



ANNELI KYLLIÄINEN

Face and Gaze Processing in Children
with Autism



ACADEMIC DISSERTATION

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Anneli Kylliäinen

ABSTRACT

Autism is a neurodevelopmental disorder characterised by serious disturbances in social interaction and communication, and restricted, repetitive behaviours. Abnormalities in face and gaze perception in children with autism are common clinical observations. The precise nature and underlying causes of these abnormalities are currently unclear. The present series of studies investigated face and gaze processing in high-functioning, school-aged children with autism.

Study I showed that another person's gaze direction automatically shifted the observer's visual attention, both in children with autism and typically developing children. Both groups of children were also able to overtly discriminate the direction of gaze from brief presented face stimuli. Thus, the orientation of attention according to another person's gaze direction and the discrimination of gaze direction seem to be preserved domains of social cognition in autism. It is possible, however, that children with autism use atypical cognitive and neural processing strategies to achieve seemingly similar behavioural outcomes. Study II demonstrated that skin conductance responses to straight gaze were stronger than responses to averted gaze in children with autism, whereas the responses of typically developing children did not differentiate between these gaze conditions. The increased psychophysiological arousal to straight gaze might have been experienced as uncomfortable by the children with autism, a finding which could be associated with the frequently observed tendency of individuals with autism to avoid eye contact. In Studies III and IV, the neural mechanisms underlying face and gaze processing were measured using magnetoencephalography in typically developing children and adults (Study III) and children with autism (Study IV). The findings of Study III suggested that the neural mechanisms underlying face processing are only partially developed in typically developing 8- to 11-year-old children. In Study IV, the electromagnetic activity elicited by the presentation of face stimuli was somewhat similar in children with autism and typically developing children. Gaze sensitive electromagnetic activity, particularly in response to straight gaze, most clearly differentiated these two groups of children.

It is speculated that the demonstrated gaze processing abnormalities might contribute to the lack of social motivation towards faces in autism. This, in turn, could lead to reduced exposure to faces during the development of children with autism and, consequently, to more general face processing difficulties.

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LIST OF ORIGINAL PUBLICATIONS

This thesis consists of the following four publications, which will be referred to by their Roman numerals:

I Kylliäinen, A., & Hietanen, J.K. (2004). Attention Orienting by Another's Gaze Direction in Children with Autism. *Journal of Child Psychology and Psychiatry*, 45, 435-444. Reprinted with permission.

II Kylliäinen, A., & Hietanen, J.K. (2006). Skin Conductance Responses to Another Person's Gaze Direction in Children with Autism. *Journal of Autism and Developmental Disorders*, 36, 517-525. Reprinted with permission.

III Kylliäinen, A., Braeutigam, S., Hietanen, J.K., Swithenby, S.J., & Bailey, A.J. (2006a). Face and Gaze Processing in Normally Developing Children: A Magnetoencephalographic Study. *European Journal of Neuroscience*, 23, 801–810. Reprinted with permission.

IV Kylliäinen, A., Braeutigam, S., Hietanen, J.K., Swithenby, S.J., & Bailey, A.J. (2006b). Face- and Gaze-Sensitive Neural Responses in Children with Autism: A Magnetoencephalographic Study. *European Journal of Neuroscience*, 24, 2679–2690. Reprinted with permission.

1. INTRODUCTION

Autism is a neurodevelopmental disorder characterised by severe abnormalities in social behaviour. These abnormalities in social behavior also differentiate autism from other developmental disorders. The earliest symptoms typically observed in children with autism are a lack of eye contact (Hutt & Ounsted, 1966) and delay in development of joint visual attention, i.e., looking where someone else is looking (Leekam, Baron-Cohen, Perrett, Milders, & Brown, 1997; Leekam, Hunnisett, & Moore, 1998; Leekam, López, & Moore, 2000). Abnormalities in gaze behaviour in autism were reported in Kanner's (1943) original description of the syndrome and are still among the diagnostic criteria for autism spectrum disorders (American Psychiatric Association, 2000). Autism-specific deficits in social cognition are currently widely studied and there are numerous reports of more general face processing abnormalities (for a review, see Schultz, 2005).

The human face is an important source of information during normal social interaction, conveying information about a person's identity, age, gender, and emotional state (Bruce, 1988). Attending to the eyes and gaze direction of others is a key skill in normal social development (see, e.g., Johnson & Farroni, 2003). The eyes are the most salient parts of the face and serve many important social functions; for example, they regulate interaction, facilitate communicative goals, and express intimacy and social control (Kleinke, 1986). The present series of studies aim to investigate face and particularly gaze processing in children with autism. In the following, I will begin by describing the nature of autism. I will then turn to the normal development of face and gaze processing before examining in more detail the face and gaze processing abnormalities observed in individuals with autism.

1.1 Autism as a neurodevelopmental disorder

Autism is diagnosed according to the presence of specific abnormalities in three behavioural domains: social interaction, communication, and repetitive behaviours. Impairments in the social domain include difficulties in developing peer relationships, sharing pleasure and interests with others, expressing emotional reciprocity, and in the use of nonverbal behaviours (e.g., eye contact, facial expressions, and gestures) to regulate social interaction. Communication deficits include delayed or absent spoken language, repetitive use of language,

and difficulties in conversation and pretend play skills. The repetitive behaviours domain includes the presence of intense interests that are narrow in focus or unusual in content, repetitive motor mannerisms, inflexible adherence to non-functional routines, and preoccupation with parts of objects. Autism (autistic disorder) is one of the five pervasive developmental disorders, the other four being Asperger's disorder, Rett's disorder, childhood disintegrative disorder, and pervasive disorder not otherwise specified. When referring to all of these conditions, the terms autism spectrum disorders and pervasive developmental disorders are used (American Psychiatric Association, 2000).

Here, I concentrate primarily on autistic disorder, particularly on high-functioning children with autism. The term 'high-functioning' refers to children with an IQ level above 70, and it differentiates these children and children with Asperger's disorder from children with autism who also have mental retardation, a common co-morbidity (e.g., Gillberg & Ehlers, 1998). The criteria differentiating high-functioning children with autism from those with Asperger's disorder are that, for high-functioning children, the onset of symptoms has been identified before three years of age and their language development has been delayed (American Psychiatric Association, 2000).

Although autism is commonly regarded as an innate disorder, most children with autism are not formally diagnosed until the second or third year of life. The precise aetiology of this biological disorder is not known. Involvement of multiple interacting genes seems to have a strong role in the development of autism (Bailey et al., 1995), and autism is only occasionally associated with identifiable medical aetiologies, for example Fragile X, Tuberous sclerosis and chromosomal abnormalities (Rutter, Bailey, Bolton, & Le Couteur, 1994). Despite the fact that there is no specific cure for autism, there is usually improvement during the course of development, especially with the help of early intense behavioural interventions (e.g., Lord & Bailey, 2002).

Despite the general acceptance of a biological basis for the disorder and a long history of research investigating cognitive abnormalities in autism, there is still no consensus with regards to the cognitive models explaining autistic abnormalities (Volkmar, Lord, Bailey, & Klin, 2004). Three influential psychological models have been proposed to explain autistic cognitive abnormalities. The theory of mind hypothesis defines social abnormalities in autism as a consequence of inability to attribute mental states (e.g., intentions, desires, and beliefs) to oneself and others (Baron-Cohen, 1995). The theory of weak central coherence is based upon findings of abnormal integration of perceptual information in individuals with autism. These findings have led to the suggestion that the internal social world of individuals with autism could also be piecemeal and lacking the overall coherence of social context and meaning (Happé & Frith, 1996). The executive dysfunction hypothesis relates autism to more general problems in guiding attention, inhibiting irrelevant responses, and planning complex behaviour which all lead to perseveration and inappropriate problem-solving (Pennington & Ozonoff, 1996). It must be emphasised, however, that these are not the only cognitive models trying to explain the

autistic abnormalities. Moreover, none of the models can fully explain the development of the complex behavioural phenotype of autism, leading some to argue that the idea of a single model of autism is implausible (Volkmar et al., 2004). The cognitive models are important, however, for helping us to identify the brain pathologies underlying autism.

Recent neurobiological and neuroimaging findings also support the notion that autism can not be explained by a single cognitive model. In general, the brains of individuals with autism do not have any gross structural abnormalities. Greater total brain volume, however, has been observed in MRI-studies (e.g., Piven, Arndt, Bailey, & Andreasen, 1996) and in post-mortem studies (e.g., Bailey et al., 1998). Enlarged brains (megalocephaly) do not seem to be present at birth but appear during the first few years, possibly due to excessive number of neurons and lack of neural pruning. This early overgrowth is followed by an early arrest in growth leading to a 'normalisation' in volume in late adolescence/early adulthood (for a review, see Courchesne, 2004). Both increases and decreases in the size of the cerebellum and the medial temporal lobe, especially in the amygdala, have been reported (for a review, see Volkmar et al., 2004). The most consistently reported microscopic pathological finding in autism is a reduction in the number of cerebellar Purkinje cells. Additionally, small cell size and increased cell packing density in the forebrain limbic system, especially in the amygdala have been reported (Kemper & Bauman, 1998) as well as neuronal disorganisation in the cerebral cortex, thought to result from abnormal neuronal migration (Bailey et al., 1998).

Functional neuroimaging studies of social cognition in individuals with autism have mainly focused on face perception and theory of mind abilities. These studies have shown hypoactivation in brain regions typically associated with these cognitive functions. For example, the regions consistently activated during the performance of tasks requiring theory of mind in healthy adults – the medial prefrontal cortex, the posterior superior temporal sulcus, and the temporal pole near the amygdala (for a review, see Frith, 2007) – all show reduced activity in individuals with autism during these tasks (Castelli, Frith, Happé, & Frith, 2002; Happé et al., 1996). Furthermore, hypoactivation in the fusiform gyrus of the ventral occipito-temporal cortex (Bailey, Braeutigam, Jousmäki, & Swithenby, 2005; Dalton et al., 2005; Pierce, Muller, Ambrose, Allen, & Courchesne, 2001; Schultz et al., 2000) and in the amygdala (Baron-Cohen et al., 1999; Critchely et al., 2000; Pierce et al., 2001) in individuals with autism is associated with their impaired processing of facial identity and facial emotional expression.

1.2 Face and gaze processing in normal development

Typically developing infants show a preference for face-like patterns from a very early age (for a review, see Maurer, 1985). Furthermore, these very young

infants show a particular preference for looking at the eyes rather than other facial features (cf., Johnson & Farroni, 2003), especially when gaze is direct/straight rather than averted (Caron, Caron, Roberts, & Brooks, 1997; Farroni, Csibra, Simion, & Johnson, 2002; Hains & Muir, 1996). During the first year of life, infants go through enormous development in their face processing skills (for a review, see Johnson & Morton, 1991); for example, they learn to recognise facial identities (for a review, see, Nelson, 2001), facial expressions (for a review, see, Leppänen & Nelson, 2006), and to follow another person's gaze direction for joint visual attention (Corkum & Moore, 1998). It has been shown that visual input during the first 6 months of life is critical for the development of further expertise in face processing (Geldart, Mondloch, Maurer, de Schonen, & Brent, 2002).

Possible explanations for newborns' preference for face-like patterns include a perceptual bias to stimuli containing a higher number of elements in the upper versus lower part of the stimulus configuration (i.e., two eyes in the human face) (e.g., Turati, Valenza, Leo, & Simion, 2005) and innate neural systems specialised for face processing. One particularly influential account of the development of neural specialisation for face processing was Johnson's and Morton's suggestion that an innate subcortical system (referred to as CONSPEC) orients a newborn's gaze towards face-like patterns, and that the resulting repeated exposure to faces leads to the emergence of cortical circuits showing specialisation for faces (referred to as CONLEARN) by approximately two months of age (Johnson & Morton, 1991). A further suggestion is that infants' right hemisphere (left visual field) advantage for processing faces is attributable to a right hemisphere superiority for processing low spatial frequencies (which dominate infants' visual abilities and are essential for processing of facial configuration) and to more rapid development of the right hemisphere (de Schonen & Mathivet, 1990).

Behavioural studies have shown that adult-like face expertise develops rather late in childhood (for reviews, see Chung & Thomson, 1995; Want, Pascalis, Coleman, & Blades, 2003) and there is a possible temporary decline in face recognition performance during early adolescence (Carey, 1992; Flin, 1985). Current neurodevelopmental models have little to say about how the adult-like cortical specialisation for faces is gained, however, although the neural basis of the face processing expertise of healthy adults has been extensively investigated. A robust brain imaging finding in adults is that the perception of an image of a face strongly activates the ventral occipito-temporal cortex, more specifically the lateral fusiform gyrus, and predominately in the right hemisphere (for a review, see Haxby, Hoffman, & Gobbini, 2002). Electroencephalographic and magnetoencephalographic evidence, in turn, shows that the face sensitive responses peak around 140-170 ms after stimulus onset (e.g., Bentin, Allison, Puce, Perez, & McCarthy, 1996; George, Evans, Fiori, Davidoff, & Renault, 1996; Sams, Hietanen, Hari, Ilmoniemi, & Lounasmaa, 1997; Swithenby et al., 1998; Taylor, George, & Ducorps, 2001; Xu, Liu, & Kanwisher, 2005) or even earlier. This early processing is considered to reflect the categorisation of a face

into a different category from other non-face objects (Braeutigam, Bailey, & Swithenby, 2001; Debruille, Guillem, & Renault, 1998; Halgren, Raij, Marinkovic, Jousmäki, & Hari, 2000; Itier & Taylor, 2002; Linkenkaer-Hansen et al., 1998; Liu, Harris, & Kanwisher, 2002; Taylor, Edmonds, McCarthy, & Allison, 2001). There is, however, debate in the face processing literature about whether the face sensitive brain activation reflects functioning of innate, face-specific mechanisms (Kanwisher, 2000) or whether it arises as a consequence of expertise related to extensive exposure to this particular stimulus category (Gauthier, Behrmann, & Tarr, 1999).

The face sensitive event related potentials (ERP's) reported in healthy adults have also been seen in children (Henderson, McCulloch, & Herbert, 2003; Taylor, McCarthy, Saliba, & Degiovanni, 1999; Taylor, Edmonds et al., 2001) and infants (e.g., Halit, de Haan, & Johnson, 2003; de Haan, Pascalis, & Johnson, 2002). The latencies of these responses, however, are longer than those observed in adults (peaking around 190-400 ms after stimulus onset). Thus, it has been proposed that the neural development of face expertise is based upon increased processing speed within the face processing mechanisms (Taylor et al., 1999). Based on ERP-findings in infants (cf., Halit et al., 2003) and fMRI-findings in older children (Passarotti et al., 2003), however, others have argued that there are more fundamental changes underlying the development of face processing expertise. It has also been claimed that increasing exposure to human faces in infancy leads to a narrowing of the perceptual window for face processing (Nelson, 2001). For example, although 6-month-old infants can discriminate the identity of monkey face stimuli, this ability has been lost by 9 months of age (Pascalis, de Haan, & Nelson, 2002).

One interesting possibility is that the eyes play a special role in the development of the neural face processing mechanisms. Johnson and Farroni (2003) argued that as the eyes are a high contrast element in a face, they direct newborns' attention toward faces. Furthermore, they suggested that this process operates in addition to the subcortical "CONSPEC" system. In support of this theory, it has been demonstrated that the amplitudes of ERP-responses of 4-month-old infants are larger to straight gaze than to averted gaze stimuli (Farroni et al., 2002). Additionally, the ERP-response in older children to an eyes-only stimulus is stronger and of shorter latency than the ERP-response to a whole face stimulus (Taylor, Edmonds et al., 2001). Moreover, there is evidence from adult studies that face and gaze processing are not independent of each other: for example, the gaze direction of a face stimulus modulates the activation of the face sensitive responses (George, Driver, & Dolan, 2001; Bentin et al., 1996; Taylor, George et al., 2001; Watanabe, Miki, & Kakigi, 2002) and affects the recognition speed (Adams & Kleck, 2003) and neural processing (Klucharev & Sams, 2004) of facial expressions.

1.3 Abnormalities of face and gaze processing in autism

The central role of face and gaze processing for the development of social skills is clear when one considers the case of autism. Abnormalities in face processing are broadly studied in the autism literature and there is copious evidence indicating impairments in the recognition of facial identity (Boucher & Lewis, 1992; Braverman, Fein, Lucci, & Waterhouse, 1989; Hauck, Fein, Maltby, Waterhouse, & Feinstein, 1998; Klin et al., 1999) and facial expression (Celani, Battacchi, & Arcidiacono, 1999; Hobson, 1986; Howard et al., 2000; Pelphrey et al., 2002; Tantam, Monaghan, Nicholson, & Stirling, 1989), and in facial gender and age identification (Hobson, 1987; Hobson, Ouston, & Lee, 1988).

It has been suggested that the abnormalities in face processing are due to unusual cognitive processing strategies, i.e., that individuals with autism process faces by relying on local features rather than on configural or holistic information. This is supported by findings suggesting that individuals with autism respond similarly to pictures of upright and of inverted faces (e.g., Davies, Bishop, Manstead, & Tantam, 1994; Hobson et al., 1988; Langdell, 1978), show no problems in recognizing face halves (Teunisse & de Gelder, 2003), and do have difficulties in recognising briefly presented facial expressions (Celani et al., 1999). All of these tasks are thought to be sensitive to configural (Freire & Lee 2001) or holistic (Tanaka, Kay, Grinnell, Stansfield, & Szechter, 1998) mode of face processing. Configural or holistic processing is shown to be preferred in normal face perception (Tanaka & Farah, 1993) and to arise very early on, during infancy (Cohen & Cashon, 2001; de Haan & Nelson, 1998). More recent studies have challenged the view that abnormalities in the processing of configural or holistic information underlie the face processing deficits in individuals with autism. For example, it has been demonstrated that the inversion of a face stimulus slows the processing speed in participants with autism as well as in typically developing participants (Joseph & Tanaka, 2003; Lahaie et al., 2006). It has also been suggested, however, that the processing of individual face features is enhanced in individuals with autism (Lahaie et al., 2006), especially when face identification is based only on the mouth region of the face (Joseph & Tanaka, 2003; Langdell, 1978). In addition, it has been proposed that the face processing abnormalities seen in individuals with autism may also be due to difficulties in processing affective states and due to a lack of engagement with other people. These affective problems may lead to reduced attention to faces in general (Hobson et al., 1988) and, therefore, may prevent the development of adult like face expertise.

It has been argued that the abnormalities in face processing exhibited by individuals with autism may also be a consequence of more general problems in low level visual processing. Deficits have been shown, for example, in visual motion perception (Gepner, Mestre, Masson, & de Schonen 1995; Gepner & Mestre 2002; Milne et al., 2002; Spencer et al., 2000) and processing of low spatial frequencies of faces (Deruelle, Rondan, Gepner, & Tardif, 2004). Low

spatial frequencies have been linked to configural processing, and greater use of low spatial frequency information has been reported in face processing in healthy adults (Fiorentini, Maffei, & Sandini, 1983; Schyns & Oliva, 1999). Brain imaging studies of basic visual processing in autism, however, have not found specific abnormalities indicative of deficits in low-level visual processing for example, in dorsal stream connectivity (Villalobos, Mizuno, Dahl, Kemmotsu, & Müller, 2005) or in retinotopic maps of the primary visual cortex (Hadjikhani, Chabris et al., 2004).

The idea that abnormalities in face processing skills could be related to different cognitive or visual processing strategies led researchers to investigate whether these differences were reflected in the functioning of the neural mechanisms underlying face processing in autism. A common finding in most of the studies has been that, in contrast to healthy adults, the brain activation elicited by faces in the ventral occipito-temporal cortex – particularly the fusiform gyrus – in individuals with autism is either weaker (Bailey et al., 2005; Hall, Szechtman, & Nahmias, 2003; Hubl et al., 2003; O'Connor, Hamm, & Kirk, 2005; Pierce et al., 2001; Schultz et al., 2000; Wang, Dapretto, Hariri, Sigman, & Bookheimer, 2004), longer in latency (McPartland, Dawson, Webb, Panagiotides, & Craver 2004; O'Connor et al., 2005) or totally lacking (Critchley, Daly et al., 2000; Pierce et al., 2001). Some studies, however, did not report differences in the activation of the fusiform gyrus between the clinical and control groups (Hadjikhani, Joseph, Snyder, & Tager-Flusberg, 2007; Hadjikhani, Joseph et al., 2004; Pierce, Haist, Sedaghat, & Courchesne, 2004). The developmental time course of the observed neural abnormalities is mainly unknown. Studies in children and adolescents with autism have concentrated on facial expression processing (Dawson, Webb, Craver, Panagiotides, McPartland, 2004; Piggot et al., 2004; Wang et al., 2004) or recognition of familiar versus unfamiliar faces (Dawson et al., 2002; Webb, Dawson, Bernier & Panagiotides, 2006) and found reduced activation or a different pattern of responses/activated areas in children with autism as compared to typically developing children. An ERP-study in children with Asperger's syndrome and control children did not find any differences, however, in the emotional expression processing (O'Connor et al., 2005).

As previously mentioned, the earliest observable symptoms of autism relate to gaze processing; lack of eye contact and delay in the development of joint visual attention (i.e., looking where someone else is looking). The development of joint visual attention has been shown to be delayed in children with autism in studies using a naturalistic (face-to-face) paradigm (Leekam et al., 1997; 1998; 2000). In normal development, joint visual attention appears during the first year of life when an infant follows an adult's gaze in order to have a shared experience of seeing the same object or event (Corkum & Moore, 1998). Children with autism, however, do not achieve this level of joint visual attention until they have reached a verbal mental age of over 4 years (Leekam et al., 1998). It has been proposed that this delay relates to a specific deficit in representing that self and other are looking at the same object (Baron-Cohen,

1995). However, there is evidence that children with autism can overtly infer where another person is looking (Baron-Cohen, 1989; Baron-Cohen, Campbell, Karmiloff-Smith, Grant, & Walker, 1995; Leekam et al., 1997), and understand that eyes are for seeing (Tan & Harris, 1991). Based on evidence that individuals with autism have specific problems in visual attention orienting with non-social cues (Casey, Gordon, Mannheim, & Rumsey, 1993; Wainwright-Sharp & Bryson, 1993), it has been suggested that the deficits in joint visual attention in autism could relate to impairments in visual attention orienting.

The absence of normal eye contact is another early clinical manifestation of autism. It has been shown that children with autism spontaneously direct their own gaze to other people less than typically developing individuals do (Hutt & Ounsted, 1966; Kasari, Sigman, & Yirmiya, 1993; Osterling & Dawson, 1994; Pederson, Livoir-Petersen, & Schelde, 1989; Phillips, Baron-Cohen, & Rutter, 1992; Tantam, Holmes, & Cordess, 1993; Volkmar & Mayes, 1990) and that there are deficits in the timing and quality of gaze behaviour (Baron-Cohen, Baldwin, & Crowson, 1997; Buitelaar, van Engeland, De Kogel, De Vries, & Van Hooff, 1991; Mirenda, Donellan, & Yoder, 1983; Swettenham et al., 1998; Willemsen-Swinkles, Buitelaar, Weijnen, & van Engeland, 1998). Furthermore, it has been demonstrated that both children (Senju, Hasegawa, & Tojo, 2005; Senju, Yaguchi, Tojo, & Hasegawa, 2003) and adults (Howard et al., 2000) with autism have difficulties in detecting straight gaze stimuli among averted gaze stimuli, whereas in control participants there are no difficulties in straight gaze detection (Howard et al., 2000). In fact, control participants detect straight gaze stimuli more rapidly than averted gaze stimuli (Senju, Hasegawa et al., 2005; Senju et al., 2003). Thus, there is some evidence that the processing of straight gaze (i.e., eye contact), in particular, is impaired in autism. It has been long hypothesised that gaze avoidance in autism could be a strategy to minimise overstimulation resulting from an unusual degree of physiological arousal elicited by eye contact (Hutt & Ounstead, 1966; Tinbergen, 1974). Although eye contact has been shown to affect psychophysiological arousal in healthy adults (Gale, Spratt, Chapman, & Smallbone, 1975; Kleinke & Pohlen, 1971; McBride, King, & James, 1965; Nicholas & Champness, 1971), physiological arousal in response to eye contact in individuals with autism has not yet been measured.

