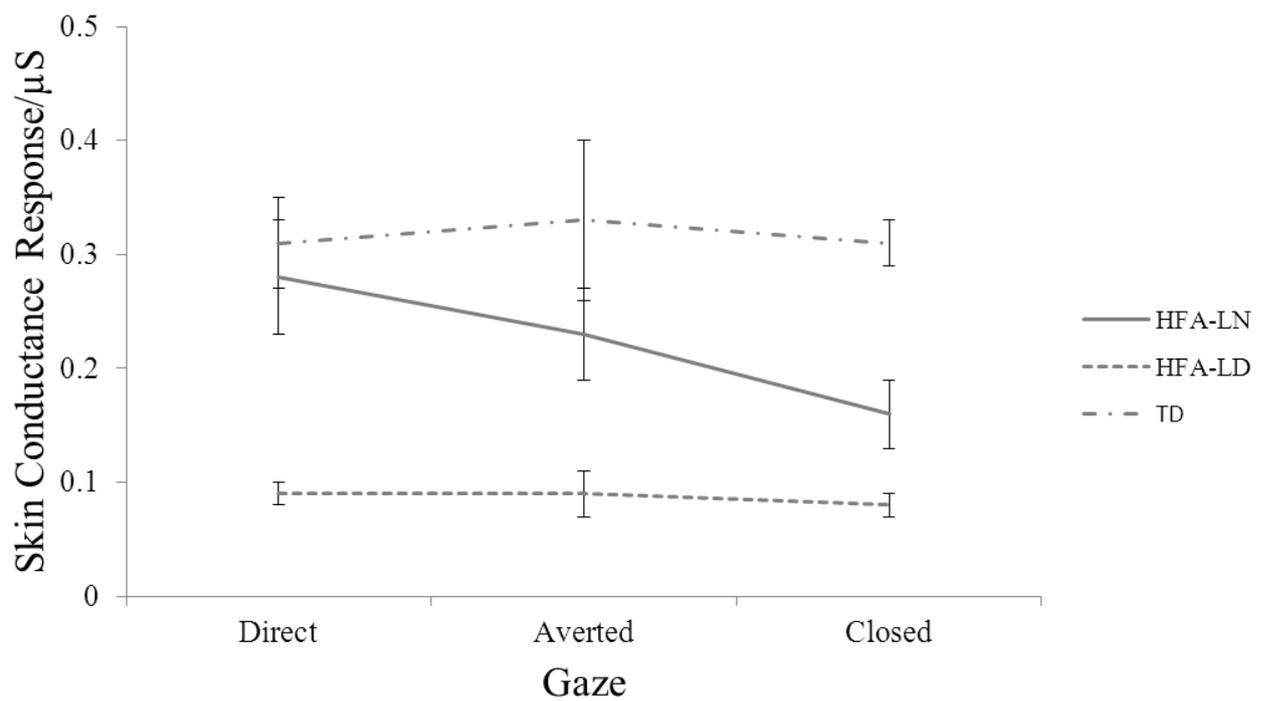


Figure 2 Skin conductance responses to eye-gaze for the TD, HFA-LN and HFA-LD groups

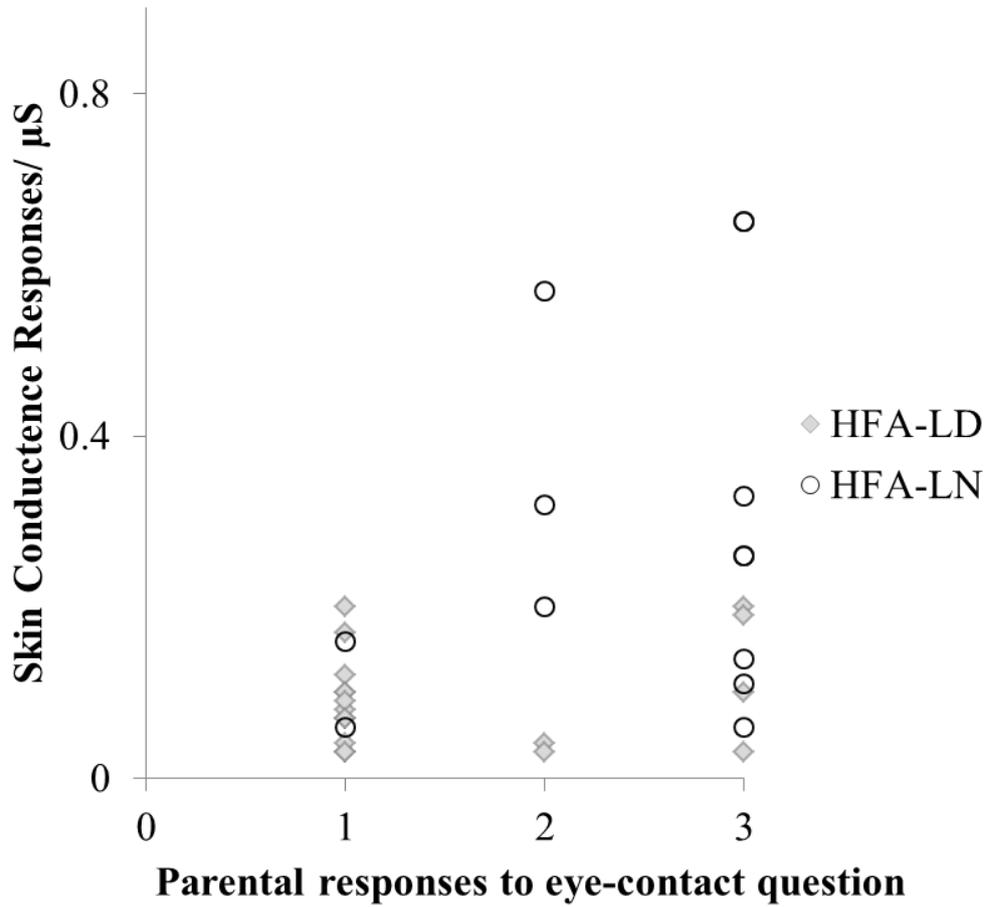


Figure 3 Parental responses to the 3 di question ‘Did you ever get the impression during the first year or so of your son/daughter’s life that they avoided eye contact with you?’ and SCR measures for direct gaze. Answers to the question are scored 1= definitely, 2 = possibly, 3 = no.

1 [Insert Figures here]

2

3

4