Interestingly, it has been shown that unlike typically developing children, children with autism rely more on the mouth region than on the eye region for facial identity recognition (Joseph & Tanaka, 2003; Langdell, 1978). Similarly, studies using accurate measurements of eye movements have shown that individuals with autism scan the mouth region of both still face images (Pelphrey et al., 2002; Spezio, Adolphs, Hurley, & Piven, 2007) and moving facial images (Klin, Jones, Schultz, Volkmar, & Cohen, 2002) more than the eye region of the face. These findings are in direct contrast to those observed in typically developing individuals. The findings have been explained by assuming that the perceptual bias for the mouth region observed in autism may reflect a strategy used to improve the understanding of verbal information in social interaction (Klin et al., 2002; Joseph & Tanaka, 2003). It has also been argued that

individuals with autism do not understand the mental significance of the eyes. These suggestions are based on findings showing impairments in recognising other people's complex mental states and intentions from images of the eyes (Baron-Cohen et al., 1995; Baron-Cohen, Wheelwright, & Jolliffe, 1997).

Despite the relatively comprehensive description of gaze perception abnormalities in autism, the neural activity related to gaze processing in autism has remained relatively unstudied. Some studies have addressed this issue, however. Brain imaging studies have shown abnormal patterns of activation when adults with autism make assumptions about another person's intentions from their eye movements (Pelphrey, Morris, & McCarthy, 2005) or describe another person's mental state from the inspection of eyes only (Baron-Cohen et al., 1999). ERP-findings of gaze processing in children with autism have shown that in contrast to age-matched control children, the responses are stronger to straight gaze than to averted gaze (Grice et al., 2005). The ERP-findings of children with autism resemble those of 4-month-old infants (Farroni et al., 2002), supporting the hypothesis of specific delay in gaze processing (Grice et al., 2005). Another ERP-study observed right lateralised and gaze direction sensitive ERP-responses in typically developing children, whereas the responses were not lateralised and were insensitive to gaze direction in children with autism (Senju, Tojo, Yaguchi, & Hasegawa, 2005). These findings seem to indicate that the neural mechanisms underlining gaze processing are abnormal or that the development of these mechanisms is delayed in autism.

A tempting possibility is that the abnormalities in the processing of eyes could play a central role in the general face processing difficulties in autism. As noted earlier, it has been suggested that the perception of the eyes have an influence on the typical development of neural face processing mechanisms by attracting newborn infants' attention towards faces (Johnson & Farroni, 2003). It is not entirely clear whether this attraction is mediated by an innate eye direction detector (Baron-Cohen, 1995) or by the visual salience of the eyes as high contrast element in a face (Johnson & Farroni, 2003). In either case, the attractive nature of the eyes may serve to maximise the infant's experience of faces as they develop adequate social skills. In the case of autism, the problems in gaze perception and behaviour, and potentially diminished attraction to eyes may reduce the amount of time the child spends looking at another person's eyes, and, therefore, another person's face. This might have an impact on more general face processing abilities and on the neural maturation of face processing.

2. THE PRESENT STUDIES

The present series of studies had four aims. The first aim was to investigate the automatic orientation of attention in response to another person's direction of gaze in children with autism (Study I). The second aim was to study psychophysiological arousal to eye contact in children with autism (Study II). Lastly, the study aimed to investigate and compare the neural mechanisms underlying face and gaze processing in typically developing children and adults (Study III) to those in children with autism (Study IV).

2.1 Automatic attention orienting to another person's gaze direction

Previously reported deficits in joint visual attention in children with autism have been studied by using a conventional, naturalistic face-to-face paradigm. In this paradigm, the child sat facing the experimenter, who made concomitant eye, head, and body movements. It was judged that joint visual attention had been established when the child repeatedly turned to look in the same direction as the adult (see e.g., Moore & Corkum, 1998). The majority of children with autism assessed with this paradigm failed to monitor an adult's head and eye movements (Leekam et al., 1997; 1998; 2000). One possible explanation is that the autistic difficulties in joint visual attention reflect impairments in visual attention orienting. Attention orienting is traditionally studied by using a spatial attention orienting paradigm (Posner, 1980). In the computer-based task, the participant is asked to detect visual targets which appear either side of the central fixation point. Before the appearance of the target, the participant's attention is directed by a cue either to the correct target location (valid condition) or to the incorrect target location (invalid condition). Normally, reaction times to detect targets are longer in the invalid than in the valid conditions. Visual attention orienting in this type of experimental circumstance can emerge without concordant eye movements and it can be automatic (i.e., not under voluntary control) in nature (Posner, 1980).

The automatic shift of attention is traditionally thought to be triggered by non-predictive (i.e., equal probability for valid and invalid cues) but salient visual peripheral events (e.g., a flash of light). Instead, centrally presented predictive (i.e., probability is higher for valid than invalid trials) symbolic cues (e.g., arrows) are considered to trigger voluntary shifts of attention (Jonides,

1981). Adults with autism have been shown to have a reduced ability to shift their attention in response to centrally presented, predictive arrow cues (Wainwright-Sharp & Bryson, 1993), although both children (Harris, Courchesne, Townsend, Carper, & Lord, 1999) and adults (Casey et al., 1993; Townsend, Courchesne, & Egaas, 1996) with autism have shown intact attention orienting in response to peripheral illumination changes.

More recently, attention orienting has been investigated using another person's gaze and/or head orientation as a directional cue. This area of research has become known as social attention orienting. In healthy adults, there is clear evidence that seeing another person's gaze and/or head orientation triggers a shift in the observer's attention. The detection of a peripherally presented target is more rapid when it appears on the same, rather than opposite side in relation to the direction of the centrally presented gaze/head cue (Driver et al., 1999; Friesen & Kingstone, 1998; Friesen, Moore, & Kingstone, 2005; Hietanen, 1999; 2002; Langton & Bruce, 1999; Ristic, Friesen, & Kingstone, 2002). Although the gaze/head cue is a centrally presented cue, it seems to fulfil the criteria for automatic or reflexive shifts of attention. Most importantly, another person's averted gaze or head shifts observer's attention to the same direction even though the gaze/head cue does not predict the direction of the following target (i.e., equal probability for valid and invalid cues) (e.g., Friesen & Kingstone, 1998).

The previous conventional joint visual attention studies have aimed to describe the abnormalities in joint visual attention in autism. The purpose of Study I was to investigate, whether the problems in joint visual attention might reflect an inability to reflexively orient one's attention according to another person's gaze direction. In fact, previous independent studies have shown that the perception of another person's laterally moving eyes triggered reflexive attention orienting in children (Swettenham, Condie, Campbell, Milne, & Coleman, 2003) and toddlers (Chawarska, Klin, & Volkmar, 2003) with autism. It must be emphasised, however, that in both of these studies the gaze direction cue involved an illusory eye movement and, therefore, it is possible that the movement of the eyes is necessary for the shifts of gaze-cued attention to occur in children with autism. In the present study, it was investigated whether *static* gaze cues will trigger comparable shifts of visual attention in children with and without autism. If the earlier findings of the orientation of attention in children with autism in response to shifts of another person's gaze merely result from the effect of illusory visual motion, one would not expect the static gaze cues in the present study to trigger shifts of reflexive visual attention in these children. In other words, no difference in reaction times between validly and invalidly cued trials would be anticipated.

2.2 Psychophysiological reactions to eye contact

Mutual gaze between two people is a strong action of social communication and has an impact on physiological arousal (Gale et al., 1975; Kleinke & Pohlen, 1971; McBride et al., 1965; Nicholas & Champness, 1971). It has been suggested that gaze avoidance in autism arises because of an unusually enhanced physiological arousal to eye contact (Hutt & Ounsted, 1966; Tinbergen, 1974). The enhanced arousal might result in eye contact being experienced as uncomfortable and, therefore, avoided by individuals with autism. Subsequently, this might contribute to the apparent lack of interest in faces, and contribute to additional face processing abnormalities in autism.

Measuring electrodermal activity is one of the most robust and well studied measures of psychophysiological arousal. Skin conductance responses refer to momentary changes in the electrical resistance of the skin reflecting the functioning of the sweat glands controlled by the sympathetic nervous system (Andreassi, 2000). When a weak, constant current is delivered through two electrodes attached to the skin, resulting changes in the skin conductance can be measured. Tonic and phasic skin conductance both refer to different aspects of psychophysiological arousal. Tonic, resting skin conductance is the baseline level of skin conductance which varies individually. Phasic skin conductance is the time-related change in conductance evoked by a discrete environmental stimulus. Skin conductance (phasic) responses to sensory stimuli have been interpreted as an indication of the stimulus' significance, novelty, and its' emotional significance to the participant, and are generally believed to be a reliable accompaniment to psychological processes such as attention and orienting reflex (Dawson, Schell, & Filion, 2000). The generators of skin conductance responses in the central nervous systems are not well known, although they are commonly related to the motivational system of the brain including medial frontal cortex and amygdala (see e.g., Critchley, Elliott, Mathias, & Dolan, 2000; Williams et al., 2001).

Several electrodermal studies have investigated responses to socially meaningful stimuli in children with autism. Palkovitz and Wiesenfeld (1980) recorded responses to a spoken sentence and found no differences in skin conductance responses between the children with autism and control children. Blair (1999) had three socially meaningful visual stimulus categories in his study; distressing, threatening, and neutral images. Contrary to the typically developing children and to the children with moderate learning difficulty, children with autism had greater skin conductance responses to distress cues than to neutral stimuli, while there was no difference between responses to the threatening and neutral stimuli. Hirstein, Iversen, and Ramachandran (2001) studied relatively low-functioning children with autism and found that there was no difference in their skin conductance responses to their mother's face and a paper cup, whereas in the control group, the skin conductance responses were stronger to the face than to the cup. The skin conductance responses to a straight

and averted gaze in autism have not been measured in the previous studies. The aim of Study II was to measure skin conductance responses to face stimuli with a straight gaze (eye contact) or an averted gaze in children with autism and typically developing children. It was hypothesised that if eye contact is associated with an unusual degree of arousal in autism, relatively stronger skin conductance responses to a straight gaze than to an averted gaze stimulus would be measured in children with autism as compared to typically developing children. In other words, the difference between skin conductance responses to straight gaze and averted gaze was expected to be larger in children with autism than in control children.

2.3 Neural correlates of face and gaze processing in children with and without autism

Despite a wealth of brain imaging, electrophysiological (for a review, see Haxby et al., 2002), and magnetoencephalographic (e.g., Sams et al., 1997; Swithenby et al., 1998) research of face processing in healthy adults and electrophysiological research of face processing in infants (for a review, see Leppänen & Nelson, 2006), the neurodevelopmental trajectory of face processing during childhood has not received that much attention. Furthermore, it is largely unknown how development within the neural pathways subserving face processing is different between children with and without autism. As described earlier, there is electroencephalographic (McPartland et al., 2004; O'Connor et al., 2005) and magnetoencephalographic (Bailey et al., 2005) evidence for face processing abnormalities in adults with autism. Previous studies with children are limited to investigations of perception of emotional expressions (Dawson et al., 2004; Piggot et al., 2004; Wang et al., 2004) or face familiarity (Dawson et al., 2002; Webb et al., 2006). As previously mentioned, the processing of other people's eyes might have special importance in typical neural development of face processing (Johnson & Farroni, 2003). It is possible, therefore, that face processing abnormalities in autism relate, at least partly, to atypical processing of the eyes. In order to further investigate this assumption, studies III and IV studied the neural correlates of face and gaze processing in typically developing children and adults (Study III) and in children with autism (Study IV).

The neural basis of face and gaze processing was studied using whole head magnetoencephalography (MEG). MEG is a non-invasive method based on detecting weak magnetic fields produced by neural activity in the brain. Magnetic fields are detected outside the head with superconducting sensors. Superconducting sensors have basically no resistance and, therefore, enable the detection of very weak currents/magnetic fields. MEG is most sensitive to tangential currents produced by the synaptic current flow of cortical pyramidal

cells, and despite the superconducting properties of the sensors, the synchronous neural activity of thousands of neurons is needed to generate a measurable current. The background noise is reduced by having the MEG scanner in a shielded room. MEG provides excellent temporal resolution (in the range of milliseconds) and a good spatial resolution as the skull and the tissue surrounding the brain do not significantly affect the magnetic fields (e.g., Hämäläinen, Hari, Ilmoniemi, Knuutila, & Lounasmaa, 1993). MEG is a particularly child-friendly method to measure brain activity as it is completely silent and a child can sit upright in the scanner and in the company of an adult if necessary.

In Study III, the neural basis of gaze and face processing in typically developing children and adults was compared in order to establish a) whether we could replicate previous ERP observations (Henderson et al., 2003; Taylor et al., 1999; Taylor, Edmonds et al., 2001) of slower processing of faces in a group of children in middle childhood (8 to 11 years of age) as compared to adults and b) whether there is any evidence for qualitative changes in the neural basis of face processing between childhood and adulthood, particularly with respect to processing of the eyes.

In Study IV, typically developing children and children with autism were compared. The aims were to study a) whether there are differences between typically developing children and those with autism in the neural activity evoked by viewing faces with straight gaze and b) whether the neural responses to straight and averted gaze in children with autism are different from those seen in typically developing children. It was expected that the neural activity evoked by faces would be different in these two groups of children and that the neural responses as a function of the gaze direction would differentiate between children with and without autism.

3. METHODS AND RESULTS

3.1 Study I: Attention orienting to gaze direction

Methods of Study I

Twelve high-functioning children with autism took part in this study. All these children had a clinical diagnosis of autism spectrum disorder and the diagnosis was confirmed using the parental Autism Diagnostic Interview -Revised (ADI-R; Lord, Rutter, & Le Couteur, 1994). Table 1 shows the scores of the clinical group on the three domains of the ADI-R. The control group comprised gender- and mental-age-matched volunteer children with no history of mental or neurological disorders. There were no significant differences between the clinical and control groups in chronological age (CA) and performance IQ, but the control children had a higher verbal IQ and full scale IQ, than the participants in the clinical group (see Table 1).

TABLE 1. Participant characteristics in Studies I and II (modified from Kylliäinen & Hietanen, 2004), * $p \leq 0.01$, ** $p \leq 0.003$.

	Group	
	Clinical	Control
N (sex)	12 (11M, 1F)	12 (11M, 1F)
CA (years; months)		
Mean (SD)	9;11 (1;10)	8;11 (2;10)
Full IQ, Mean (SD)	91 (17)	106 (7)*
Verbal IQ, Mean (SD)	90 (19)	109 (8)**
Performance IQ ,Mean (SD)	95 (16)	102 (7)
ADI-R, Mean (SD)		
Social Domain (cut off 10)	18.7 (4.5)	
Communication Domain (cut off 8)	14.1 (3.1)	
Stereotypy Domain (cut off 3)	7.3 (2.5)	

In the first task of Study I, the children were asked to detect a laterally presented target (an asterisk) that was preceded by a face cue with either straight or averted gaze (to the left or right). Trials began with the presentation of a fixation point (1000 ms) followed by the stimulus face appearing on the screen for 200 ms. The face was followed by the target, which was presented either on the left or the right side of the screen (see Figure 1). The design comprised of three different, randomly presented conditions, each with an equal probability of occurrence: congruent (gaze averted to the same side as the target), incongruent (gaze averted to the opposite side of the target), and neutral (a straight gaze with the target on the left or right). The time interval between the onset of the face cue and the onset of the target (stimulus-onset-asynchrony, SOA) was given two values: 200 ms and 800 ms. Participants indicated target detection by pressing a single, centrally located response key. The main dependent variable was reaction time measured from the appearance of the target.

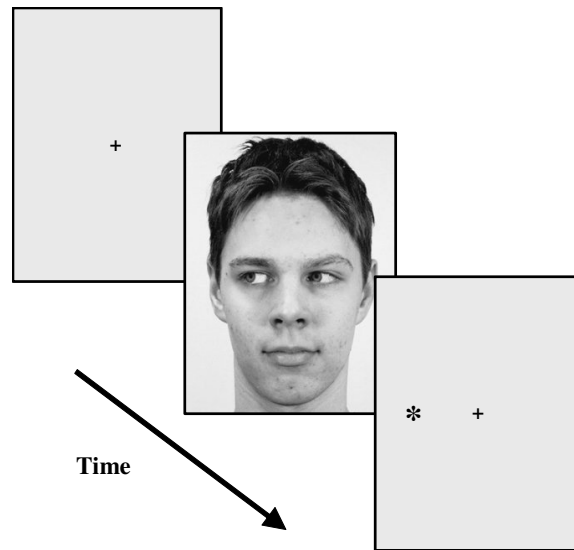


FIGURE 1. The sequence of stimulus events on a single trial in Study I. The figure illustrates a congruent condition in which the gaze is directed to the same side as the following target.

In the second task of Study I, the same children were asked to discriminate whether the person on the screen looked straight ahead (at them) or, from a child's point of view, to the left or right. The presentation time of the face stimuli was the same as in the first task (200 ms). This task was planned to show and confirm that the children with autism were able to perceive gaze direction, thus, excluding the possibility that potential impairments in gaze-cued attention orienting could be explained by perceptual problems in discriminating gaze direction. The main dependent variable in this task was recognition accuracy. Although rapid responses were not required, the response times were also measured.

Results of Study I

Because main focus was in possible differences in the reaction times between the congruent and the incongruent conditions, for the sake of brevity, only the findings regarding these comparisons are described here. The results of the first task in Study I showed that, at the SOA of 200 ms, the reaction times were shorter in the congruent than incongruent condition in both groups of children. Similarly, at the SOA of 800 ms, the reaction times were shorter in the congruent than in the incongruent condition in both groups (Figure 2). Thus, the results showed that, in *both* groups of children, another person's static gaze direction triggered an automatic shift of visual attention.

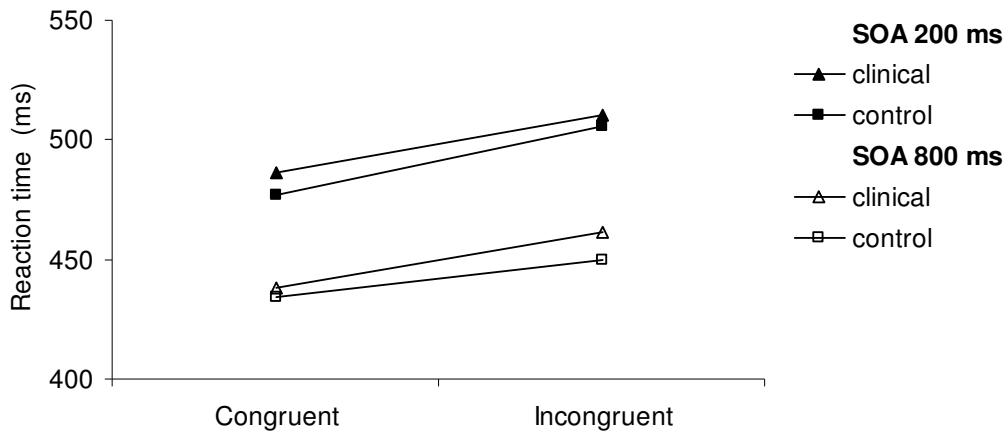


FIGURE 2. Mean reaction times in the gaze-cuing task of Study I. The reaction times are presented as a function of stimulus condition, SOA, and group.

The second task of Study I confirmed that children in both groups were able to discriminate gaze direction in stimuli presented for a short time (Table 2). There was no difference in the percentage of total response errors between the clinical (3.4%) and control (4.9%) groups. In the clinical group, the children made somewhat more errors when the gaze was averted to the left compared with gaze averted to the right or straight gaze. This difference, however, was not significant (but was approaching it). There were no differences in number of errors between the conditions in the control group. The mean response times did not differ between the groups.

TABLE 2. The mean percentages of response errors and the mean response times as a function of gaze conditions and group in gaze direction discrimination task of Study I (modified from Kylliäinen & Hietanen, 2004).

Group	Gaze direction		
	Left	Straight	Right
Clinical			
Errors (%)	6.1	4.0	0.0
Response time (ms)	846	902	836
Control			
Errors (%)	2.8	6.5	5.6
Response time (ms)	774	782	786

3.2 Study II: Psychophysiological reactions to eye contact

Methods of Study II

Study II included the same children who participated in Study I (see Table 1). Skin conductance responses (SCR) to face stimuli with a straight gaze (eye contact) or an averted gaze were measured. The face stimuli were filmed with a video camera. By using the zoom an impression was created in which the faces appeared to be looming towards the participant. Each film clip lasted 6 seconds and was presented on a computer screen. After the stimulus presentation, the children were asked whether the person looked straight at the child, or whether the person's gaze was averted. Thus, the children were explicitly asked to attend to the eyes of the stimulus face.

A total of 12 face stimuli were presented in a random order, 6 of which had straight gaze and 6 with averted gaze. Half of the faces were female and the other half male. The inter-stimulus-interval (ISI) was 25-35 seconds. Two electrodes were coated with electrode gel and attached to the child's left hand (middle and index fingers). The electrodermal activity was recorded with a standard methodology. The SCR as a dependent variable was defined as the maximum amplitude change from baseline (defined at the stimulus onset) within a 5-second time window starting 1 second after the stimulus onset until the end of the stimulus presentation. The mean value of SCR was computed across all stimulus presentations in each category, including those without a measurable response as a zero response. The result of these calculations is a measure of the magnitude of the skin conductance responses; a measure that combines response size and response frequency (cf., Dawson et al., 2000).

Results of Study II

Behavioural accuracy of the gaze direction discrimination (straight or averted) was high in both groups of children, and there was no difference between the clinical (97 %) and control (99 %) groups in the mean percentages of correct responses. The skin conductance responses seemed to be overall smaller in the clinical group than in the control group, but the difference was not statistically significant. Children with autism had greater skin conductance responses to stimuli with the straight than the averted gaze. There was no difference in skin conductance responses to the straight and averted gaze conditions in the control group (Figure 3).

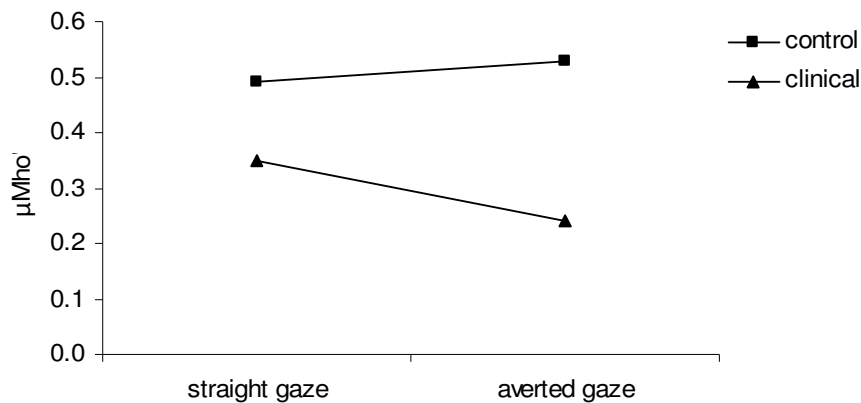


FIGURE 3. Mean skin conductance responses to gaze stimuli in Study II. The responses are shown as a function of gaze direction and group (modified from Kylliäinen & Hietanen, 2006).

3.3 Studies III and IV: Neural correlates of face and gaze processing in children with and without autism

Methods of Studies III and IV

Ten typically developing boys (mean age = 9 years, 1 month; range = 7;10-10;11; SD = 1;2) and twelve adult men (mean age = 30 years, 6 months; range = 23;9-51;10; SD = 8;0) participated in Study III. The boys in Study III also participated in Study IV and were age- and IQ-matched with ten boys (mean age

= 9 years, 10 month; range = 7;8-12;1; SD = 1;5) with a clinical diagnosis of autism spectrum disorder. The Autism Diagnostic Interview -Revised (ADI-R; Lord et al., 1994) was completed with the children's parents, and all children in the clinical group met the ADI algorithm criteria for autism. There were no significant differences between the clinical and control groups in chronological age, mental age, full scale IQ, verbal IQ, and performance IQ (see Table 3).

TABLE 3. Participant characteristics in Study IV (modified from Kylliäinen et al., 2006b).

	Group	
	Clinical	Control
N	10	10
CA (years; months)		
Mean (SD)	9;10 (1;5)	9;1 (1;2)
Full IQ, Mean (SD)	91 (17)	103 (6)
Verbal IQ, Mean (SD)	93 (16)	104 (10)
Performance IQ, Mean (SD)	92 (20)	101 (7)
ADI-R, Mean (SD)		
Social Domain (cut off 10)	20 (4.2)	
Communication Domain (cut off 8)	15 (3.7)	
Stereotypy Domain (cut off 3)	7 (2.3)	

In Studies III and IV, a whole-head MEG scanner was used to record electromagnetic brain responses whilst the participants performed two tasks. In both tasks, participants had to decide whether pairs of sequentially presented images depicted the same individual or the same motorbike. The gaze condition was always the same within a pair of images. Sequentially presented pairs of images were used in order to ensure that attention was paid to briefly presented images, to elicit priming effects, and to elicit neural activity with short latencies for faces (e.g., Braeutigam et al., 2001). In the first task, the stimuli were pictures of faces in which the eyes were either open (50 image pairs) or closed (50 image pairs), and pictures of motorbikes (50 image pairs). The motorbike images constituted a non-face control stimulus category and the eyes closed images were used to control for the presence of visible eyes in the face stimuli. The second task involved only pairs of faces with gaze averted to the left (50 image pairs) or right (50 image pairs). Although the averted gaze condition in task 2 was planned to be contrasted with other stimulus categories in task 1, it was presented in a separate task in order to reduce the length of the tasks, thus making them more tolerable for children. In half of the trials the second image was a repetition of the first image and in half of the trials it was different (see Figure 4). Each image was presented for 200 ms with an interval of 1000 ± 100 ms between the first and second images of a pair. Participants responded by

pressing two response buttons using their right hand. The potential overlap between the neural activity associated with processing of the face and the subsequent motor response was minimised by cueing the key press with a visual prompt (a picture of a hand in which the response fingers were marked). The visual prompt was presented 1400 ± 100 ms after the second image and was displayed for 400 ms.

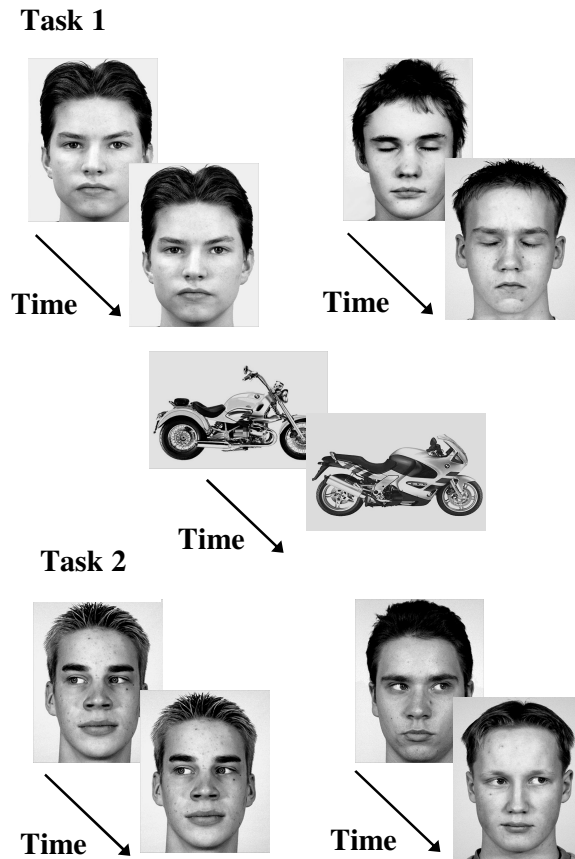


FIGURE 4. Examples of the stimulus pairs used in task 1 (eyes open – same identity; eyes closed – different identity; motorbike – different model) and task 2 (eyes left – same identity; eyes right – different identity) of Studies III and IV.

Maps of local signal strength were obtained from the root-mean-square (rms) amplitudes of each detector pair of the scanner. Head movement was monitored by measuring position before and after each experimental run. For each participant, evoked responses were calculated for each task condition, stimulus type, and both stimuli within a pair for latencies from 0 to 800 ms after stimulus onset. Given that the responses to the second image did not vary according to whether this image was the same as the first image of the pair, the data from both types of image pairs (same or different) were pooled for statistical robustness, yielding 10 types of evoked responses (straight gaze, closed, left, right, motorbikes; first and second image for each stimulus category). Significant

differences between evoked responses were sought using a time-dependent measure, $P(t)$. This method is conceptually similar to common event-related potential techniques of comparing evoked peak amplitudes across participants. The measure takes into account the data from all detectors and does not require the prior identification of peaks in the evoked responses (Braeutigam et al., 2001).

Results of Study III

The overall performance accuracy was high in both adults (94%) and children (92%). Both groups were more accurate for faces (95%) than motorbikes (89%). In the adults, the first peak of evoked activity following the first images of the face-pairs was observed over occipital regions at about 90 ms after stimulus onset (Figure 5). Low amplitude neuronal activity was observed around 30-60 ms before the first peak. Strong evoked activity was next observed at about 135 ms after stimulus onset, strongly lateralised over right inferior occipito-temporal regions and accompanied by weaker signals over left inferior occipito-temporal and right anterior temporal areas. The right-lateralised evoked responses were stronger for the first images in face-pairs than for the first images of motorbike-pairs.

In the children, the first peak maximum of evoked activity occurred in posterior regions approximately 60 ms after stimulus onset. This short latency activity did not depend on either image type or stimulus order within a pair, and was stronger and more localised than the response observed in adults at a similar latency. This was followed by a very strong response in comparison with adults at 100 ms, localised predominately over posterior regions. The strong evoked response at 100 ms had a shorter latency for all face categories compared with motorbikes. Furthermore, all responses evoked by bikes that occurred later than 100 ms were delayed by 10–30 ms compared with those evoked by faces. At 135 ms, a weak bilateral response was detected over occipito-temporal cortex, which contrasted with the strong, right lateralised response observed in adults (Figure 5). Although the 135-ms responses to the second image in the pair in all stimulus categories were reduced in children, this reduction was not significant as it was in the adult data. The differences noted here between the child and adult data indicate that adult-like face sensitivity in extrastriate areas is only partially developed by middle childhood. Furthermore, the primary visual areas might still be involved in face processing during relatively late stages of development.

In task 2, averted gaze (both to the left and right) evoked a response in children over the right inferior occipito-temporal regions at 245 ms (Figure 7, top row). This response was weak or absent for straight gaze, eyes closed, and motorbikes in task 1. There was no evidence for such a response in the adult data. This finding seems to suggest that as with face processing, there are differences in the neural processing of gaze direction in children and adults.

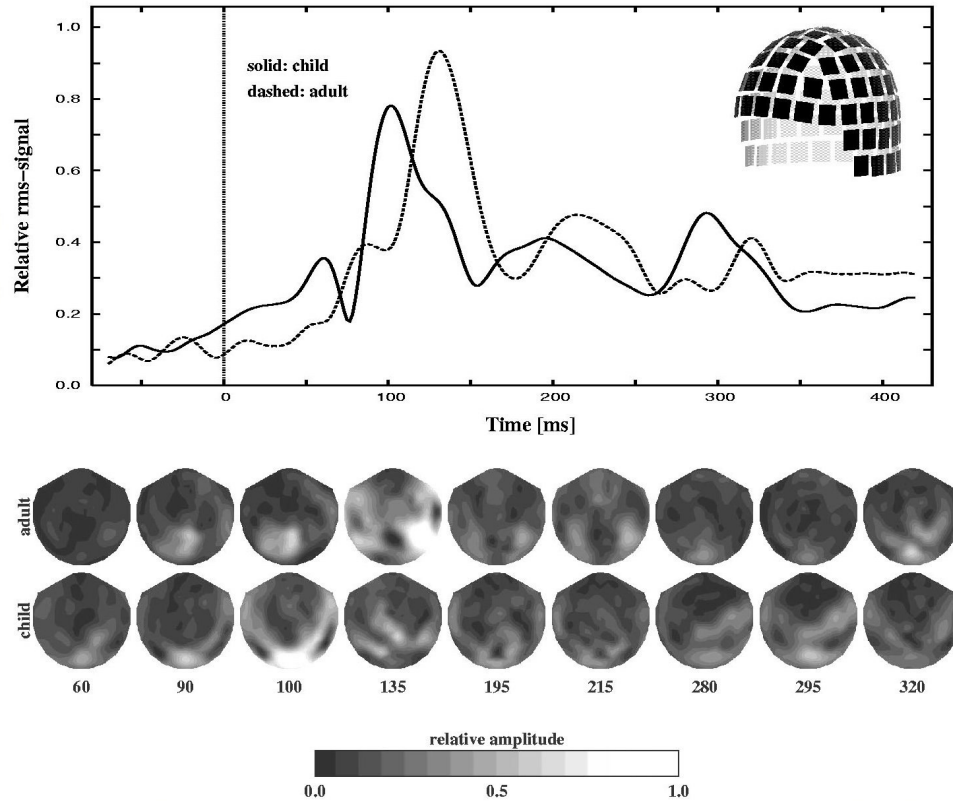


FIGURE 5. Top: Grand root-mean-square (rms) signals following first face (straight gaze) images in Task 1 (dashed line - adult; solid line – child; stimulus onset at 0). The inset shows the helmet shaped array of detectors used to record neural responses to static images. Bottom: Spatial distribution of local rms-signals to first faces in Task 1 (top row - adult; bottom row - child). For presentation of data, the detectors have been projected into two dimensions (right ear on the right, front at the top). The maps show neuronal activity at selected latencies between 60 and 320 ms after stimulus onset, corresponding to peaks in either of the rms-signals above (modified from Kylliäinen et al., 2006a).

Results of Study IV

In Study IV, the performance accuracy for faces was better in the typically developing control children (95%) than in the children with autism (87%). Both groups responded more accurately during the face condition compared with the motorbike condition, and there was no difference in performance accuracy for motorbikes between the control (86%) and the clinical (80%) groups.

The overall pattern of neural responses was largely similar in both groups of children. This pattern of responses was markedly different to that observed for adults in Study III. There were also, however, some significant differences

between the clinical and control children and these differences are described in the following.

The first peak maximum of evoked activity occurred in posterior regions at around 60 ms after stimulus onset in both groups. This short latency response was followed by a strong response at 100 ms, localised predominately over posterior regions. In children with autism, the neural responses to the first images in face-pairs at 100 ms were indistinguishable from those observed in the control children. The weak bilateral response evoked by faces at approximately 135 ms was somewhat weaker in children with autism than in control children but this difference did not reach the set significance level (Figure 6). Thus, it seems that the early categorisation process of faces is relatively similar in children with and without autism.

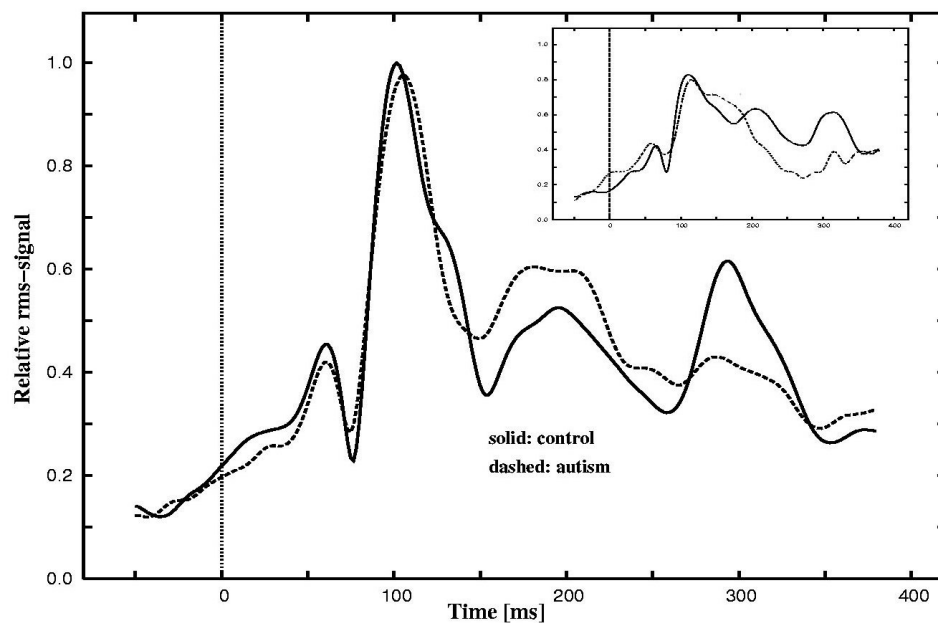


FIGURE 6. Rms-signals following the first face (straight gaze) images in Task 1 (solid line – control children; dashed line – children with autism; stimulus onset is at 0). The inset on the right shows grand rms-signals following the first motorbike images in Task 1 (modified from Kylliäinen et al., 2006b).

The responses to motorbikes at 100 ms seemed to be right lateralised in children with autism but not in the control children. At 135 ms, the responses to motorbikes were significantly stronger than the responses to faces only in children with autism. There was no evidence for longer response latencies to motorbikes than to faces in the clinical group, whereas such a difference was observed in the control group.

There was a response at around 240 ms over left superior temporal, parietal, and inferior occipito-temporal cortices that was stronger to straight gaze than to other image categories in the clinical group. In the control group, there was a

response at the same latency to averted gaze over right inferior occipito-temporal cortices. This response was strongly reduced, but not absent in the clinical group (Figure 7).

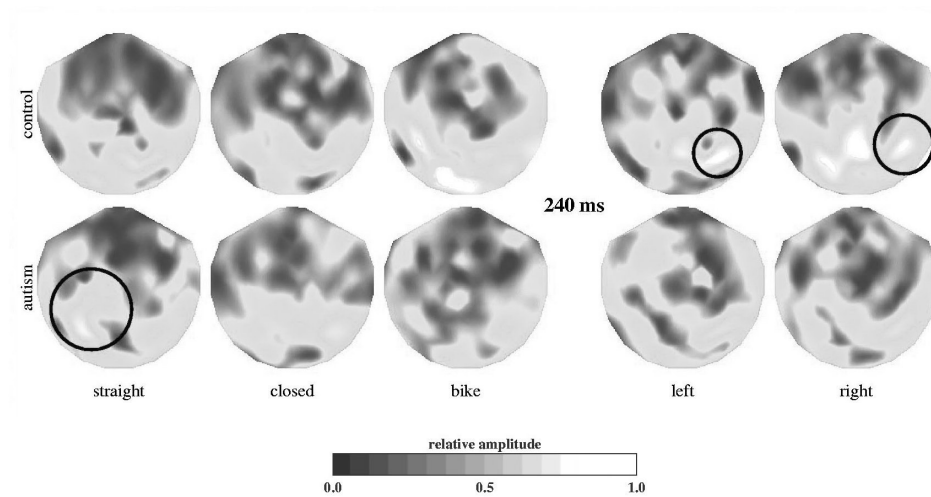


FIGURE 7. Local rms-signals following the first images in Task 1 (straight, closed, bike) and Task 2 (left, right). Top row represents the control group; bottom row represents the clinical group. The circles indicate the regions where within group analyses revealed significant differences between conditions (modified from Kylliäinen et al., 2006b).

4. DISCUSSION

Abnormalities in face and gaze processing in autism are frequently reported both clinically and in experimental studies. The present series of studies investigated the underpinnings of these abnormalities. The findings of Study I showed that another person's static gaze direction triggered an automatic shift of visual attention both in children with autism and in typically developing children. The children in both groups were also able to overtly discriminate the direction of gaze from static gaze stimuli with a relatively short presentation time (200 ms). The findings of Study I, therefore, suggest that the delay in the development of joint visual attention in autism does not reflect impairments in automatic gaze-cued attention orienting. Study II revealed that the children with autism exhibited greater psychophysiological arousal (electrodermal activity) in response to seeing straight gaze compared with seeing averted gaze, whereas there was no difference in the psychophysiological response elicited by these two gaze conditions in the typically developing children. If the enhanced arousal to the straight gaze is experienced as uncomfortable by the children with autism, this finding could provide one explanation for the frequently observed tendency of individuals with autism to avoid eye contact.

Electromagnetic brain activity was measured in order to investigate the neural mechanisms underlying face and gaze processing in typically developing children and adults (Study III) and in children with autism (Study IV). The results of Study III suggested that in middle childhood (8 to 11 years of age) the neural mechanisms underlying face processing appear to be less specialised than they are in adults. The findings of Study IV indicated that, in addition to many similarities in these neural mechanisms in children with and without autism, the gaze sensitive neural responses of these two groups differed.

In the following, I will discuss the findings of these four studies in more detail. Furthermore, I will speculate on the possibility that children with autism learn to use compensatory mechanisms for their deficits in the area of social cognition. Additionally, I will suggest that the abnormalities in the processing of eyes may impede the development of face processing skills in autism. Finally, I will consider the possibility that the neural abnormalities in face processing in individuals with autism are related to diminished face experience during development.

4.1 Preserved automatic attention orienting to another person's gaze direction in autism

The results from Study I indicated that another person's laterally averted static gaze shifted the observer's attention to the same direction, not only in typically developing children but also in children with autism. This evidence of intact reflexive attention orienting to social gaze cues in autism has been supported in two more recent studies (Senju, Tojo, Dairoku, & Hasegawa, 2004; Vlamings, Stauder, Son, & Mottron, 2005). Thus, these findings suggest that the well-documented delay in the development of joint visual attention in autism (Leekam et al., 1997; 1998; 2000) does not reflect impairments in automatic gaze-cued attention orienting. Previous studies using peripheral, non-social cues in children (Harris et al., 1999) and adults (Casey et al., 1993; Townsend et al., 1996) with autism have also demonstrated preserved automatic attention orienting. In this respect, the results of Study I are consistent with previous studies using non-social attentional cues.

There is robust evidence that uninformative, centrally presented gaze cues can trigger reflexive shifts of visual attention (e.g., Driver et al., 1999; Friesen & Kingstone, 1998; Hietanen, 1999). In addition, it has recently been shown that also centrally presented, uninformative and biologically irrelevant arrow cues can elicit reflexive attention orienting (Hommel, Pratt, Colzato, & Godijn, 2001; Ristic et al., 2002; Tipples, 2002). As only the former cue is social in nature, it is interesting to compare the strength of the cuing effect triggered by face and the strength of the cuing effect triggered by arrow cues in individuals with autism, given the social deficits exhibited by these individuals. Two recent studies (Senju et al., 2004; Vlamings et al., 2005) addressed this issue by comparing arrow cuing and gaze cuing in autism. Vlamings et al. (2005) demonstrated that although both types of non-predictive cues triggered an automatic shift of attention in adults with and without autism, the typically developing adults had longer reaction times overall in the gaze cue condition than in the arrow cue condition, whereas the adults with autism showed no differences in reaction times between the two cueing tasks. The authors suggested that the increased reaction times in the face condition for typically developing adults resulted from the fact that they – but not the adults with autism – found the eyes to be more salient stimuli than symbolic arrows. This finding was supported in a recent study, which demonstrated longer reaction times in the gaze cue condition compared to the arrow cue condition in typically developing adults (Hietanen, Nummenmaa, Nyman, Parkkola, & Hämäläinen, 2006). Using a similar non-predictive cuing task, Senju et al. (2004) showed that children with autism were slower in the arrow cuing task than in the gaze cuing task, whereas there was no such a difference in the control group. Following the line of Vlamings et al.'s (2005) reasoning this would mean that children with autism had longer overall reaction times in the arrow cuing than in the gaze cuing task because they found arrow cues to be more salient than face cues.

In a second task, Senju et al. (2004) presented the invalid (i.e. incorrectly cued) trials four times more frequently than the valid (i.e. correctly cued) trials. In typically developing children, the cueing effect to the expected (incorrectly cued) location was found in the arrow condition but not in the gaze condition. It seemed, therefore, that typically developing children could control the attention orienting (i.e., inhibit the automatic orienting according to the cue direction) better in the arrow cuing task than in the gaze cuing task. One interpretation of this result is that gaze-cued attention orienting is more automatic than arrow-cued attention orienting and, therefore, is more difficult for typically developing children to control voluntarily. This interpretation is in line with that suggested by Friesen, Ristic and Kingstone (2004) when reporting similar type of results with typically developing adults. In contrast, in Senju et al. (2004) study, the children with autism exhibited the cueing effect to the unexpected (correctly cued) location in both conditions. Thus, it seems that the children with autism could not voluntarily control their responses in either cueing task. Taken together, these findings indicated qualitative differences between the clinical and control groups in their reflexive attention orienting to gaze and arrow cues. One interpretation is that the gaze cued attention orienting might not have been as social in nature for the individuals with autism as it was for the typically developing individuals.

Thus, although the gaze cues seem to trigger reflexive shifts of attention also in children with autism it is possible that, nevertheless, gaze cued attention shifts are based on functioning of different cognitive and neural mechanisms in children with and without autism. A recent fMRI-study reported that reflexive attention orienting in response to arrow and gaze cues is based on different neural mechanisms despite the similarities in the behavioural outcome (Hietanen et al., 2006). This finding further supports the evidence from patients with brain-lesions indicating that attention orienting triggered by gaze and arrow cues may rely on different neural mechanisms (Akiyama et al., 2006; Kingstone, Friesen, & Gazzaniga, 2000; Vuilleumier, 2002). These findings could indicate that the seemingly similar behavioral performance in the attention orienting task by children with autism and typically developing children in these studies may have been achieved using different neural mechanisms. The children with autism may have compensated for their deficits in social cognition by using mechanisms normally subserving processing of non-social information.

The MEG-findings of Study IV provided some evidence of different neural responses to gaze stimuli in children with autism and in typically developing children. In Study IV, the averted gaze condition elicited an electromagnetic response 240 ms after stimulus onset in typically developing children. This response was stronger for averted gaze condition than for straight gaze and closed eyes conditions. This gaze direction sensitive response was reduced in children with autism. This finding is in keeping with the study by Senju, Tojo et al. (2005), who reported a right lateralised, gaze direction sensitive ERP-response at around 280 ms in typically developing children that was neither lateralised nor gaze direction sensitive in children with autism. Pelphrey et al.

(2005) measured neural activity in an fMRI study in which the stimulus face was either looking at the peripheral target (a congruent trial) or looking at another location (an incongruent trial). The findings demonstrated that the superior temporal sulcus (STS) was activated in response to gaze shifts both in individuals with and without autism. Only in individuals without autism, however, did the activity in STS differentiate between congruent and incongruent gaze shifts. These findings indicate that there are differences in the neural processing of averted gaze between individuals with autism and typically developing individuals.

One recent study, however, did not find a cueing effect in the non-predictive gaze cueing task in adolescents and young adults with autism (Ristic et al., 2005). It is possible that methodological differences may explain the inconsistency in the findings between Ristic et al. (2005) and other studies (including the present Study I) investigating this effect. In both Study I and the other more recent studies (Senju et al., 2004; Vlamings et al., 2005), the centrally-presented face cue disappeared from the screen before the peripheral target appeared. In the study by Ristic et al. (2005), however, the centrally presented face cue remained on the screen when the peripheral target appeared to the left or right side of the computer screen. As such, participants would have to disengage their attention from the fixated face stimulus before it could be shifted towards the new stimulus. It has been shown that individuals with autism have problems in disengaging their attention from a fixated stimulus (e.g., Casey et al., 1993). It is possible, therefore, that difficulties in disengaging from the centrally presented face cue might have affected the results in the non-predictive gaze cuing task by Ristic et al. (2005). Furthermore, the stimuli used in Ristic et al.'s study (2005) were schematic faces instead of real faces as in other studies, which may also have produced different findings. It has been argued that individuals with autism have difficulties in understanding symbolic, representative information (Hermelin & O'Connor, 1970; Tager-Flusberg, 1985; Wainwright-Sharp & Bryson, 1993). Therefore, it could be that two small circles with black dots (eyes) above a tiny circle (nose) and a straight horizontal line (mouth) surrounded by a bigger circle (face) are not seen as a face by individuals with autism, particularly when the time allowed to process the stimulus is short and rapid responses are required. In the study by Ristic et al. (2005) gaze cuing was achieved also in participants with autism in a predictive gaze cuing task when the cue face remained on a screen long enough (≥ 300 ms) before the appearance of the target. In this task, the probability of the valid trials was as high as .80 and the number of trials was doubled (up to 672 trials) as compared to the non-predictive gaze cuing task. The authors argued this indicating that the individuals with autism might learn to orient their attention according to the social cue without capturing its social relevance.

The findings from the gaze direction discrimination task in Study I further supported the previous findings (Baron-Cohen, 1989; Baron-Cohen et al., 1995; Leekam et al., 1997) that children with autism are able to overtly discriminate the direction of another person's gaze. Study I extended previous findings by

demonstrating that the direction of gaze can be recognised even with a short presentation time (200 ms), without simultaneous head orientation cues, and without anything in the visual field to which the gaze is directed.

Taken together, it might seem that children with autism process another person's gaze direction in a similar way to typically developing children, and that this social information is sent to the systems subserving visual attention orienting. Nevertheless, it is possible that individuals with autism use atypical strategies for processing visual information from gaze direction. According to other recent attention orienting studies (Senju et al., 2004; Vlamings et al., 2005), it seemed that unlike control participants, individuals with autism did not benefit from the salience of the face/gaze cues as compared to arrow cues. Individuals with autism may also have abnormalities in the neural substrates involved in processing of another person's averted gaze, as suggested by Study IV and Senju, Tojo et al. (2005). In general, these findings emphasise the importance of considering the role of compensatory mechanisms in the future studies of social cognition in autism.

4.2 Atypical arousal to eye contact in autism

In Study I, we aimed to confirm that the children were looking at the eye-region of the stimulus face and the results showed that their attention was shifted in the same direction as the stimulus face's averted gaze direction and that they were able to overtly discriminate the gaze direction. It is commonly observed, however, both in clinical and experimental settings that individuals with autism do not look at the eyes of other people (Klin et al., 2002; Pelphrey et al., 2002; Spezio et al., 2007) and that they have abnormalities in the use of eye contact (e.g., Volkmar & Mayes, 1990). Nevertheless, the underlying cause of their gaze aversion remains unsolved. In Study II, the possibility that gaze avoidance in autism arises because of unusually enhanced physiological arousal to eye contact (Hutt & Ounsted, 1966; Tinbergen, 1974) was examined. The findings revealed that children with autism exhibited stronger skin conductance responses to the perception of straight gaze than averted gaze, whereas there was no such difference in typically developing children. Thus, the heightened physiological arousal to eye contact in children with autism might, at least partly, explain the tendency to gaze avoidance in autism.

The stronger skin conductance responses to straight gaze than to averted gaze in the children with autism could indicate that children with autism interpret another person's direct gaze as hostile or as expressing intimacy at a level which is experienced as uncomfortable. Recently, it has been shown that the length of time spent fixating the eyes of another person was positively correlated with amygdalar and right fusiform gyrus activation in adolescents and adults with autism spectrum disorder (Dalton et al., 2005). The association between the gaze fixation time and the amygdalar activation was interpreted as indicating that

individuals with autism spectrum disorder become negatively over-aroused while looking at another person's eyes.

The specific problems in the perception of a face with straight gaze in autism have been demonstrated in behavioural studies. Both children and adults with autism have difficulties in detecting straight gaze stimuli among averted gaze stimuli, whereas straight gaze facilitates gaze detection in control participants (Howard et al., 2000; Senju et al., 2003; Senju, Hasegawa et al., 2005). The MEG-findings of Study IV also indicated atypicalities in the neural processing of straight gaze in children with autism. Straight gaze elicited a greater electromagnetic response than averted gaze at around 240 ms after stimulus onset only in children with autism. This type of response was not seen in typically developing children or adults (Study III). This gaze direction-sensitive finding is broadly in line with Grice et al.'s (2005) recent study reporting an anterior mid-line component at 200-260 ms that was stronger to straight gaze than to averted gaze in young children with autism but not in control children and adults.

It is possible that atypical neural processing of straight gaze in children with autism is a consequence of abnormal use of eye contact. If individuals with autism do not find looking at the other person's eyes comfortable, they are unlikely to be motivated to have an eye contact. This could lead to a general lack of interest in looking at faces, and the resultant reduced exposure to faces might contribute to the abnormal development of face expertise in individuals with autism. Indeed, it has been suggested that the lack of neural specialisation for faces in individuals with autism is due to diminished experience of processing faces (Schultz et al., 2000; Grelotti, Gauthier, & Schultz, 2002). The lack of interest in looking at faces might be evident from very early on in the development of autism. It has been shown that 6-month-old siblings of children with autism, who are at enhanced risk for developing autism, fixate their mother's eyes less than 6-month-old infants with no known risk for developing autism (Merin, Young, Ozonoff, & Rogers, 2006).

4.3 The protracted neurodevelopmental maturation of face processing in typical development

In Study III, electromagnetic activity associated with face and gaze processing was measured and compared in 8- to 11-year-old typically developing children and in typically developing adults. Although the behavioural performance in a matching task was similar in the children and the adults, the electromagnetic responses elicited by faces showed major dissimilarities between the groups.

The strongest face sensitive response in children arose 100 ms after stimulus onset and seemed to originate from midline occipital cortex. This response was much more prominent in children than in adults for all image categories. The 100-ms response differentiated between the categories of face and motorbike

stimuli because it was of shorter latency for faces than motorbikes. This finding is consistent with a previous ERP-study (Taylor, Edmonds et al., 2001) which also demonstrated that the latency of an evoked response at around 100 ms was shorter for faces than other stimulus categories. In general, the prominent face sensitive response at 100 ms in children might indicate that the primary visual areas have a special role in face processing and that the primary visual areas still play a strong role in face processing at this relatively late stage of development.

The strongest face sensitive response in adults occurred 135 ms following stimulus onset and was right lateralised. Given that the signal topography, the increased signal amplitude (as compared to responses to motorbikes), and amplitude reduction upon repetition of an image are consistent with previous observations (e.g., Braeutigam et al., 2001; Campanella et al., 2000), this response was assumed to correspond to what has commonly been labelled as the N170 face response in the ERP literature. Electromagnetic activity was observed in the children at the same latency, although the response was weaker and more bilateral. Furthermore, this response did not significantly differentiate between the faces and motorbikes in terms of signal strength in children. These findings suggested that adult-like face sensitivity in extrastriate areas is only partially developed by the middle childhood. Unlike previous ERP-studies (Henderson et al., 2003; Taylor et al., 1999; Taylor, Edmonds et al., 2001), the latencies of the face sensitive electromagnetic responses were not longer in children compared with adults. The bilateral nature of the MEG signal at 135 ms in children was, however, in line with previous ERP-findings showing that the right hemisphere dominance typically seen in adults is not evident before the age of 12 years (Taylor et al., 1999). It seems likely that the discrepancy between studies in the latency of face sensitive responses reflects differences in spatial resolution and sensitivities between the technologies used. The findings of Study III supported the fundamental, qualitative developmental changes in neural bases of face and gaze processing between children and adults (cf., Halit et al., 2003; Passarotti et al., 2003).

Another interesting finding of Study III was that averted gaze elicited significantly stronger activation than straight gaze (or eyes closed) at 245 ms in children. This response apparently originated in inferior occipital cortex and was strongly right lateralised. This type of response did not occur in response to motorbikes and was not seen in adults. It has been argued that the eyes have a special role in the development of face processing abilities (Johnson & Farroni, 2003). It seems possible, therefore, that the hemispheric lateralisation of face processing may follow the lateralisation of averted gaze processing. This hypothesis is, however, rather speculative and needs further exploration.

4.4 Abnormal development of neural processing of face and gaze in children with autism

In Study IV, electromagnetic activity associated with face and gaze processing in 8- to 12-year-old children with autism was studied in comparison to typically developing children. Unexpectedly, the electromagnetic activity elicited by the presentation of face stimuli was, in general, relatively similar in the two groups of children. Specific abnormalities were found in the neural correlates associated with gaze processing in children with autism. Furthermore, the neural processing of non-face objects (motorbikes) showed rather marked dissimilarities between the groups. Nevertheless, the behavioural performance showed the opposite pattern of results; the performance accuracy for motorbikes was similar in the two groups of children, whereas the performance accuracy for faces was better in the control group than in the clinical group.

The response at 135 ms, thought to correspond to the N170-response in ERP-studies with healthy adults was somewhat weaker in children with autism than in typically developing children. This decrease, however, was not as robust as shown in adults with autism vs. typically developing adults (Bailey et al., 2005; McPartland et al., 2004). A previous ERP-study by O'Connor et al. (2005) found no difference between children with Asperger's syndrome and control children in the N170-response to faces, whereas in the adults with Asperger's syndrome the N170-response to faces was weaker than in the control adults. It is possible that the insignificant weakness of the 135-ms response in children with autism vs. typically developing children is a developmental precursor to the more robust finding of lack of face sensitive activation at this latency in adults with autism. If true, the apparent development of abnormal neural correlates of face processing in adults with autism could reflect the lack of experience of faces during the development. This line of reasoning, however, seems to be inconsistent with studies reporting significant differences between children with and without autism as young as three to four years of age in studies investigating ERP-responses to fearful versus neutral faces (Dawson et al., 2004) and to familiar versus unfamiliar faces (Dawson et al., 2002; Webb et al., 2006). The findings from these ERP-studies are not, however, entirely compatible with the findings of Study IV. These previous studies investigated ERP-responses at latencies which were longer (> 300 ms) than those in our study. The long latency responses have been associated with face familiarity, attention allocation, and memory processes (for a review, see de Haan, Johnson, & Halit, 2003), and not with the recognition or categorisation of a face as a face amongst other type of stimuli, i.e., processes related to the ERP-responses at short latency (around 100-200 ms after stimulus onset) (e.g., Eimer, 2000; Liu et al., 2002). In these ERP-studies with younger children with autism, the findings were interpreted to indicate that abnormalities in social attention modulate the experiences of the infant with autism from very early on (Dawson et al., 2002).

Interestingly, it has been shown that the so-called fusiform face area in the ventral occipito-temporal cortex responded more to cartoon characters (Digimons) than familiar and unfamiliar faces in a boy with autism who was a Digimon-enthusiast (Grelotti et al., 2005). This finding supports the views (e.g., Gauthier, Behrmann et al., 1999; Tarr & Gauthier, 2000) that the fusiform gyrus is specialised for processing visual patterns with which a person has acquired extensive experience (expertise). Previous studies have shown, for example, that car enthusiasts and bird-watchers (Gauthier, Skudlarski, Gore, & Anderson, 2000) or healthy adults who have been trained to discriminate artificial statue figures (Gauthier, Tarr, Anderson, Skudlarski, & Gore, 1999) show enhanced fusiform activity in response to these stimulus categories compared with participants who are not specialised. Thus, the enhanced fusiform activity in the Digimon-enthusiast with autism to Digimon-characters could be interpreted as supporting the theory that the lack of specialised neural activity to faces in individuals with autism is, indeed, a consequence of reduced exposure to faces.

As noted above, the present results indicated that there was no difference in the face sensitive response at 135 ms between children with autism and typically developing children. This finding was in contrast to those of previous studies observed in adults with and without autism (Bailey et al., 2005; McPartland et al., 2004; O'Connor et al., 2005). It is possible that the improvement of the intervention programs which nowadays also include training of social skills may explain the finding. The current type of intervention programs may have influenced the neural development of face processing in present-day children with autism by emphasising the importance of looking at people's faces, thus providing increased experiences of faces during the development (cf., O'Connor et al., 2005).

The present results also showed that around 240 ms after stimulus onset, there were differences in the electromagnetic responses between the children with autism and typically developing children in respect to gaze direction. Namely, at this latency, children with autism had a stronger response to straight gaze than to averted gaze, whereas in typically developing children this type of response was not seen. Furthermore, at the same latency, typically developing children had a right lateralised response to averted gaze that was reduced in children with autism. It is possible that these differences in the gaze-sensitive responses reveal something about the general face processing difficulties exhibited by individuals with autism. Typically developing infants prefer to look at faces with straight gaze compared to faces with averted gaze (Caron et al., 1997; Farroni et al., 2002; Hains & Muir, 1996) or closed eyes (Batki, Baron-Cohen, Wheelwright, Connellan, & Ahluwalia, 2000). It has also been shown in typically developing infants (Farroni, Massaccesi, Menona, & Johnson, 2007), children (Hood, Macrae, Cole-Davies, & Dias, 2003), and adults (Hood et al., 2003; Vuilleumier, George, Lister, Armoni, & Driver, 2005) that eye contact facilitates the memory of the facial identity. It is possible that processing of the eye region of a face somehow enhances the normal development of the face processing.

As speculated earlier, the tendency to avoid eye contact in children with autism might lead to more general face processing abnormalities. Interestingly, it has been shown that activity in the face sensitive area of the fusiform gyrus was strongly and positively correlated with the amount of time spent fixating the eyes of the face image presented in adults with autism (Dalton et al., 2005). It has also been suggested that differences in the duration of gaze fixation in the control and the clinical groups may contribute to the inconsistent results in the imaging literature of face processing in autism (Dalton et al., 2005; Hadjikhani et al., 2007; Jemel, Mottron, & Dawson, 2006). In the imaging studies that did not find reduced activation of the fusiform face sensitive areas in individuals with autism (Hadjikhani et al., 2007; Hadjikhani, Joseph et al., 2004; Pierce et al., 2004), it is possible that the participants in the clinical and the control group may have exhibited similar inspections of eyes when viewing faces, while the clinical and control groups in the studies that did find differences in this area might have exhibited different viewing patterns (Critchley, Daly et al., 2000; Hall et al., 2003; Hubl et al., 2003; Pierce et al., 2001; Schultz et al., 2000; Wang et al., 2004). This is speculative, however, as gaze patterns were not explicitly measured. It should be noted that, in Study IV, the face stimuli were presented only for 200 ms, and were presented so that the preceding fixation location was matched with the point between the eyes in the subsequent face stimulus. It is likely, therefore, that the amount of time fixating the eye region in the two groups was approximately equal in Study IV. It does not seem plausible, therefore, that the differences in the amount of time spent fixating the eye region could account for the differences in the gaze-sensitive responses between the two groups of children.

One unexpected finding of Study IV was that the electromagnetic activity elicited by the presentation of motorbikes appeared to be atypical in children with autism. In contrast to the control children, the 100-ms response evoked by motorbikes in children with autism occurred largely over right extrastriate cortex. In typically developing children, the motorbike responses were consistently 10-30 ms slower than responses to faces, whereas the delay was not significant in children with autism. Furthermore, the response to motorbikes at 135 ms was stronger than the response to faces only in children with autism. These findings are largely consistent with Webb et al.'s (2006) recent study showing that ERP-responses around 300 ms to objects were faster than those to faces in toddlers with autism, whereas normally developing toddlers showed reversed pattern of latencies. They also demonstrated that, at the same latency, young children with autism had stronger responses to object than face stimuli. In the control children, there was no difference in the amplitudes of the responses between the two stimulus categories. The authors explained these findings by suggesting that toddlers with autism might exhibit preferential processing abilities for nonsocial as compared to social stimuli (Webb et al., 2006). This may be a consequence of the abnormalities in social attention/motivation evident at a young age in infants who are later diagnosed with autism (Osterling & Dawson 1994). It is also possible that, in children with autism, an atypical

pattern of responses to non-face objects, such as motorbikes, interferes with the normal development of face processing and is related to more general visual processing abnormalities in autism (cf., Jemel et al., 2006). This suggestion naturally needs further investigation and should be researched with a comprehensive battery of non-face, object categories. In conclusion, the current MEG-findings seem to indicate that neural abnormalities in face processing in individuals with autism are related to the lack of face experience during the development. It is not, however, clear at the moment which factors underlie this lack of interest.

4.5 Concluding remarks

A number of conclusions can be drawn from the studies discussed above. Firstly, the studies demonstrated that the perception of another person's averted gaze triggered an automatic shift of visual attention both in children with autism and in typically developing children. The children in both groups were also able to overtly discriminate between another person's averted or direct gaze. Secondly, children with autism exhibited stronger electrodermal activity in response to straight gaze than to averted gaze, whereas there was no difference in electrodermal activity between these gaze conditions in typically developing children. Thirdly, the findings indicated that in typical development, the neural mechanisms subserving face perception are still less specialised in middle childhood than in adulthood. Fourth, the face sensitive neural responses were relatively similar in children with autism and in typically developing children. The most prominent difference between these two groups of children was found in gaze sensitive responses, particularly in response to straight gaze.

The present series of studies demonstrated that some aspects of social cognition were preserved in children with autism. Alternatively, it was possible that the high-functioning children with autism were able enough to use compensatory cognitive and neural mechanisms in the present series of laboratory tasks and, therefore, exhibited seemingly intact abilities of social cognition. The ability to compensate for the socio-cognitive problems might be most optimal in the laboratory settings in which situational distracters are minimised and the task demands are very clear. It may be that the ability to compensate for these problems is restricted to high-functioning children and does not apply to low-functioning children with autism. Wide variation in the level of cognitive functioning and autistic behaviours in individuals within the autism spectrum disorder challenge all the research in this area.

It was speculated that the face processing abnormalities in autism relate to atypical processing of the eyes; in particular, to processing of straight gaze (i.e., eye contact). It should be emphasised that the abnormalities in the neural processing of faces ought to be seen as a part of potential abnormalities in a more distributed social perception network (cf., Hadjikhani et al., 2007; Schultz,

2005). The functioning of this network is likely to be affected by early social motivation including, for example, the attraction of typically developing infants towards faces. As previously suggested, the development of social motivation might be abnormal from very early on in autism. An interesting possibility is that the eyes play a central role in triggering and maintaining this social-motivational behaviour. The influence of gaze behaviour abnormalities on broader face processing deficits in autism should be investigated in future studies. By increasing this understanding it might be possible to guide the planning of the early intervention programs in an effective way in order to alleviate the devastating difficulties children with autism encounter in their every-day social interactions.

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Attention orienting by another's gaze direction in children with autism

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Background: The aim of this study was to investigate attention orienting triggered by another's gaze direction in autism. **Method:** Twelve high-functioning children with autism and gender- and age-matched normal control children were studied using two tasks. In the first task, children were asked to detect laterally presented target stimuli preceded by centrally presented facial cue stimuli in which gaze was either straight ahead or averted. The direction of the cue was either congruent, neutral, or incongruent with respect to the laterality of the target stimulus. In the second task, children were asked to discriminate the direction of eye gaze. **Results:** The results showed that another person's static gaze direction triggered an automatic shift of visual attention, both in children with autism and in normally developing children. The children in both groups were also able to overtly discriminate the direction of the gaze. **Conclusion:** These results seem to suggest that, in children with autism, the visual system processes information about another person's gaze direction and sends this information to those areas that subserve reflexive attention orienting. However, future studies are needed to investigate whether the processing of eyes and gaze direction relies on similar neural mechanisms in children with autism and in normally developing children. **Keywords:** High-functioning autism, attention orienting, gaze direction, reaction time. **Abbreviations:** ADI-R: Autism Diagnostic Interview-Revised.

Autism is a neurodevelopmental disorder characterised, among other things, by impairments in reciprocal social interaction and communication. One of the earliest signs of a disturbance in social interaction in autism is an impairment in joint attention. Autistic impairments in joint attention are related to a variety of behaviours, including problems in looking, touching, pointing, and showing behaviours (Baron-Cohen, 1989; Landry & Love-land, 1988; Mundy, Sigman, Ungerer, & Sherman, 1986; Sigman, Mundy, Sherman, & Ungerer, 1986). Here, we concentrate on joint visual attention, i.e., looking where someone else is looking. Especially, we will focus on how children with autism process information from other people's gaze direction for social attention.

In normal development, joint visual attention appears during the first year of life when infants start to follow an adult's gaze in order to have a shared experience of seeing the same object or event (Corkum & Moore, 1998). The normal development of joint visual attention has been studied using a naturalistic paradigm in which an infant is placed in a face-to-face interaction with an adult, and the infant's ability to use the adult's direction of attention as a cue for locating a rewarding object (e.g., a toy) is recorded (Butterworth & Jarrett, 1991; Corkum & Moore, 1995; Moore & Corkum, 1998; Scaife & Bruner, 1975). Joint visual attention is judged to be established if the infant repeatedly turns to look in the same direction as the adult (Scaife & Bruner, 1975). Different kinds of visual cues have been used in these experiments: a congruent head and eye turn, an eye turn without a head turn, a head turn

without an eye turn, and head and eye turns in opposite directions (Corkum & Moore, 1995, 1998). These studies have shown that eye direction alone affects infants' orienting only after 18 months of age. Younger infants, aged between 8 and 12 months, ignore information about eye orientation and turn their heads to targets within their own visual field according to another person's head orientation information alone (Corkum & Moore, 1998).

Recently, joint visual attention has also been investigated in laboratory experiments, allowing more stringent control of the attention orienting stimuli. Hood, Willen, and Driver (1998) reported that infants as young as 10 to 28 weeks old could shift their gaze in the same direction as an adult's gaze. Hood and colleagues presented computerised face cues with a straight and an averted gaze followed by a peripheral target which appeared either on the same or opposite side to the direction of gaze. The infants' eye movement recordings showed that the infants were faster to orient to the target that appeared on the side where the face looked. However, Farroni, Johnson, Brockbank, and Simion (2000) argued that the orienting effect Hood et al. reported could have been, in fact, due to a motion cue present in the cue stimuli. Namely, in the study by Hood and colleagues, the gaze cue gave an impression of eye gaze shifting to the left or right. To test this possibility, Farroni et al. ran an experiment where the eyes of the face cue remained stationary, but the face was displaced laterally. Eye movement recordings from 16- to 21-week-old infants showed that saccadic reaction times were shorter to target locations that were congruent with the direction of lateral displacement

of the face. Further, to confirm that the infants' attention was cued by the motion cue, they showed, in another experiment, that when the illusory movement of the pupils was eliminated, static gaze direction did not affect infants' saccadic reaction times to lateral targets.

A number of recent experimental studies have focused on the nature of abilities children with autism possess in joint visual attention (Baron-Cohen, 1989; Baron-Cohen, Campbell, Karmiloff-Smith, Grant, & Walker, 1995; Leekam, Baron-Cohen, Perrett, Milders, & Brown, 1997; Leekam, Hunnisett, & Moore, 1998; Leekam, López, & Moore, 2000; Tan & Harris, 1991). This research has shown that children with autism possess basic knowledge about eyes and seeing. They understand that eyes are for seeing (Tan & Harris, 1991) and they are able to infer when a person is looking at them (Baron-Cohen et al., 1995). They are also, for example, capable of picking out a specific object in a room that another person is looking at (Baron-Cohen, 1989) or report which object another person is fixating on in a photograph (Leekam et al., 1997).

In contrast to these preserved abilities, ability to orient spontaneously towards adults' direction of attention has been found to be impaired in children with autism. Leekam et al. (1997) compared children with autism, Down syndrome, and normally developing children using the naturalistic paradigm. They found that the majority of the children with autism failed to monitor an adult's head and eye movements, whereas children with Down syndrome and normally developing children repeatedly turned to look in the same direction as the adult. However, the spontaneous gaze-monitoring ability seems to be related to the developmental age of a child with autism (Leekam et al., 1998). Children with autism who had a verbal mental age over four years were able to follow another person's head and eye direction spontaneously. This result was shown by using both the conventional naturalistic paradigm and by observing the children in a play situation with an adult. Hence, it has been argued that individuals with autism might suffer from a specific delay in joint visual attention and that they need more time to establish this ability than normally developing children. Preschool children with autism resemble 8- to 12-month-old typically developing infants in their joint visual attention skills (Leekam et al., 2000). In Corkum and Moore's (1998) study, 40% of normally developing infants from 8 to 12 months of age were able to follow an adult's head and eye direction if the target was within their visual field. The same proportion of preschool-aged children with autism spontaneously followed the adult's head and eye direction in the study by Leekam et al. (2000).

An interesting possibility is that the deficiencies in joint visual attention in autism reflect impairments in visual attention orienting. Attention orienting in autism has been studied using the classic spatial

cueing tasks (Posner, 1980). In these computer-based tasks, the subject is required to detect visual targets which appear, for example, on the left or right side of a central fixation point. Before the onset of the target stimulus, the subject's attention is directed to one of the possible target locations by a cue. The cue (e.g., a peripheral light flash or a centrally presented arrow) provides valid or invalid information about the location of the target. Typically, reaction times to detect targets are shorter in the valid than in the invalid cue conditions. This result has been interpreted as suggesting that the preceding cue triggers a shift in the subject's attention which, in turn, leads to enhanced processing of information in the cued spatial location (Posner, 1980). The shift of attention can be triggered exogenously by the onset of an uninformative (i.e., equal probability for valid and invalid cues) but salient visual peripheral event (e.g., a flash of light). In contrast, endogenous orienting is considered to be under voluntary control and it emerges after centrally presented informative (i.e., probability is higher for valid than invalid trials) symbolic cues (e.g., arrows) (Jonides, 1981). Both types of attention orienting can emerge without concordant eye movements (Posner, 1980).

Townsend, Courchesne, and Egaas (1996) used peripheral illumination changes as cues and found that adults with autism as well as normal controls had shorter reaction times in the valid than invalid conditions. Similar results were reported in adult autistic savants (Casey, Gordon, Mannheim, & Rumsey, 1993) and children with autism (Harris, Courchesne, Townsend, Carper, & Lord, 1999). Wainwright-Sharp and Bryson (1993) used centrally presented arrow cues and found that adults with autism showed the attention orienting effect (at long cue-target intervals), whereas Swettenham, Milne, Plaisted, Campbell, and Coleman (2000) reported that children with autism showed a reduced ability to shift attention followed by central arrow cues. In this study, however, exogenous shifts of attention seemed to be intact (Swettenham et al., 2000). Interestingly, a few studies, in adults with autism, have found difficulties in attention orienting specifically when attention must be shifted to the left side of the visual field (Casey et al., 1993; Wainwright-Sharp & Bryson, 1993). This result has been suggested to indicate that individuals with autism may have impairments in the right parietal systems devoted to spatial orienting.

Recently, the study of social attention orienting and the spatial cueing paradigm have been brought together. There is clear evidence that seeing another person's gaze and/or head direction triggers a shift in the observer's attention. Adult subjects detect a peripherally presented target more rapidly when it appears on the same rather than the opposite side to the direction of the gaze/head cue (Driver et al., 1999; Friesen & Kingstone, 1998; Hietanen, 1999, 2002; Langton & Bruce, 1999; Ristic, Friesen, &

Kingstone, 2002). These results are compatible with a wealth of neurophysiological evidence suggesting that the visual system contains specialised brain mechanisms sensitive to gaze direction (e.g., George, Driver, & Dolan, 2001; Perrett, Hietanen, Oram, & Benson, 1992). Also, Baron-Cohen (1995) has proposed an innate neural module for eye direction detection (EDD) that is central for development of joint visual attention. There are some preliminary results suggesting that children with autism fail to orient their attention using gaze/head direction cues in a spatial cueing task. Swettenham et al. (2000) investigated attention orienting triggered by social stimuli using a computer-based paradigm. The orienting cue was a head (full profile) facing either to the left or to the right. The direction of another person's head as a cue did not affect the reaction times of the children with autism, whereas a clear cueing effect was reported for the normal children. It is noteworthy that the mean age of the children was slightly over ten years in both groups and their non-verbal abilities were matched. Thus, in both groups the children had reached an age in which behavioural observations have shown children to follow another person's head and eye direction spontaneously (cf. Leekam et al., 1998).

To summarise, it is extensively reported that children with autism are impaired in orienting towards other people's direction of attention, although some evidence suggests that, rather than being permanently impaired, these children might suffer from a developmental delay in joint visual attention. Children with autism who have reached a certain level of mental age (over four years) have been shown to be able to orient towards another person's head and eye direction. However, these studies have employed observations in naturalistic situations where the attention directing cues have often involved concomitant eye, head, and body movements. Moreover, in these studies, the cues have also involved visual motion. Based on classic paradigms in attention orienting research, recent studies with healthy adults have shown that centrally presented static gaze and/or head direction cues elicit rapid shifts of visual attention. The aim of the present study was to investigate whether children with autism orient their attention according to another person's static gaze direction. Interestingly, there is one earlier study showing that centrally presented static *head direction* cues do not elicit attention shifts in children with autism, not even in children whose mental age, based on knowledge from naturalistic observations, would lead one to expect such an orienting to occur. However, an averted *gaze direction* embedded in a full view of a face might enjoy a special status as an attention directing cue.

The present paper reports children's performance in two tasks. In the first task, children with autism and their matched controls were asked to detect laterally presented target stimuli preceded by a face

cue with a straight or an averted gaze. In this task, the time interval between the onset of the cue stimulus and the onset of the reaction signal (stimulus-onset-asynchrony, SOA) was given two values: 200 ms and 800 ms. The SOA of 200 ms was selected because, in earlier studies (in adults) using centrally presented social cues (Driver et al., 1999; Friesen & Kingstone, 1998; Hietanen, 1999, 2002; Langton & Bruce, 1999), SOAs between 100 and 300 ms have been shown to result in the attention orienting effect. At longer SOAs (approaching 1000 ms), the attention orienting effect by social cues diminishes (Ristic et al., 2002) or disappears completely (Friesen & Kingstone, 1998; Langton & Bruce, 1999). However, Wainwright-Sharp and Bryson (1993) reported a study in adults with autism showing that central arrow cues did not result in attention orienting at short SOAs (100 ms), whereas an orienting effect was achieved at long SOAs (800 ms). Therefore, we were interested in studying whether the attention orienting by gaze cues follows a similar time course for normally developing children and children with autism. As there was earlier indication for differences in orienting to the targets in the left and right visual fields in subjects with autism (Casey et al., 1993; Wainwright-Sharp & Bryson, 1993), the effect of visual field was also investigated.

The second task investigated whether the children were able to overtly discriminate gaze direction in face stimuli when using the same presentation time of stimuli as in the attention-orienting task (200 ms). This task was planned to confirm that, in the case of impaired attention orienting by the gaze cues, the children with autism were able to perceive gaze direction. In order to ensure that the children with autism had acquired the ability for joint visual attention (cf., Leekam et al., 1998) and were old enough to understand the instructions of the tasks and to participate cooperatively in the behavioural experiments, only high-functioning children with autism who had a mental age above six years were selected.

Methods

Subjects

The subjects comprised 12 school-aged children with autism spectrum disorders and their gender- and mental-age-matched controls. The parents of the clinical group were all administered the Autism Diagnostic Interview-Revised (ADI-R; Lord, Rutter, & Le Couteur, 1994) and all participants met the algorithm criteria for autism. Table 1 shows the scores of the clinical group on three domains in ADI-R, social domain (cutoff score for diagnosis of autism is 10), communication domain (cutoff score 8), and stereotypy domain (cutoff score 3). Normal control children were volunteers and had no history of mental or neurological disorders. The groups were individually matched for mental age (WISC-R). There were no significant differences between the clin-

Table 1 Subject characteristics

	Group	
	Clinical	Control
<i>N</i> (sex)	12 (11M, 1F)	12 (11M, 1F)
CA (years; months)		
Mean (SD)	9;11 (1;10)	8;11 (2;10)
Range	7;4–14;1	6;1–16;0
MA (years; months)		
Mean (SD)	9;3 (2;11)	9;5 (2;10)
Range	6;8–16;0	6;6–16;0
Full IQ		
Mean (SD)	91 (17)	106 (7)
Range	67–122	101–124
Verbal IQ		
Mean (SD)	90 (19)	109 (8)
Range	69–124	94–123
Performance IQ		
Mean (SD)	95 (16)	102 (7)
Range	67–117	95–118
ADI-R		
Social Domain		
Mean (SD)	18.7 (4.5)	
Range	11–24	
Communication Domain		
Mean (SD)	14.1 (3.1)	
Range	8–18	
Stereotypy Domain		
Mean (SD)	7.3 (2.5)	
Range	3–12	

M: male; F: female; CA: chronological age; MA: mental age; IQ: intelligence quotient; ADI-R: Autism Diagnostic Interview-Revised.

ical and control groups in chronological age, mental age, and performance IQ, but the normal controls had a higher verbal IQ, $t(22) = 3.35$, $p \leq .003$, and full scale IQ, $t(22) = 2.79$, $p \leq .01$, than the clinical group (see Table 1).

Attention orienting by gaze direction

Stimuli. A male face with a neutral expression was pictured with a digital camera in ambient lighting conditions. Three pictures were taken: a front view of the face with straight ahead gaze and front views of the face with gaze averted 30° to the left or right. The facial stimuli were presented on a 20-inch computer monitor (1024 × 768, 75Hz, Apple Multiple Scan Display). The head subtended 14° and 10° vertically and horizontally, respectively. The reaction signal was an asterisk subtending 1° and its distance from the fixation point was 7°. The fixation point was located in the middle of the screen and the face cues were aligned so that the fixation point was located on the ridge of the nose between the eyes. Stimulus presentation and data collection were controlled by the PsyScope computer program which was running on a Power Macintosh 7100/80 computer.

Design and procedure. A trial began with the appearance of a fixation point for 1000 ms. Next, the face stimulus appeared on the screen for 200 ms.

The face was followed by the reaction signal (an asterisk) which appeared either on the left or right side of the fixation point until a response was made (see Figure 1). The stimulus-onset-asynchrony (SOA) between the onset of the face stimulus and reaction signal had two values, 200 and 800 ms.

The children's heads were held in a fixed position by a head-rest at a distance of 55.0 cm from the computer monitor. The children were asked to fixate and maintain their fixation throughout each trial. They were instructed to press a single response key located in a midsagittal plane as soon as they detected the asterisk on the screen. The face cues with left, straight, and right gaze direction were equiprobably presented and each cue was followed as often by left and right targets. It was emphasised that the face gave no information whatsoever about where the target asterisk would appear on each trial. Subjects were asked to use one hand at a time for pressing the response key and each child performed the task using both left and right hand. The task contained 120 experimental trials and 12 'catch' trials on which no target was presented. The aim of the catch trials was to discourage anticipatory responses. Prior to the experimental trials, 10 practice trials, which included examples of each experimental condition as well as catch trials, were presented to the children.

The experimental procedure was carefully explained to the child with the aid of cartoon pictures. The experimenter sat behind the child throughout the experimental procedure and initiated every trial by pressing a remote button. The child's eye movements were monitored by using a mirror on the wall behind the computer monitor. This method for monitoring eye movements has also been used in other studies (e.g., Rizzolatti, Riggio, Dascola, & Umiltà, 1987; Umiltà, Riggio, Dascola, & Rizzolatti, 1991). In this way the experimenter was able to ensure that the child was looking at the monitor before initiating a trial. Also, it

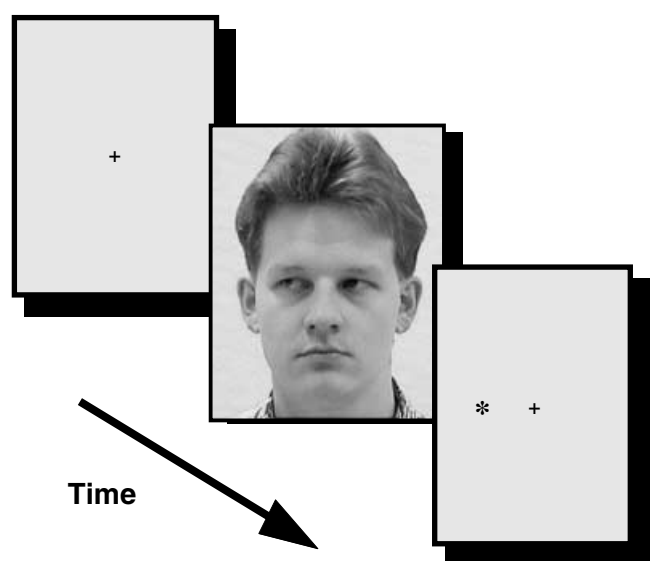


Figure 1 The sequence of stimulus events on a single trial in the attention orienting by gaze-direction task. The figure illustrates a condition in which the gaze was directed to the same side as the reaction signal (congruent condition)

was possible to ensure that the child fixated the fixation point. The children were rewarded with a token after task completion.

In sum, the experimental design included three within-subject variables: gaze congruency (congruent = gaze averted to the same side as the reaction signal, incongruent = gaze averted to the opposite side as the reaction signal, and neutral = a straight gaze with the reaction signal on the left or right), SOA (200 ms and 800 ms), and visual field of the target presentation (left and right).

Discrimination of gaze direction

This task was used to investigate whether the children were able to overtly discriminate gaze direction from pictures with the same stimulus presentation time (200 ms) as in the attention-orienting task.

Stimuli. The same pictures and apparatus as in the attention-orienting task were used.

Design and procedure. A trial began with a fixation point appearing on the screen for 1000 ms followed by the presentation of a face stimulus for 200 ms. Children were asked to discriminate whether the person on the screen looked straight ahead (at them) or, from a child's point of view, to the left or right. The responses were given by pressing the middle, left, or right response key, respectively. It was also pointed out to the children that correct choices were more important than the speed of responses. Left, straight, and right gaze directions were equiprobably presented. The task contained 30 trials in a random order with 6 practice trials.

The experimenter sat behind the child throughout the experimental procedure and initiated every trial by pressing a button as in the attention-orienting task. The children were rewarded with a token after task completion.

Results

Attention orienting by gaze direction

In this task, the children detected targets which were preceded by a face cue with a straight or an averted gaze. First, responses with reaction times shorter than 150 ms and longer than 1500 ms were eliminated from subsequent calculations. Secondly, trials in which reaction times exceeded a time-window of \pm two standard deviations from each child's mean were also excluded from subsequent analyses. Based on these criteria, 6.4% of trials were excluded. There was no difference between the children with autism (6.0%) and controls (6.8%) in the percentage of excluded trials (Mann-Whitney, $U = 56$, n.s.).

The data were analysed with a gaze congruency (3) \times SOA (2) \times visual field (2) \times group (2) ANOVA (split-plot design). This analysis showed that there were significant main effects of gaze congruency, $F(2, 44) = 7.35$, $p < .002$, and SOA, $F(1, 44) = 55.68$, $p < .001$. The reaction times were shorter at the SOA of 800 ms (436 ms) than at the SOA of 200 ms (481

Table 2 Mean reaction times (and SEM) as a function of gaze congruency, SOA, and group

Group	Gaze congruency		
	Congruent	Neutral	Incongruent
Clinical			
200 ms SOA	486 (37.7)	511 (46.4)	510 (48.6)
800 ms SOA	438 (39.8)	439 (32.3)	461 (45.5)
Control			
200 ms SOA	477 (32.1)	494 (36.0)	506 (42.0)
800 ms SOA	434 (31.8)	456 (35.2)	450 (35.6)

ms). Most interestingly, the main effect of group was not significant ($p > .9$), nor did it significantly interact with any other main effects (gaze congruency, $p > .8$; SOA, $p > .5$; visual field, $p > .3$). None of the other two-way or higher-order interactions were statistically significant. Table 2 shows the mean reaction times for different stimulus conditions. Because the main effect of visual field was not significant nor was visual field interacting with any other main effect, the data are presented averaged across the visual field of the target.

The lack of the effects of group and interaction between group and condition was confirmed with further analyses. Because the main effect of visual field was not significant in the four-way ANOVA, it was removed from further analyses. Two two-way ANOVAs (separately for the SOAs of 200 ms and 800 ms) were performed. At the SOA of 200 ms, the main effect of gaze congruency was significant, $F(2, 44) = 5.13$, $p < .01$, indicating that there was a difference in the reaction times between congruent (481 ms), neutral (502 ms), and incongruent (508 ms) stimulus conditions. The main effect of group was not significant ($p > .8$), nor was the interaction between group and gaze congruency ($p > .7$). Because the effect of group and the interaction between group and gaze congruency were not significant, the effect of gaze congruency was investigated in more detail by combining the data across the groups. Planned pairwise comparisons (t -tests, two-tailed) revealed that, at the SOA of 200 ms, the reaction times were shorter in the congruent than in the neutral condition, $t(23) = 2.4$, $p \leq .02$, whereas there was no difference in the reaction times between the neutral and incongruent conditions.

At the SOA of 800 ms, the main effect of gaze congruency was also statistically significant, $F(2, 44) = 3.32$, $p < .05$, showing that there was a difference in the reaction times between congruent (436 ms), neutral (447 ms), and incongruent (456 ms) conditions. Also, at the SOA of 800 ms, the main effect of group ($p > .9$) and the interaction between group and gaze congruency ($p > .1$) were not significant. Planned pairwise comparisons revealed that, at the SOA of 800 ms, there was no difference in the reaction times between the congruent and neutral or between the neutral and incongruent

conditions. Given that the main effect of gaze congruency was significant, the pairwise comparison between the congruent and incongruent condition was naturally significant, $t(23) = 2.7$, $p \leq .01$.

In order to analyse whether the reaction times were confounded by the children's intelligence, these two analyses were also performed using verbal and full scale IQ as covariates. These analyses showed that the group differences remained non-significant even when the effects of VIQ and FIQ were removed.

Discrimination of gaze direction

In this task, the children were asked to discriminate the direction of gaze (straight, right, or left from the child's point of view) by pressing one of the three response keys. The data from one child with autism were excluded from further analyses because of technical problems with data collection. Even though speeded responses were not asked for, response times were also analysed. Response times which exceeded a time-window of \pm two standard deviations from each child's mean were rejected from data analysis. Based on these criteria, 4.8% of the trials were excluded. Table 3 shows the mean percentages of response errors and mean response times in three task conditions in both groups.

Two non-parametric Friedman's ANOVAs were performed on the error data from clinical and control subjects. These analyses showed that the effect of gaze direction was marginally significant in the group of clinical subjects, $\chi^2_F(2) = 5.2$, $p = .076$. These children made most errors when the gaze was directed to the left, whereas there were no errors when the gaze was directed to the right. The effect of gaze direction was not significant in the control group, $\chi^2_F(2) = 3.3$, $p = \text{n.s.}$ There was no difference in the percentage of total response errors between the groups of clinical subjects (3.4%) and controls (4.9%), Mann-Whitney, $U = 49.5$, n.s. For the response time data, a two-way ANOVA (split-plot design) showed that the main effects of gaze direction and group were not significant. The interaction between gaze direction and group was also non-significant.

Table 3 Results of the gaze-direction discrimination task. The mean percentages of response errors and the mean response times are shown in three task conditions for clinical and control subjects

Group	Gaze direction		
	Left	Straight	Right
Clinical			
Errors (%)	6.1	4.0	0.0
Response time (ms)	846	902	836
Control			
Errors (%)	2.8	6.5	5.6
Response time (ms)	774	782	786

Discussion

In this study, children with autism and their matched controls were tested using an attention-orienting task in which subjects were asked to detect peripherally presented target stimuli (cf., Posner, 1980). Instead of the traditionally used peripheral light flashes or central arrow cues, the targets were preceded by a face with a straight or an averted gaze. The gaze direction was either congruent, incongruent, or neutral (straight gaze) with respect to the location of the target. The results showed that another person's gaze direction triggered an automatic shift of visual attention both in children with autism and in normally developing children. We also studied the subjects in a second task, in which they were asked to make an overt three-choice discrimination of gaze direction (left, straight, or right). These results showed that the children in both groups were able to discriminate the direction of gaze.

The present study produced two main findings. First, the results indicated that the children with autism were able to overtly recognise the direction of another person's gaze. This result is consistent with several previous studies (Baron-Cohen, 1989; Baron-Cohen et al., 1995; Leekam et al., 1997). It also extends previous work by showing that the recognition of gaze direction is possible from facial images which are presented for a relatively short period of time (200 ms), without concordant head orientation (cf. Leekam et al., 1997), and when the target of the stimulus face's attention is not shown (cf., Baron-Cohen, 1989; Baron-Cohen et al., 1995). Secondly, and more importantly, the results showed that another person's static gaze direction triggers an automatic shift of attention in high-functioning children with autism. This is an interesting finding for two reasons. First, even though there are previous results from studies using the naturalistic paradigm that high-ability children with autism are able to follow another person's head and eye direction spontaneously (Leekam et al., 1998, 2000), it is possible that the attention orienting was cued, in these studies, not only by head and eye direction but the direction of (eye and head) movement also (cf., Farroni et al., 2000). The present study shows that perception of static laterally oriented eyes is enough to trigger attention shifts both in normally developing children and in high-functioning children with autism. Second, the present results are in contrast to a previous study which showed that static head direction cues did not elicit attention shifts in relatively able children with autism (Swettenham et al., 2000). The present results, thus, suggest that gaze direction as an attention-orienting cue is processed differently from head direction and that this information is used for attention orienting in high-functioning children with autism. Below, we will return to this topic in more detail.

Because the design included a straight (neutral) as well as congruent and incongruent gaze-direction conditions, it was possible to measure reaction time shortening and lengthening by congruent and incongruent gaze direction, respectively, with respect to the reaction times in the neutral trials. At the SOA of 200, the results showed that the reaction times were shorter in the congruent than neutral trials, whereas there was not a significant difference between reaction times in the neutral and incongruent conditions. This pattern of result is considered to be typical for exogenous attention orienting by uninformative peripheral cues (e.g., Posner, 1980) and it has also been reported previously in normal adults using gaze direction (Friesen & Kingstone, 1998) and head orientation (Hietanen, 2002) cues. At the SOA of 800, there was also a significant cueing effect as manifested in the reaction time difference between congruent and incongruent conditions, but neither of these conditions significantly differed from the neutral one. Recently, Ristic et al. (2002) reported a gaze cueing effect also at long cue-target intervals (up till 1005 ms) for both adults and normally developing 3- to 5- year-old children. However, because the design in that study did not include a neutral condition, we cannot compare the present result regarding the lack of orienting effect between congruent and neutral and between neutral and incongruent conditions at the longer SOA. The results also showed that the overall reaction times were shorter at the SOA of 800 than 200 ms. This shortening of the reaction times as a function of the SOA is a typical result reflecting the effects of several factors (e.g., arousal and subjective expectancy) on reaction times after any cue event (for a review, see Niemi & Näätänen, 1981).

It is of particular interest to reflect on how the present study relates to previous studies that investigated attention orienting in autism using other than social cues. It has been suggested that attention orienting by gaze cues has hallmarks which relate it more strongly to reflexive than voluntary attention orienting (Friesen & Kingstone, 1998). In studies using peripheral cues (Casey et al., 1993; Harris et al., 1999; Townsend et al., 1996), reaction times were shorter on valid than invalid trials in both children with autism and control children. In this respect, therefore, the present results are concordant with those studies and indicate that the involuntary attention-orienting mechanisms, whether triggered by peripheral illumination changes or central gaze cues, are intact in autism. Instead, when centrally presented arrow cues were used, adults with autism did not show faster reactions on valid than invalid conditions (Wainwright-Sharp & Bryson, 1993). There is considerable agreement that this latter type of cue may not elicit reflexive but voluntary shifts of attention (Jonides, 1981). This distinction is very important. Also, Minshew, Luna, and Sweeney (1999), investigating reflexive and

volitional saccadic eye movements, suggested that children with autism do not have difficulties in reflexive shifts of attention, whereas voluntary orienting, which appears later in development (Enns & Brodeur, 1989), is dysfunctional in autism.

In the previous studies showing the peripheral cueing effect with adult individuals with autism, the difference between the reaction times in valid and invalid conditions was greater for adults with autism than control subjects (Casey et al., 1993; Townsend et al., 1996). This pattern of results was interpreted to reflect problems in the disengagement component of attention in subjects with autism. Current theories of spatial attention propose that attention functions are comprised of three components: disengagement, shift, and engagement of spatial attention. Attention has to be disengaged from the current target of interest first, and only after that can it be shifted towards and re-engaged by a new stimulus (Posner, Inhoff, Friedrich, & Cohen, 1987). On invalid trials, attention must be disengaged from the (invalidly) cued location before it can be shifted to the target location. Therefore, the lengthening of the reaction times on invalid trials has been suggested to reflect problems, especially in the disengagement component of attention.

Why, then, was the difference between reaction times in congruent and incongruent conditions not greater for the children with autism than normally developing children in the present study? In the previous exogenous attention-orienting studies using peripherally illuminated squares as cues (Casey et al., 1993; Harris et al., 1999; Townsend et al., 1996), the frames of the squares remained visible in the visual periphery throughout the trials. It is possible that this feature of the paradigm could have amplified the disengagement problems on invalid trials, in those studies. Once triggered and shifted in the wrong (invalidly cued) location, attention may be harder to disengage from a location containing salient visual features than from an 'empty' location. Because there were no peripheral cueing events or visual objects present, in this study, it is possible that the autistic problems in attention disengagement were not manifested here.

Previous studies have been inconsistent regarding the findings about the lateralisation of attention orienting in autism. In some studies, there were no differences in attention orienting to the left and right visual fields (e.g., Harris et al., 1999; Townsend et al., 1996), whereas in some other studies it was found that the adults with autism were slower in orienting attention from the right to the left than from the left to the right in the invalid conditions (Casey et al., 1993; Wainwright-Sharp & Bryson, 1993). In the present study, there were no significant differences in the attention orienting to the left and right between the groups of children with autism and controls. Instead, in the task requiring discrimination of gaze direction, we found a marginal effect

indicating that the children with autism made more errors in discriminating the gaze directed to the left than to the right. At the moment, it may be futile to speculate on this result any further. It is noteworthy, however, that this marginal impairment was found for discriminating left gaze directions, i.e., the same direction where some previous studies showed impaired attention orienting.

What do these results tell us about gaze direction processing in autism? The processing of gaze and gaze direction are developmentally very early functions. This has been shown in recent behavioural (Batki, Baron-Cohen, Wheelwright, Connellan, & Ahluwalia, 2000) as well as in electrophysiological studies (Taylor, Edmonds, McCarthy, & Allison, 2001). There is also a wealth of neurophysiological evidence suggesting that the occipito-temporal visual system contains specialised brain mechanisms sensitive to the eyes, eye-movements, and gaze direction (e.g., Allison, Puce, & McCarthy, 2000; George et al., 2001; Hoffman & Haxby, 2000; Kawashima et al., 1999; Perrett et al., 1992; Wicker, Michel, Henaff, & Decety, 1998). Therefore, at first look, one might be inclined to interpret the results of the present study showing that, in children with high-functioning autism, the (ventral) visual system processes another person's static gaze direction in much the same way as in normally developing children, and that this information is sent to those (parietal) systems that subserve visual attention orienting (Posner & Dehaene, 1994).

However, it is possible that the high-functioning children with autism might use a different strategy for processing visual information from gaze direction than normally developing children. For example, it is possible that the children with autism could base the analysis of gaze direction on some low-level simple visual features, i.e., they do not process the eyes as eyes embedded in the facial context. It has been suggested that the luminance contrast between the dark iris and white sclera is an important perceptual cue of gaze direction (cf., Gibson & Pick, 1963; Kobayashi & Kohshima, 1997). It is possible that the children with autism might use this contrast information to derive geometric information from the eyes (see Leekam et al., 1997), and, therefore, the analysis could rely on some other neural mechanisms than those usually involved in gaze/face processing. Recently, Ristic et al. (2002) provided evidence for suggesting that uninformative biologically irrelevant arrow cues as well as biologically relevant gaze cues can trigger reflexive shifts of attention, but that these effects, indeed, are not based on the functioning of the same brain mechanisms. This line of reasoning could also explain why Swettenham and colleagues (2000) did not achieve a cueing effect with relatively able children with autism when using images of a head facing either to the right or left. It could be that the visual analysis of the head orientation for

social attention orienting cannot be solved by basing the analysis on some low-level simple visual features, whereas the direction of the eyes could be derived from certain low-level features.

There is recent evidence suggesting that face processing involves different regions of brain activity in adults with autism and in normal controls (Schultz et al., 2000; Swithenby, Bräutigam, Bailey, Joussmäki, & Tesche, 2000). These results suggest that the adults with autism seem to use the same regions of cortex to process faces and non-face objects. Thus, face processing in autism might be relying on processing of local features instead of holistic information (e.g., Tanaka & Farah, 1993; Tanaka, Kay, Grinnell, Stansfield, & Szechter, 1998) or configurational information (Searcy & Bartlett, 1996) typical in normal face processing. It is a matter for future studies to continue on this line of research and investigate whether the perception of eyes and gaze direction relies on similar cognitive and neural processes in children with autism and in normally developing children.

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Skin Conductance Responses to Another Person's Gaze in Children with Autism

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The effects of another person's gaze on physiological arousal were investigated by measuring skin conductance responses (SCR). Twelve able children with autism and 12 control children were shown face stimuli with straight gaze (eye contact) or averted gaze on a computer monitor. In children with autism, the responses to straight gaze were stronger than responses to averted gaze, whereas there was no difference in the responses to these gaze conditions in normally developing children. Thus, these results showed that eye gaze elicited differential pattern of SCR in normally developing children and in children with autism. It is possible that the enhanced arousal to eye contact may contribute to the abnormal gaze behaviour frequently reported in the context of autism.

KEY WORDS: High functioning autism; skin conductance responses; electrodermal activity; eye contact; gaze direction.

Eye contact is a powerful stimulus in social interaction. People are very accurate at discriminating whether another person is looking straight at them or whether the gaze is averted, especially when the other person's face is seen from straight ahead (Anstis, Mayhew, & Morley, 1969; Cline, 1967; Gibson & Pick, 1963; Masame, 1990; Wade & Jones, 1982; Vecera & Johnson, 1995). Gaze direction also serves many other important social functions: it provides information about attentiveness to communication, regulates interaction, facilitates communicational goals, and expresses intimacy and social control (Argyle, 1975; Kleinke, 1986). From early infancy, gaze behaviour has a special role in social development. Infants are known to preferentially fixate face-like stimuli (for a review, see Maurer, 1985), they prefer faces with eyes open (Batki, Baron-Cohen,

Wheelwright, Connelan, & Ahluwalia, 2000) and especially faces with straight gaze (Caron, Caron, Roberts, & Brooks, 1997; Farroni, Csibra, Simion, & Johnson, 2002; Hains & Muir, 1996).

The significance of gaze behaviour in social development becomes evident in the case of developmental disorders such as autism, which is characterised by serious disturbances in communication and social interaction. Abnormalities in eye contact in autism have been reported since Kanner's (1943) original definition of the syndrome and it is still one of the diagnostic criteria for autism spectrum disorders (DSM-IV; APA 1994). In empirical studies of gaze behaviour in autism, research has concentrated on (i) possible lack of eye contact and (ii) on presumable deficits in the use of gaze to control social interaction. In studies concentrating on the amount of eye contact, the results have shown that individuals with autism *spontaneously* direct their own gaze to other people less than normally developing individuals (Hutt & Ounsted, 1966; Kasari, Sigman, & Yirmiya, 1993; Osterling & Dawson, 1994;

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Pederson, Livoir-Petersen, & Schelde, 1989; Phillips, Baron-Cohen, & Rutter, 1992; Tantam, Holmes, & Cordess, 1993; Volkmar & Mayes, 1990). Studies investigating the use of gaze in social interaction have, in turn, shown deficits in timing and quality of gaze behaviour (Baron-Cohen, Baldwin, & Crowson, 1997; Buitelaar, van Engeland, De Kogel, De Vries, & van Hooff, 1991; Mirenda, Donellan, & Yoder, 1983; Swettenham *et al.*, 1998; Willemsen-Swinkles, Buitelaar, Weijnen, & van Engeland, 1998).

It has been suggested that these abnormalities in gaze behaviour may arise because of a variety of reasons. For example, individuals with autism do not understand the mental significance of the eyes; they show impairments in recognising other people's complex mental states and intentions from the eyes (Baron-Cohen, Campbell, Karmiloff-Smith, Grant, & Walker, 1995; Baron-Cohen, Wheelwright, & Jolliffe, 1997). Studies measuring eye-movements during looking at facial images have shown that individuals with autism scan the mouth region more than the eye region of the face, a pattern of results which is opposite to that observed in normally developing individuals (Klin, Jones, Schultz, Volkmar, & Cohen, 2002; Pelphrey *et al.*, 2002). Also, unlike normally developing children, children with autism rely in their face (identity) recognition more on the mouth region than on the eye region (Joseph & Tanaka, 2003). These findings have been explained by assuming that the perceptual bias to the mouth region observed in autism may reflect a strategy to improve the understanding of verbal information in social interaction (Klin *et al.*, 2002; Joseph & Tanaka, 2003). Recently, it has also been suggested that deficits in the neural mechanisms dedicated to the processing of another person's straight gaze (eye contact) might participate in the disturbances in development of social behaviour (Senju, Yaguchi, Tojo, & Hasegawa, 2003). It has been shown that both children (Senju *et al.*, 2003) and adults (Howard *et al.*, 2000) with autism have difficulties in recognising gaze stimuli with an eye contact among serially presented averted-gaze stimuli. That the deficit is specifically related to the processing of eye contact is supported by the findings that individuals with autism can make overt discriminations of where other people are looking (Baron-Cohen *et al.*, 1995; Kylliäinen & Hietanen, 2004; Leekam, Baron-Cohen, Perrett, Milders, & Brown, 1997; Tan & Harris, 1991) and that seeing of another person's averted gaze direction triggers an automatic shift of visual attention comparably in the clinical and control groups

(Chawarska, Klin, & Volkmar, 2003; Kylliäinen & Hietanen, 2004; Senju, Tojo, Dairoku, & Hasegawa, 2004; Swettenham, Condie, Campbell, Milne, & Coleman, 2003).

In the present study, we were interested in investigating the effect of another person's direct gaze on children with autism. In the past, it has been suggested that the avoidance of gaze in autism reflects an unusual degree of arousal elicited by eye contact (Hutt & Ounsted, 1966; Tinbergen, 1974). As an important element in social interaction gaze, indeed, affects physiological arousal (Kleinke, 1986). There are studies showing that, in healthy adult subjects, EEG arousal (decreased alpha activity) is higher to eye contact than to averted gaze (Gale, Spratt, Chapman, & Smallbone, 1975). Also, in some studies, heart rate has been found to be higher in an eye contact condition compared to a condition without eye contact (Kleinke & Pohlen, 1971), and eye contact has been shown to elicit greater skin conductance responses than unreciprocated gaze (McBride, King, & James, 1965; Nicholas & Champness, 1971). However, there are also studies showing no difference in physiological arousal between eye contact and unreciprocated gaze. For example, Leavitt and Donovan (1979) reported that pictures of gazing and non-gazing infants presented on a television monitor did not result in differential skin conductance responses in observing mothers. Also in another study by Donovan and Leavitt (1980), there were only marginal differences in skin conductance responses between straight gaze and averted head (without eye contact) conditions. In the present study, we investigated the effects of *gaze direction* on skin conductance responses in normally developing children and in children with autism. Despite the early suggestions of increased arousal to eye contact in autism (Hutt & Ounsted, 1966; Tinbergen, 1974), physiological arousal to straight and averted gaze in autism has not actually been measured.

Skin conductance response (SCR) refers to momentary changes in the electrical resistance of the skin reflecting the functioning of the sweat glands controlled by the sympathetic nervous system (Andreassi, 2000, pp. 193–196). Skin conductance responsiveness has been interpreted to be a sensitive method for collecting physiological data on the stimulus significance, novelty, and its' emotional content to the subject, and it is generally believed to be a reliable accompaniment of psychological processes such as attention and orienting reflex (Dawson, Schell, & Fillion, 1990). Skin conductance (phasic)

responses to sensory stimuli in children with autism have been mostly studied using auditory stimuli (van Engeland, 1984; Palkovitz & Wiesenfeld, 1980; Stevens & Gruzelier, 1984) and more rarely using both auditory and visual stimuli (Barry & James 1988; van Engeland, Roelofs, Verbaten, & Slangen, 1991; James & Barry, 1984). Studies with auditory stimuli have produced somewhat conflicting results. In van Engeland's (1984) study, children with autism were split into two subgroups: high and low general arousal. The children in the high general arousal subgroup had higher mean amplitude in skin conductance responses than normally developing children. In the studies by Barry and James (1988, see also James & Barry, 1984), the mean SCR to auditory stimuli was found to be higher in the group of children with autism than in the group of normally developing children. On the other hand, other studies have found no difference in responsiveness to auditory stimuli between children with autism and normally developing children (Palkovitz & Wiesenfeld, 1980; Stevens & Gruzelier, 1984) nor between children with autism and mentally retarded children (Stevens & Gruzelier, 1984). The mental age of the children had no effect on these results. In studies using visual stimuli (simple geometric figures), there has been some evidence showing that high functioning children with autism are hyporesponsive (van Engeland *et al.*, 1991), whereas mildly or moderately retarded children with autism are hyperresponsive to visual stimuli as compared to normally developing children (Barry & James 1988; James & Barry, 1984).

Only a few electrodermal studies have used socially meaningful stimuli. Palkovitz and Wiesenfeld (1980) used a spoken sentence as a stimulus and failed to differentiate between the children with autism and control children. However, the authors argued that their stimulus sentence ("listen to me") was more commonly used with the children with autism than with control children and, therefore the significance of the stimulus might not have been comparable in both groups. Blair (1999) had three socially meaningful visual stimulus categories in his study; distressing (e.g., a crying face), threatening (e.g., a pointed gun), and neutral (e.g., a book) images. When the responses were averaged across all the stimulus categories, the children with autism did not differ in their responsiveness from the normally developing children or from the children with moderate learning difficulty. However, in a further analysis, it was found that only in the group of children with autism did the children have greater skin

conductance responses to distress cues than to neutral stimuli, while there was no difference between responses to the threatening and neutral stimuli. Hirstein, Iversen, and Ramachandran (2001) studied relatively low-functioning children with autism and found that there was no difference in SCR between looking at their mother's face and looking at a paper cup. In a control group consisting of both children and adults, there were stronger SCRs to a face than to a cup.

In most of the previous studies, the general experimental procedure was quite simple. In studies using auditory stimuli, SCR was measured while the children heard sounds of different amplitude and frequency without any task, i.e., without a demand to respond in a certain way to different kinds of stimuli. In fact, the children were asked to ignore the tones they were hearing (van Engeland, 1984; Palkovitz & Wiesenfeld, 1980; Stevens & Gruzelier, 1984). In the studies using visual stimuli, children were usually asked to pay attention to the stimuli by either just encouraging to maintain their attention on the screen (Barry & James 1988; Blair, 1999; Hirstein *et al.*, 2001; James & Barry, 1984), by asking to fixate on the target stimulus, or by requiring the children to count the number of a certain type of stimuli (van Engeland *et al.*, 1991).

In the present study, skin conductance responses of high functioning children with autism and normally developing children were measured to face stimuli with straight gaze (eye contact) or averted gaze shown on a computer monitor. After the stimulus presentation, the children were asked whether the person looked straight at the child or whether the person's gaze was averted. Hence, in this study, the children were especially asked to pay attention to the stimuli. It was expected that if eye contact with another person is associated with an unusual degree of arousal in autism, perceiving another person with a straight gaze would elicit relatively stronger skin conductance responses in comparison to an averted gaze in children with autism than in normally developing children.

METHODS

Participants

Twelve school-aged children with autism took part in this study. All these children were clinically diagnosed to have an autism spectrum disorder. Additionally, the parents were administered the

Autism Diagnostic Interview -Revised (ADI-R; Lord, Rutter, & Le Couteur, 1994) and all the children met ADI algorithm criteria for autism. Table I shows the scores of the clinical group on the three domains of the ADI-R, communication domain (cutoff score for diagnosis of autism is 8), social domain (cutoff score 10), and stereotypy domain (cutoff score 3). Normal gender- and mental-age-matched control children were volunteers and had no history of mental or neurological disorders. The groups were individually matched for mental age (WISC-R). There were no significant differences between the clinical and control groups in chronological age, mental age, and performance IQ, but the normal controls had a higher verbal IQ, $t(22)=3.35$, $p \leq .003$, and full scale IQ, $t(22)=2.79$, $p \leq .01$, than the clinical group (see Table I). The children were the same as in our previous study investigating reflexive gaze-cued attention orienting (Kylliäinen & Hietanen, 2004).

Table I. Subject Characteristics

	Group	
	Clinical	Control
<i>N</i> (sex)	12 (11M, 1F)	12 (11M, 1F)
<i>CA</i> (years; months)		
Mean (<i>SD</i>)	9;11 (1;10)	8;11 (2;10)
Range	7;4–14;1	6;1–16;0
<i>MA</i> (years; months)		
Mean (<i>SD</i>)	9;3 (2;11)	9;5 (2;10)
Range	6;8–16;0	6;6–16;0
<i>Full IQ</i>		
Mean (<i>SD</i>)	91 (17)	106 (7)
Range	67–122	101–124
<i>Verbal IQ</i>		
Mean (<i>SD</i>)	90 (19)	109 (8)
Range	69–124	94–123
<i>Performance IQ</i>		
Mean (<i>SD</i>)	95 (16)	102 (7)
Range	67–117	95–118
<i>ADI-R Communication Domain</i>		
Mean (<i>SD</i>)	14.1 (3.1)	
Range	8–18	
<i>Social Domain</i>		
Mean (<i>SD</i>)	18.7 (4.5)	
Range	11–24	
<i>Stereotypy Domain</i>		
Mean (<i>SD</i>)	7.3 (2.5)	
Range	3–12	

M: male; F: female; CA: chronological age; MA: mental age; IQ: intelligence quotient; ADI-R: Autism Diagnostic Interview-Revised.

Stimuli

Frontal views of a female and a male face with a neutral expression were filmed with a video camera. The models were asked to maintain straight gaze or gaze averted to the left or right. By using the zoom of the camera, an impression was created in which the faces appeared to be looming towards the subject (see Fig. 1). Moving images, particularly those which are known to be arousing, are associated with an increase in the magnitude of skin conductance responses, and they improve the viewer's attention to stimuli (Detenber, Simons, & Bennett, 1998; Simons, Detenber, Roedema, & Reiss, 1999). As measured from the computer monitor, the inter-ocular distance of the stimulus face subtended 5° and 13° in the first and last frames of the film clip, respectively. The film clips had duration of 6 s. The facial stimuli were presented on a 20-inch computer monitor (1024×768, 75 Hz, Apple Multiple Scan Display).

Physiological Measurements

The electrodes were coated with electrode gel and attached to the palmar surface of the medial phalanges of the index and middle fingers on the children's left hand, which had been cleaned with an antiseptic liquid. Power Lab 400 equipment was used to measure the skin conductance. Data collection was controlled by Power Lab Chart v3.6 computer programme running on a Power Macintosh 7100/80 computer. The sampling rate was 100/s.

Design and Procedure

Children sat in a comfortable chair in front of a monitor at a distance of 70 cm. The cubicle was isolated with portable walls. The experimental procedure was carefully explained to the child with the aid of cartoon pictures showing the sequence of different events during the task. The children were asked to fixate in the middle of the screen and they were asked not to talk and to stay as still as possible.

In total, 12 face stimuli were presented in a random order, 6 faces with a straight gaze and 6 faces with an averted gaze. Half of the faces were female and the other half male. The inter-stimulus-interval (ISI) was 25–35 s. After the presentation of each face (during the ISI), the children were asked whether the person they had just seen had a straight or an averted gaze direction. This confirmed that the children had to look at the face on the monitor. The children's eye movements were also monitored using a

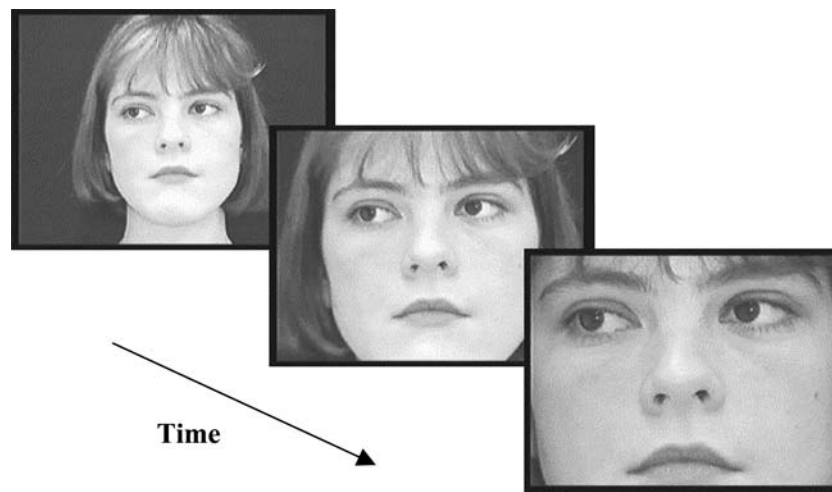


Fig. 1. By showing three separate pictures the figure illustrates the impression of a looming face which was created by using the zoom of the camera. The film clips had a duration of 6 s. Published with consent.

video-camera above the computer monitor. The children were rewarded with a token after the task completion. The experimental procedure lasted around 15–20 min.

Data Analysis

The experimental design included one within-subject variable: gaze direction (straight or averted) and one between-subject variable: group (clinical or control). The SCR was defined as the maximum amplitude change from baseline (defined at the stimulus onset) during a 5-s time window starting after 1 s from the stimulus onset till the end of the stimulus presentation. Responses contaminated by children's body movements or technical problems with the measurement were eliminated from subsequent analysis. Also, trials in which the child did not concentrate on the computer screen during the stimulus presentation were rejected. This evaluation was done by using the video tapes of the monitoring of the child's eyes. Because of all these reasons, 21% of trials were eliminated. There was no significant difference between the clinical subjects (24%) and controls (18%) in the mean percentages of the eliminated trials (Mann–Whitney, $U = 55$, n.s.). After this, the mean value of SCR was computed across all stimulus presentations in the category including those without a measurable response as a zero response. This method of calculation results in the *magnitude* of the galvanic skin conductance responses; a measure that combines response size and response frequency (cf., Dawson *et al.*, 1990). There was no significant

difference between the clinical and control group in the number of non-response trials (Mann–Whitney, $U = 59$, n.s.).

RESULTS

Regarding the behavioural data, there was no difference between the clinical subjects (97%) and controls (99%) in the mean percentages of correct responses to gaze direction (straight or averted) (Mann–Whitney, $U = 65$, n.s.). For physiological data, the normality of the distribution was tested and it showed that the data were not normally distributed (Kolmogorov–Smirnov, $D(48) = .140$, $p = .02$). Square root and logarithmic transformations, which are commonly used with positively skewed distributions (e.g., Clark-Carter, 1997), did not remove the skewness of the distribution. Thus, all further analyses were performed using non-parametric tests.

Figure 2 shows the mean skin conductance responses as a function of gaze direction and group. The overall mean (averaged across straight and averted gaze conditions) of the skin conductance responses in the clinical group (mean = $.29 \mu\text{Mho}$, $SD = .17$) was weaker than the mean responses in the control group (mean = $.51 \mu\text{Mho}$, $SD = .37$). However, this difference was not statistically significant (Mann–Whitney, $U = 48$, $p = .17$). The effect of gaze direction was tested separately in the clinical and control groups. Wilcoxon's signed ranks tests showed that the effect of gaze direction was significant in the

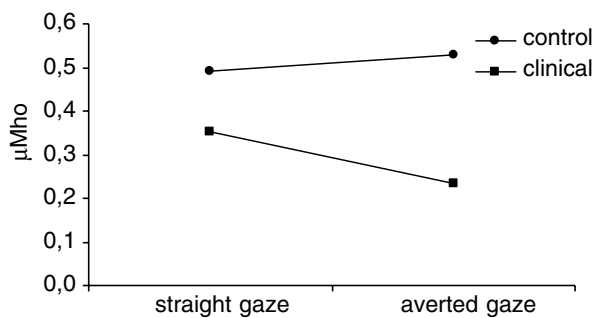


Fig. 2. Mean skin conductance responses as a function of gaze direction and group.

group of autistic subjects, $T=11$, $p=.028$; the responses were stronger to straight gaze (mean = .35- μ Mho, $SD=.22$) than to averted gaze (mean = .24- μ Mho, $SD=.14$). However, in the control group, there was no difference in the responses between straight gaze (mean = .49 μ Mho, $SD=.41$) and averted gaze (mean = .53 μ Mho, $SD=.32$) conditions, $T=31$, $p=.86$.

In order to analyse whether the skin conductance responses were affected by the children's intelligence, correlations between SCRs and verbal, performance, and full scale IQs were performed. There was no significant correlation between SCRs and any of the intelligence measures either in the clinical group or in the control group.

DISCUSSION

Skin conductance responses (SCR) to another person's gaze direction (straight and averted gaze) were measured in children with autism and in normally developing children. First, the present results showed that, although the overall SCR level seemed to be lower in the group of children with autism than in the control group, the difference was not statistically significant. This finding is in line with Blair's (1999) study in which the children with autism were only marginally ($p=.062$) hypo-responsive to meaningful visual stimulus categories (i.e., to neutral as well as to distressing and threatening stimuli) as compared to normally developing children. Secondly, and more importantly, in normally developing children, there was no difference in SCR between straight gaze (eye contact) and averted gaze conditions, whereas in children with autism the responses to straight gaze were stronger than those to averted gaze. In the following, we will separately discuss the

findings related to the SCR to gaze direction in the normally developing children and in children with autism.

The results of this study revealed that there was no significant difference in SCR between eye contact and averted gaze in the normally developing children. In some previous studies with healthy adults, eye contact produced greater electrodermal activity than unreciprocated gaze (McBride, King, & James, 1965; Nicholas & Champness, 1971). In other studies, however, such a difference has not been found (Donovan & Leavitt, 1980; Leavitt & Donovan, 1979). In the early study by Nicholas and Champness (1971) with reasonable control of the stimulus conditions, the procedure, however, differed in two important ways from the present procedure. First, in the study by Nicholas and Champness, the stimulus person was actually sitting in the front of the subject, whereas in the current study computerised stimuli were used. Second, Nicholas and Champness collected data for alternating 10-s periods when the eye contact was held and when the eye contact was released. A period of released eye contact is not entirely comparable with the condition of averted gaze in the present study. This possible explanation for the differences between the results of the earlier studies and the present one is also supported by other previous studies. In their study with adults, Donovan and Leavitt (1980) found only a marginal difference in SCR between eye contact and averted head conditions and, in another study, they (Leavitt & Donovan, 1979) found no difference in SCR of mothers who were shown gazing and non-gazing infants. The data were collected, in both studies, during presentations of static computerised images separated by 25–45-ms long inter-stimulus-intervals.

As expected the pattern of SCR results was different in the children with autism than in normally developing children. In children with autism, the SCR was stronger to straight than to averted gaze suggesting, thus, that, in these children, a stronger level of arousal may be triggered by eye contact than by averted gaze. It has long been argued, without actually measuring physiological responses to gaze direction, that individuals with autism avoid eye contact with others in order to reduce their physiological arousal (Hutt & Ounsted, 1966; Tinbergen, 1974). Thus, the present data seem to fit with this suggestion. Recent studies using accurate measurements of eye movements have also provided evidence for that individuals with autism tend to look more at the mouth than eye region of the face, whereas the

eye region is more commonly the focus of fixation in the normal face scanning (Klin *et al.*, 2002; Pelphrey *et al.*, 2002). Because, in the present study, the children were asked to answer to the question of where the person on the screen was looking at, they had to look at the eye region of the stimulus faces. This fact together with the special feature of the stimulus presentation (looming faces) might have contributed to the finding of stronger physiological responses to straight gaze (eye contact) than averted gaze in children with autism.

The higher arousal to eye contact than averted gaze in autism may reflect the interpretation of another person's direct gaze as a hostile signal or a signal expressing intimacy at a level which is experienced uncomfortable. In early infancy, the eye contact with a primary caregiver is very important in establishing affection bond between the child and a caregiver. This early gaze behaviour is not only for regulating social interaction but is thought to be also one of the precursors for later social development (Jaffe, Stern, & Perry, 1973). Thus, if the enhanced physiological arousal to eye contact is reflecting the fact that eye contact is experienced as uncomfortable in individuals with autism it is not surprising that eye contact is avoided. Followingly, this may contribute to the development of disturbances in social behaviour from very early on.

So far, the present results have been interpreted in light of giving support to our hypothesis that straight gaze elicits stronger SCR than averted gaze in children with autism in comparison to normally developing children. However, one could also argue our results showing that averted gaze elicited unusual low level of physiological arousal in the children with autism. In fact, further analyses of the results showed no significant difference in SCR in the straight gaze condition between the groups (Mann-Whitney, $U=62$, n.s.), whereas a significant difference was found in SCR between the groups in the averted gaze condition (Mann-Whitney, $U=36$, $p=.039$). The comparison between the groups is, however, very problematic. Although, in the present study, the overall SCR level was not statistically significant between the clinical and control groups, high functioning children with autism have been shown to exhibit generally lower responses to visual stimuli as compared to normally developing children (van Engeland *et al.*, 1991). Therefore, one should be cautious in interpreting between-group differences. In order to answer to the question of whether the differential SRC to straight and averted gaze in

children with autism reflected enhanced responses to eye contact or attenuated responses to gaze aversion, our design would have necessitated a control stimulus. However, the choice of an appropriate control stimulus is not that straightforward. The experimental and control stimuli should be identical with respect to all stimulus features except that under investigation, i.e., the direction of gaze in this case (cf., Jonides & Mack, 1984, p. 31). Thus, one possible control stimulus to be used in a present type of a study would be a face with eyes closed. If the results of an experiment including such a control stimulus showed that (a) the SCRs to straight, averted, and closed eyes are indistinguishable in the group of control children, and (b) that, in the group of children with autism, SCRs to the control stimulus are at the level of responses either to straight gaze or averted gaze (or between them), it would be relatively straightforward to answer to the question of whether straight gaze produced enhanced responses or whether averted gaze produced attenuated responses (or both). However, if such an experiment showed a different pattern of results, it would lead to reasoning of whether a face with closed eyes was, after all, an appropriate control stimulus.

For the present time, regardless of the line of interpretation, the present results *did* show that eye gaze elicited differential pattern of SCR in normally developing children and in children with autism. It is obvious that the question of enhanced physiological arousal to eye contact (cf., Hutt & Ounsted, 1966; Tinbergen, 1974) in autism must be revisited by other studies using well-controlled experimental design and measurements. Meanwhile, the present study can be regarded as an opening on this interesting line of research.

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Face and gaze processing in normally developing children: a magnetoencephalographic study

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Abstract

Magnetoencephalography (MEG) was used to study the neural mechanisms underlying face and gaze processing in ten normally developing boys aged between 8 and 11 years and 12 adult males. The participants performed two tasks in which they had to decide whether images presented sequentially in pairs, depicted the same person or the same motorbike. In the first task, the participants saw pictures of faces in which the eyes were either open or shut and pictures of motorbikes. In the second task, participants saw pairs of faces with gaze averted to the left or right. In children there was no evidence of the face sensitive, low amplitude short latency (30–60 ms) activity seen previously in adults. A strong, midline posterior response at approximately 100 ms was observed in children, which was earlier and somewhat stronger to faces than to motorbikes; in adults the signal at this latency was weak. A clear face sensitive response was seen in adults at 135 ms, predominantly over the right inferior occipito-temporal regions. Although activity was observed in the children at the same latency, it was less prominent, not lateralized and was evoked similarly by faces and motorbikes. Averted gaze conditions evoked strong right-lateralized activity at approximately 245 ms in children only. These findings indicate that even in middle childhood the neural mechanisms underlying face processing are less specialized than in adults, with greater early activation of posterior occipital cortices and less specific activation of ventral occipito-temporal cortex.

Introduction

Adult expertise in processing human faces has been demonstrated in many behavioural studies (e.g. Bruce, 1988). The first evidence that some neural structures might be specialized for processing faces came from patients who were selectively unable to recognize familiar faces after acquired neurological lesions (reviewed in Farah, 1995). Further support for neural specificity came from the single cell recordings in non-human primates that identified neurons in the temporal cortex that responded specifically to faces (e.g. Desimone, 1991; Perrett *et al.*, 1992). More recently, neuroimaging (fMRI and PET) studies in human adults (e.g. Haxby *et al.*, 1994; Clark *et al.*, 1996; Kanwisher *et al.*, 1997; McCarthy *et al.*, 1997) have shown that regions of the ventral occipito-temporal cortex are activated selectively by faces, especially the lateral fusiform gyrus and predominantly in the right hemisphere.

Electrophysiological studies using scalp electrodes (e.g. Bentin *et al.*, 1996; George *et al.*, 1996), depth electrodes (e.g. Allison *et al.*, 1999; McCarthy *et al.*, 1999) and whole-head magnetoencephalography (e.g. Sams *et al.*, 1997; Swithenby *et al.*, 1998; Taylor *et al.*, 2001a; Bailey *et al.*, 2005; Xu *et al.*, 2005) have detected a face sensitive response peaking approximately 140–200 ms after stimulus onset, most prominently over the right inferior occipito-temporal cortex. Although this response is commonly referred to as the N170 (or M170 in MEG), there are considerable variations in peak latency

across studies, which themselves sample different neural sources. Face specific responses have also been identified before the N170 response, particularly at approximately 100 ms after stimulus onset (Debruille *et al.*, 1998; Linkenkaer-Hansen *et al.*, 1998; Halgren *et al.*, 2000; Taylor *et al.*, 2001b; Itier & Taylor, 2002; Liu *et al.*, 2002). The response at approximately 100 ms has been related to categorization of the image as a face rather than identification of an individual face, which is presumed to occur at a later stage of processing (Liu *et al.*, 2002). Furthermore, both event-related potential (ERP; Seeck *et al.*, 1997) and magnetoencephalographic (Braeutigam *et al.*, 2001) studies in adults suggest that low amplitude face-specific activity can be detected as early as 30–60 ms after stimulus onset. This short latency response is seen most clearly during sequential matching tasks, precedes the activation of primary visual cortex and involves activation of the right anterior temporal and right occipito-temporal cortices (Braeutigam *et al.*, 2001).

The development of expertise in face processing is still rather poorly understood. An adult level of face expertise is achieved relatively late in development, with performance still improving during adolescence (reviewed in Chung & Thomson, 1995; Want *et al.*, 2003). This long developmental trajectory is of some interest, considering that newborn infants show a preference for face-like patterns compared with other stimuli (reviewed in Maurer, 1985), that there is significant development in the ability to process faces during the first year of life (Johnson & Morton, 1991; Corkum & Moore, 1998; de Haan & Nelson, 1998), and that adequate visual input during the first year of life seems to be critical for the subsequent acquisition of normal face processing expertise (Geldart *et al.*, 2002).

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Most neural studies of the development of face processing expertise have used electrophysiological methods. Face sensitive ERP-responses have been identified in both infants and children, but the latencies of the responses are longer than the N170-response observed in adults (e.g. Bentin *et al.*, 1996; George *et al.*, 1996). Bilateral face sensitive responses have been reported in infants from 3 to 12 months old at latencies of 290 ms and 400 ms after stimulus onset (e.g. de Haan *et al.*, 2002; Halit *et al.*, 2003). In children, Taylor *et al.* (1999) observed face-sensitive responses at a latency of approximately 190–270 ms; these were faster and right lateralized in the older children. Thus, these developmental studies raise the question of whether during development the neural basis of face processing simply speeds up. On the other hand, ERP data have also been used to argue that there are more fundamental developmental changes in the neural mechanisms underlying face processing (cf. Halit *et al.*, 2003). This proposal is in keeping with imaging findings suggesting relatively late development of hemispheric specialization for face processing and a more distributed pattern of activation in children than adults (Passarotti *et al.*, 2003).

One possible developmental change in the brain mechanisms underlying face processing is in the neural resources devoted to processing the eyes. Infants' preference for face-like stimuli is claimed to relate largely to the presence of the eyes (cf. Johnson & Farroni, 2003). Infants prefer faces with eyes open (Batki *et al.*, 2000) and with straight gaze (Hains & Muir, 1996; Caron *et al.*, 1997; Farroni *et al.*, 2002), and in 4-month-old infants the 240 ms ERP response is stronger to straight than to averted gaze (Farroni *et al.*, 2002). Also, in children the evoked responses to an eyes-only stimulus are stronger and of shorter latency than the response to a whole face (Taylor *et al.*, 2001b). These findings in children apparently parallel the observation in adults that gaze direction modulates activation of the face sensitive fusiform area (Bentin *et al.*, 1996; George *et al.*, 2001; Taylor *et al.*, 2001a).

The aims of this study were to investigate the neural basis of face and gaze processing in children using whole head magnetoencephalography (MEG; e.g. Hämäläinen *et al.*, 1993) in order to establish: (i) whether we could replicate previous observations of delayed ERP responses to faces in middle childhood compared to adults; (ii) whether there is any evidence for qualitative changes in the neural basis of face processing between childhood and adulthood, particularly with respect to the processing of the eyes, and (iii) whether the short latency face processing pathways observed in adults are also identifiable in children and, if so, whether these are particularly sensitive to the eyes.

Materials and methods

Participants

Ten normally developing children and 12 healthy men took part in this study. The children ranged in age from 7 years and 10 months to 10 years and 11 months (mean \pm SD, 9.1 ± 1.1 years). They were an age and IQ matched control group for children with autism recruited for a study reported elsewhere. The mean age of the adults was 30.5 years (SD, 8.0 years). No participant had any known neurological or psychiatric disorder. All participants had normal or corrected-to-normal vision and were right-handed. The children, their parents and adult participants gave informed consent (Helsinki Declaration) before experimentation.

Stimuli

The participants viewed static, grey-scale images of faces of Finnish adolescent boys (without eye glasses, facial hair or ear rings) and

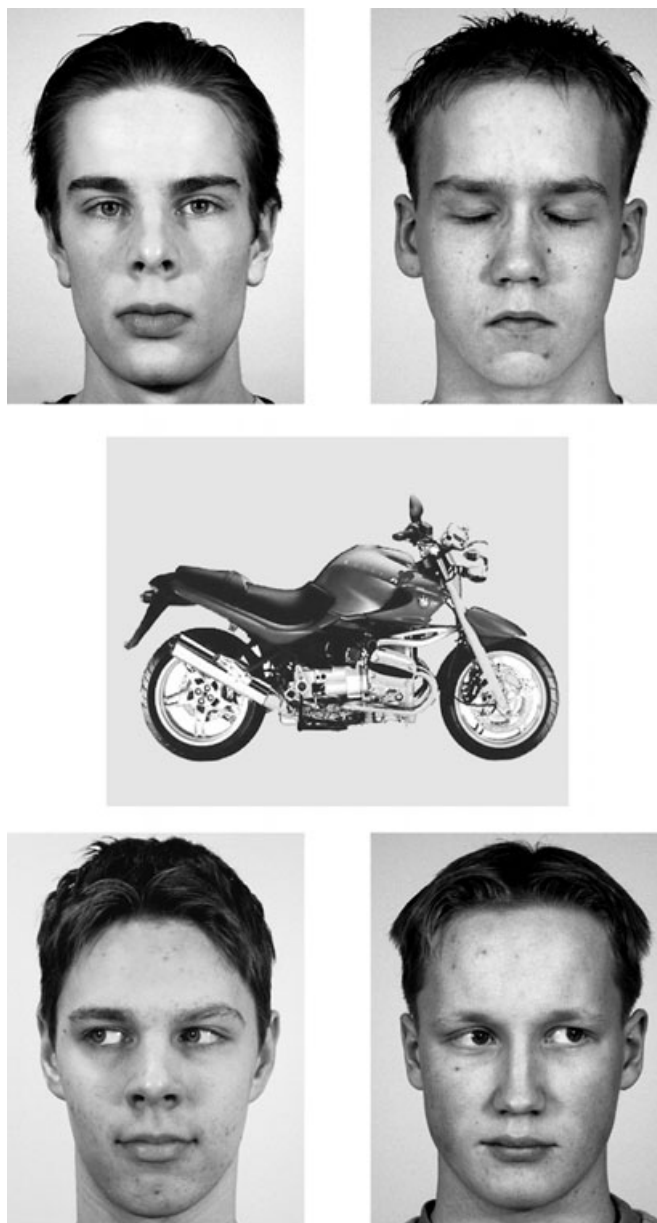


FIG. 1. The visual stimulus categories used in task 1 (eyes open, eyes shut, and motorbikes) and in task 2 (eyes left and eyes right).

images of motorbikes (all motorbikes pointed to the left) (see Fig. 1). Motorbikes were chosen as a complex comparison stimulus likely to be of interest to boys. Moreover, motorbikes have some symmetry, are rich in details and have spatial frequencies similar to faces (see e.g. Swithenby *et al.*, 1998). The images were projected onto a screen placed 90 cm in front of participants' eyes whilst they sat under the MEG-helmet. The images were standardized for luminosity (42 ± 8 cd/m²) and size (subtended $10^\circ \times 8^\circ$ at the eye). Each image was displayed for 200 ms, based on a pilot study with children.

Design and procedure

The participants performed two matching tasks that required attention to be paid to the face and allowed identification of previously reported

(Swithenby *et al.*, 1998) priming effects for faces as well as rapid pathways for face processing (Braeutigam *et al.*, 2001).

Both tasks involved sequential presentation of pairs of images of the same type. The second image followed the first after a delay of 1000 ± 100 ms. Participants were asked to respond by pressing a key under the right index finger if the second image was a repetition of the first image and a key under the middle finger if it was different. The overlap between the neural activity associated with processing of the face and the subsequent motor response was minimized by cueing the key press with a visual prompt, consisting of a hand in which the response fingers (buttons) were marked with different colours. The visual prompt followed 1400 ± 100 ms after the second image and was displayed for 400 ms. A red fixation point was displayed during the interstimulus-interval (ISI) of 1600 ± 200 ms. An optical-fibre feedback system was used to measure the delay from the computer trigger to stimulus presentation (32 ms for this study). All the latencies reported below have been corrected for this delay and refer to the exact time of stimulus presentation.

In Task 1, the image pairs comprised adolescent boys with either straight gaze (50 image pairs) or eyes shut (50 image pairs) and pairs of motorbikes viewed in profile (50 image pairs). In half of the trials the second image was a repetition of the first image and in half of the trials it was different. The task was completed in two runs with balanced content. On average each run lasted 6 min and 10 s (including 10 s of baseline data).

In Task 2, the procedure was exactly the same as in Task 1. Participants viewed pairs of images of adolescent boys' faces, in which the eyes were directed either to the left (50 image pairs) or the right (50 image pairs). In this task, direction of gaze was always the same within a pair of images but the identities of the individuals were different in half of the image pairs. The boys were the same as those seen in Task 1. The task was completed in two runs and on average each run lasted 4 min and 10 s (including 10 s baseline data).

During each experiment a progress bar was displayed for a few seconds after blocks of 20–25 trials. This was designed to help participants judge how much longer the experimental run would last. After each run the children were rewarded with a token (a plastic toy animal) that they had selected before the experiment. During the measurements a researcher sat on each side of the participant.

Data acquisition

All measurements were performed using a VectorviewTM neuro-magnetometer in the Brain Research Unit of the Low Temperature Laboratory, Helsinki University of Technology. The system comprises a helmet-shaped array of 102 pairs of orthogonal, first-order planar gradiometers. The outputs of each pair of sensors are most sensitive to the tangential current flow in the region directly below the detectors. The sum of the local root-mean-square (rms) signal from each sensor pair is a measure of current strength.

The data were sampled at 600 Hz (0.01–200 Hz anti-alias filter). Artefacts were identified by recording the electrooculogram (EOG) and the electrocardiogram (ECG). Foam inlays were used with the children to compensate for the slightly oversized helmet and head movement was monitored by measuring head position before and after each experimental run. If necessary, head position was adjusted between runs to maintain an overall position accuracy of ± 5 mm across runs for each child. Individual pre-auricular-nasion (PAN) coordinates were co-registered with the device system in order to verify that all the children's heads had the same relative position with respect to the helmet. No participant had dental braces or other metal implants.

Time-series analysis

For each participant, average evoked responses based on all runs were calculated for latencies from 0 to 800 ms after stimulus onset according to task condition, stimulus type and image position within a pair. An unreported analysis did not reveal differences when further subdividing the data according to second-same vs. second-different images. Thus the data were pooled for statistical robustness, yielding ten types of evoked responses (straight gaze, closed, left, right, motorbikes; first and second image for each stimulus category). Prior to further analysis, average signals were filtered between 0.2 and 30 Hz (roll-off 0.5 Hz), and normalized to the signal variance within a baseline interval of 0–200 ms before stimulus display.

Significant differences between evoked responses were sought using a previously described time-dependent measure $P(t)$ (Braeutigam *et al.*, 2001). This method is conceptually similar to techniques of analysing event-related potentials by comparing evoked peak amplitudes across participants. The measure takes into account the data from all detectors and does not require *a-priori* identification of peaks in the evoked responses.

$$P(t) = \text{probability}(\chi^2), \text{ where } \chi^2 = -2 \sum_{i=1}^N \ln[n_i(t)]$$

where N denotes the number of channels. For each channel, $n_i(t)$ is an appropriately chosen local, non-parametric measure of the significance of the differences between matched evoked responses across participants within a participant group. Restricting the analysis to matched samples yields a robust measure in sensor space, where absolute amplitudes may be influenced by non-physiological factors, such as head-to-detector distance. Then, $P(t)$ describes significance across the entire helmet of the channel differences (as a function of time). In this study, intervals with $P(t) < 0.01$ were considered significant, where n_i denotes a Friedman analysis of variance (f_i) used to compare the responses to the five types of stimuli in Tasks 1 and 2 (separately for first and second images). A Wilcoxon *posthoc* test (w_i) was employed for pair-wise comparisons when $P(t)$ indicated significant variation. In the case of comparisons between responses to first and second images, n_i denotes a Wilcoxon test (w_i) applied to images of the same type. For each such interval with $P(t) < 0.01$, the set of all values n_i (Friedman and/or Wilcoxon) provided the spatial distribution of significance of the differences between evoked responses. Those distributions were used to identify significant regions at the group level, as well as individually. For each identified significant latency, spatial maps of local rms-signals (amplitude maps) as a measure of neuronal activity were calculated. In this study only a relatively small number of statistical comparisons (out of all possible combinations) were made, using strictly matched data sets.

Source estimation

Equivalent current dipole (ECD) estimation was performed using CurryTM software, utilizing a homogeneous sphere as the volume conductor. The sphere was centred on the base of the perpendicular from the nasion to the line joining the pre-auricular points (PAN head co-ordinate system) for each participant. An ECD was calculated for each individual and each time slice for first images in both tasks. A fitted ECD was considered acceptable if: the goodness-of-fit parameter was greater than 0.7, the located position was stable to within 5 mm in each co-ordinate over at least three consecutive time slices, and the confidence volume did not exceed 1 cm^3 .

A note on data analysis

This study used a MEG helmet constructed for average adult head size, i.e. the helmet was suboptimal for studying children. Although every effort was made to achieve the same alignment in the helmet of all children's heads, some effects outside experimental control had to be allowed for. Consequently, the analysis emphasized non-parametric statistics applied to signals from individual channels. A relatively large array of detectors (approximately one-half of all channels over the posterior parts of both hemispheres) was used for source estimation. The large array results in a lower goodness-of-fit compared with other studies, which typically have used only a small subset of channels, but the stability and confidence criteria used ensure that the detected differences in source locations are reliable.

Results

All 12 adult males completed both runs of Tasks 1 and 2. Task performance was very high for faces ($96 \pm 1\%$ standard error of mean in Task 1 and $93 \pm 2\%$ in Task 2) and motorbikes ($92 \pm 1\%$). The 4% difference between face and motorbikes in Task 1 was statistically significant ($P < 0.001$). Eight out of ten children completed both runs of Tasks 1 and 2; two children did not perform Task 2 because of technical problems. Overall accuracies for the children were: $94 \pm 1\%$ (faces in Task 1); $86 \pm 1\%$ (motorbikes in Task 1) and $95 \pm 1\%$ (faces in Task 2). The difference between performance accuracy for faces and motorbikes in Task 1 was statistically significant ($P < 0.006$). In children, premature (before the prompt) key presses occurred in 5% of all trials (14% in one child), but these were all relatively late after stimulus onset (1270 ± 20 ms) and did not interfere with analysis of the MEG data. In both adults and children a small number of epochs ($< 0.8\%$) had to be excluded from MEG analysis due to eye blink or other artefacts.

The results of the MEG analysis are reported in the remainder of this section, beginning with an overview of the findings in both groups of participants followed by a detailed description of the MEG data from the children. For ease of presentation, the data are shown as grand-mean evoked responses. Nevertheless, all reported effects were identifiable at the individual level in at least six out of ten children and eight out of 12 adults (see Fig. 4 for illustrative traces). All differential effects were identified using the measure $P(t)$ and the criterion $P(t) < 0.01$.

Evoked signals in adults

In adults, the first peak of evoked activity following first face images was observed over occipital regions at approximately 90 ms after stimulus onset (Fig. 2; note that all rms-signal peaks are shown as positive, irrespective of the polarity of the underlying evoked responses). These responses were highly variable across participants, tasks and stimuli, without any observable pattern beyond the occipital location. The preceding (30–60 ms), low amplitude neuronal activity observed in these adults (not visible in Fig. 2 due to scaling) is consistent with the stimulus and/or task specific activity reported previously (Seeck *et al.*, 1997; Braeutigam *et al.*, 2001; Bailey *et al.*, 2005). A detailed analysis of these responses is not reported here. Strong evoked activity was next observed at approximately 135 ms after stimulus onset, strongly lateralized over the right inferior occipito-temporal regions and accompanied by weaker signals over the left inferior occipito-temporal and right anterior temporal areas. The right-lateralized evoked responses were stronger for first face

images than for first motorbike images [$P(t) < 0.01$], but there was no difference in latency between the two types of response. The data from Tasks 1 and 2 showed that these responses were independent of gaze condition (straight ahead, eyes shut, or averted). The amplitudes of the right-lateralized responses approximately 135 ms were significantly reduced for the second compared with the first images across all stimulus categories in both tasks [$P(t) < 0.01$ between 130 and 145 ms; see Fig. 4 bottom for individual traces].

Between 180 and 240 ms after stimulus onset, evoked responses were observed over bilateral occipito-temporal, posterior parietal and prefrontal cortical regions. These responses varied across participants and appeared to be independent of stimulus type and task condition. At approximately 280 ms, a highly localized response over occipital cortices followed both first and second faces, but not motorbike images. At approximately 320 ms [$P(t) < 0.01$ between 310 and 335 (ms)], an evoked response seen over occipital cortices was stronger for second than for first images, independent of image type.

Evoked signals in children

First faces (eyes straight) evoked a complex sequence of field patterns in all children (see Fig. 2 for amplitude maps for Task 1 first face image data). Typically, the first maximum of activity was evoked in posterior regions at approximately 60 ms after stimulus onset. This short latency activity was stronger and more localized than that observed in adults at a similar latency and was present in response to all stimuli. The short latency response was followed by a very strong maximum at 100 ms, localized predominately over posterior regions, in contrast with the much weaker response seen in adults. Subsequently, relatively weak evoked responses were identified at approximately 135, 195, and 295 ms after stimulus onset. These later responses were widespread, with activity observed to varying degrees over inferior occipito-temporal, parietal, temporal, and prefrontal brain regions. At approximately 135 ms, the weak bilateral responses detected over occipito-temporal cortex contrasted with the strong right lateralized response observed in adults (Fig. 2). At latencies up to approximately 400 ms, relatively weak evoked responses were also observed over occipital regions. In the children, all stimuli elicited widespread responses between approximately 450 and 750 ms (data not shown) that were not seen in the adults; these late responses were too varied across participants for a meaningful analysis. In what follows, the responses in children are described in more detail, ordered by task and latency.

Task 1 in children

The evoked responses at 60 ms did not depend on either image type or image position within a pair. At 100 ms the responses were the same for the two types of first faces (eyes straight and closed), but non-significantly weaker and significantly later ($P < 0.01$) by approximately 10 ms for first motorbikes. At 100 ms (110 ms for motorbikes), second images elicited lower signal amplitudes than first images, but the differences were only significant for faces with closed eyes [$P(t) < 0.01$ between 95 and 115 (ms)]. Signal topographies elicited by motorbikes were broadly similar to those evoked by faces but, from 100 ms onwards, all responses evoked by bikes were delayed by 10–30 ms compared with those evoked by faces (Fig. 3).

At 130 ms to 140 ms after stimulus onset, the evoked responses were bilateral. As in adults, there was a response over the right inferior occipito-temporal cortices detectable for the three image types

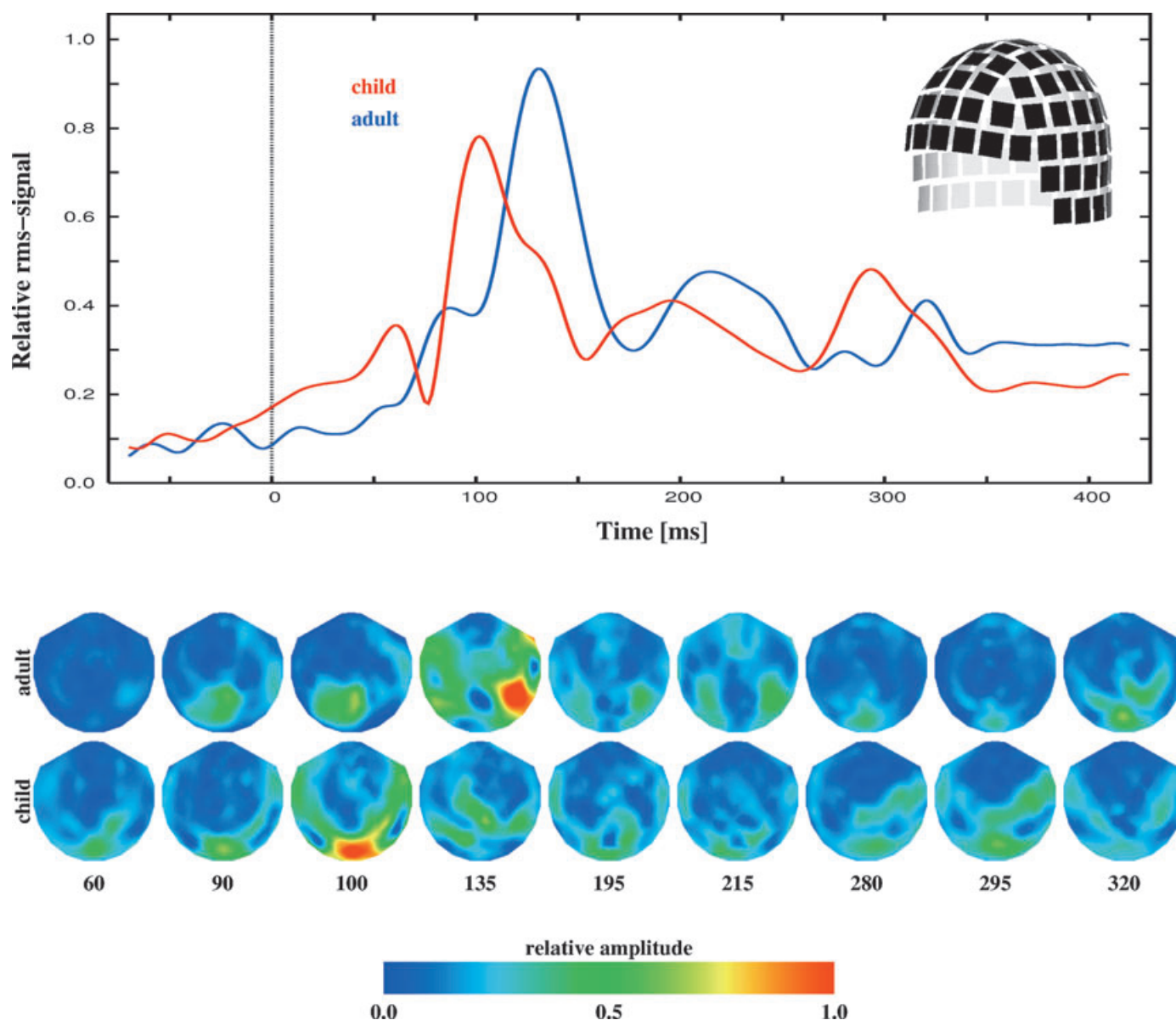


FIG. 2. (Top) Grand root-mean-square (rms) signals following first face (eyes straight) images in Task 1. The curves have been obtained by summation over all participants within a participant group (blue, adult; red, child; stimulus onset at 0) and channels. The inset shows the helmet shaped array of detectors used to record neural responses to static images. Each black plate represents two first-order gradiometers (channels) measuring two orthogonal spatial gradients of the magnetic field. These are most sensitive to the tangential neuronal currents in the region below the detectors. (Bottom) Spatial distribution of local rms-signals to first faces in Task 1. The maps have been obtained by summation over all participants (upper row, adult; lower row, child) and the two detectors at each site. For presentation of data, the detectors have been projected into two dimensions (right ear on the right, front at the top). The maps show neuronal activity at selected latencies between 60 and 320 ms after stimulus onset, corresponding to peaks in either of the rms-signals above. In general, responses in adults and children are similar in terms of absolute signal strength, but very dissimilar in terms of signal topography. In this and the following figures, all global rms curves were normalized to 3.5 fT/cm. Local rms maps were normalized to 7 fT/cm in this figure, and to 5 fT/cm in the following figures.

(straight eyes, closed eyes, and motorbikes; see Fig. 4, top-left). The response was later for motorbikes but, unlike in adults, of similar amplitude for faces and motorbikes. There were no significant differences between the responses following first or second images, although the former were stronger for straight eyes and motorbike stimuli (this effect does not hold in the case of closed-eye stimuli). Individual peaks in the waveforms at approximately 130 ms were identified in eight children showing amplitude reduction for second images over right inferior occipito-temporal cortices (illustrative traces are shown in Fig. 4, bottom). In these eight children, responses to first and second face images (eyes straight) peaked at 128 ± 1.3 ms and

123 ± 1.4 ms, respectively (difference not significant). There was no evidence that peak latency was negatively correlated with age ($P = +0.18$, not significant).

Task 2 in children

In Task 2, the short latency activity elicited by faces with averted gaze was very similar to the activity evoked by the face images in Task 1 (Fig. 4, top). There was some evidence for decreased signal power for second images: at 100 ms first left gaze images evoked

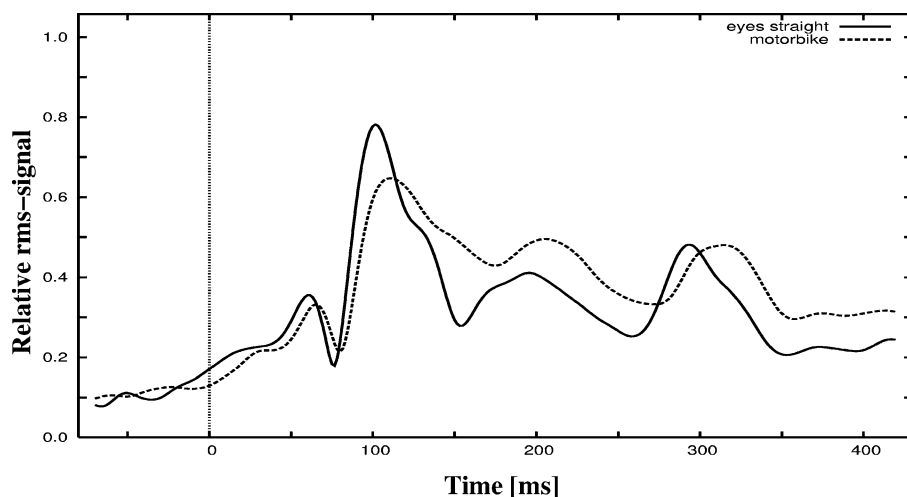


FIG. 3. Children's grand rms-signals following first face (eyes straight) and motorbike images in Task 1. The responses evoked by face and motorbike images are broadly similar in terms of signal amplitude and topography. For latencies longer than approximately 100 ms, responses elicited by motorbikes are delayed by 10–30 ms compared to faces.

insignificantly stronger activity than second left gaze and at 135 ms the weak right inferior occipito-temporal responses were insignificantly stronger for the first compared to the second images in both gaze categories (see also Fig. 4, top-right). In contrast to these similarities between the data from the two tasks, averted gaze images (both left and right) evoked a response in children over right inferior occipito-temporal regions between 245 and 260 ms (Fig. 5, bottom) that was weak or absent for straight eyes, eyes closed and motorbikes in Task 1; this response was not seen in the adults.

Source localization in children

At 60 and 100 ms robust ECD sources were identified in seven children for each type of first image. The ECD analysis did not reveal differences in either latency or strength between the generators of the 60- and 100-ms responses evoked by faces and motorbikes, or between the generators of the 100-ms responses evoked by the two types of face images in Task 2. A paired comparison of ECD sources showed that the generators of the 60-ms response were located consistently anterior and superior to the generators of the 100-ms response (Table 1). All ECD sources located consistently within the posterior, midline regions of the individual heads, regardless of image type. The number of robust dipole source obtained for signals at 135 ms in children was too low for statistical analysis.

Discussion

Face and gaze processing were studied using magnetoencephalography (MEG) in boys aged between eight and 11 years and in adult males. In children and adults behavioural performance was significantly better for faces than for motorbikes, in line with previous behavioural findings (see e.g. Bruce, 1988; Chung & Thomson, 1995). Moreover the behavioural performance of both groups was indistinguishable for faces. The adult MEG data were broadly consistent with previous electrophysiological studies (e.g. Bentin *et al.*, 1996; Swithenby *et al.*, 1998), in which prominent responses are observed in the latency range 140–200 ms over right extrastriate cortices that are strongest for faces. In the present data, the prominent peaks occur slightly earlier than the latency range reported in the literature. We assume, however, that the right lateralized response at approximately 135 ms in adults corresponds to what is commonly labelled the N170/M170, as signal topography, face-

specificity of signal amplitudes (here compared to motorbikes), and amplitude reduction upon repetition (second images) match previous observations.

Despite the similar behavioural performance of the children and adults, the evoked responses in children showed little if any similarities with the adult waveforms. Firstly, in children the responses at short latency (< 60 ms) were relatively strong, localized and, in contrast to the findings in adults, did not reveal any sensitivity to either task or stimulus type (cf. Seeck *et al.*, 1997; Braeutigam *et al.*, 2001; Bailey *et al.*, 2005). Secondly, the 100 ms midline posterior signal was much more prominent in children in response to all image categories than in adults and of shorter latency for faces than motorbikes. Thirdly, the latency of extrastriate responses at approximately 135 ms in children matched closely those observed in adults, but in children these responses were not lateralized and were not significantly sensitive to faces in terms of signal strength. Finally, the averted gaze condition evoked strong right lateralized activity at approximately 245 ms in children; this response was not evident in adults.

In children the strong evoked response at approximately 100 ms was of shorter latency for faces than motorbikes. There was also some evidence of larger responses to first than second images and this effect was greater for faces than bikes. These findings suggest that the underlying neural network is to some extent already specialized for dealing with faces. Conceivably the putative face sensitive response reflects rather inefficient processing in the visual cortex of children, as the relatively high signal strength implies coherent activation of a larger number of neurons and/or synapses. These MEG data are in line with the findings from previous neurophysiological studies of children (Taylor *et al.*, 2001b) and adults (Debruille *et al.*, 1998; Linkenkaer-Hansen *et al.*, 1998; Halgren *et al.*, 2000; Itier & Taylor, 2002; Liu *et al.*, 2002), which suggest that activation at approximately 100 ms distinguishes between faces and control stimuli. It is unlikely that the response at 100 ms simply reflects the processing of low-level features of visual stimuli, because in adults the latency and the amplitude of this response is increased for inverted compared with upright faces in both EEG (Itier & Taylor, 2002; Linkenkaer-Hansen *et al.*, 1998) and MEG studies (Linkenkaer-Hansen *et al.*, 1998). Furthermore, Liu *et al.* (2002) found that the MEG response at 100 ms was stronger when a face was correctly perceived as a face, compared to when the stimulus was wrongly categorized as a non-face, indicating some categorization of faces at this latency.

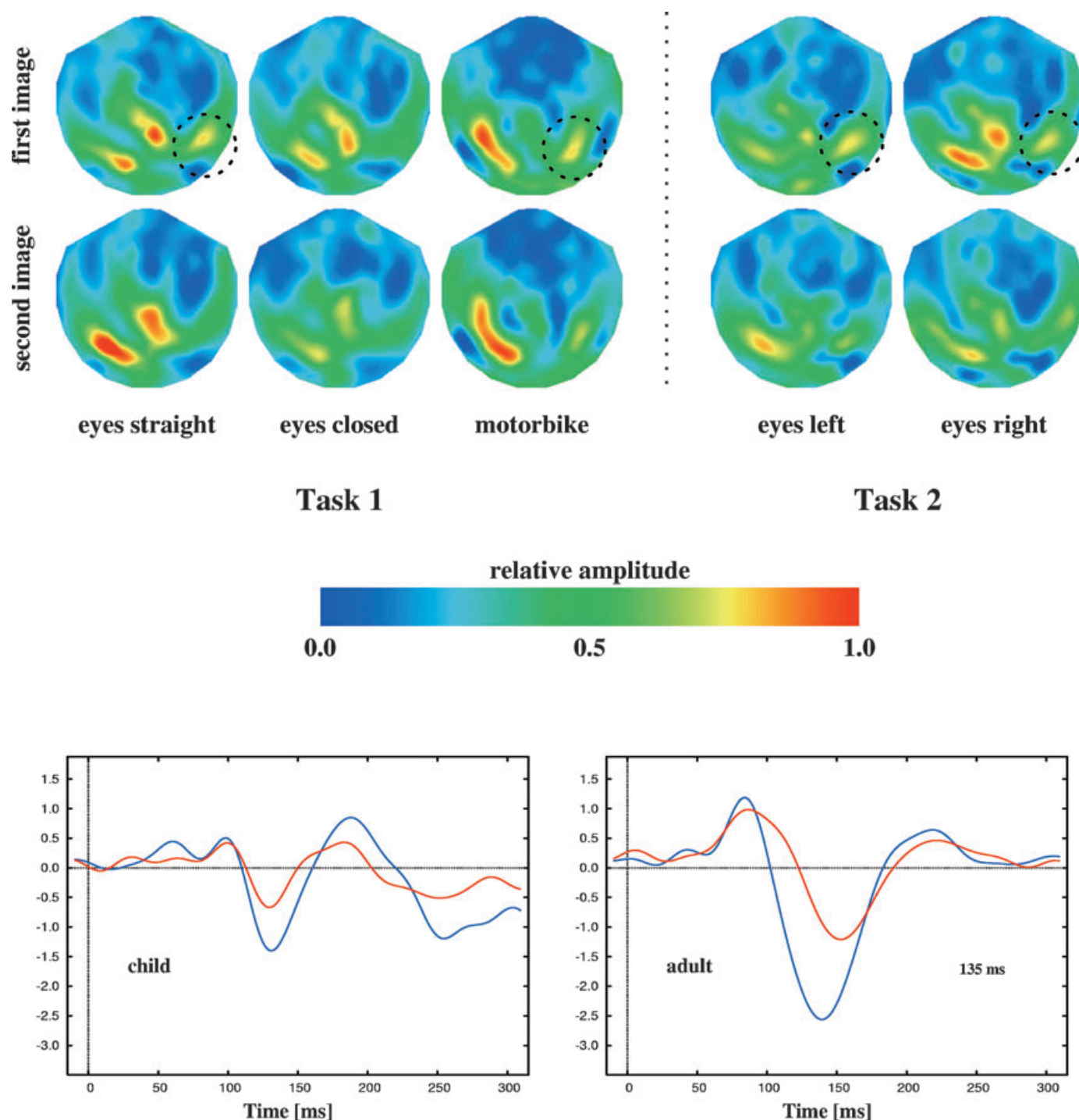


FIG. 4. (Top) Root-mean-square signal distribution of neuronal activity for children at 130 ms (faces) and 140 ms (motorbikes) after stimulus onset. At this latency, a strong, right lateralized response is observed in adults (see Fig. 2), whereas activity is weaker and more widespread in children. In particular, a response observed over the right inferior occipito-temporal regions (dotted circles) is not stronger following face images compared to non-face images. This response is reduced in amplitude for second images but the difference does not reach significance. (Bottom) Evoked signals following first straight gaze (blue) and second straight gaze (red) stimuli in one child (left) and one adult subject (right). These traces illustrate the grand-mean presentation above. A clear peak in the waveforms at approximately 130 ms was seen over the right inferior occipito-temporal regions (time in ms after stimulus onset; 0-level indicated by horizontal line). The data were taken from the same channel at a site corresponding broadly to the T6 location of the 10–20 EEG system. At this latency, signal amplitudes are stronger in adults than in children. Responses to second images are of smaller amplitude compared with responses to first images in both participant groups. This reduction in amplitude is particularly strong in adults.

Localization of the strongest signals and dipoles in this study suggests that the response at 100 ms originates from midline occipital cortex (the lack of MRI scans prevents a more precise assessment of source locations). Face sensitive activity at 100 ms may originate from

V1 or V2 (Halgren *et al.*, 2000). Thus, our results would be in line with a recent neural modelling study by Acerra *et al.* (2002), which argued that V1 feeds forward to extrastriate cortex the spatial frequencies of face like patterns, starting early in development with

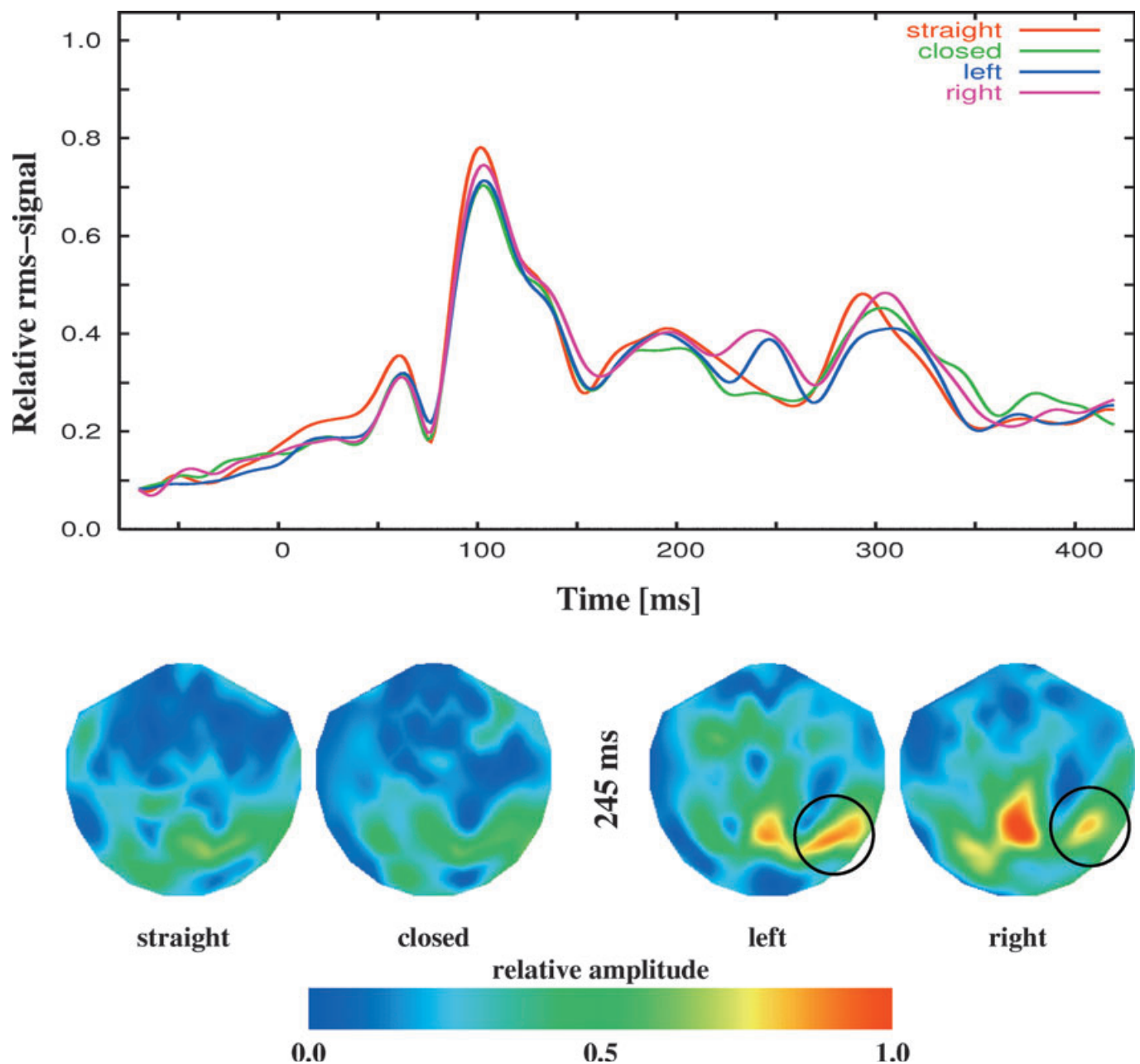


FIG. 5. (Top) Root-mean-square-signals following first face images in Task 1 and Task 2. (Bottom) At approximately 245 ms after stimulus onset, averted gaze elicits a response over the right occipito-temporal (the circles indicate the regions of spatial significance according to $w_i < 0.01$) in children. In these data, this response is independent of the left–right direction of the gaze. Second faces with averted gaze elicit similar responses.

the simplest patterns and progressively increasing the complexity of the relevant visual information. Alternatively, face sensitive activity at 100 ms could be generated in the inferior occipital gyri (IOG). The IOG is a part of a distributed neural system for face processing whose functioning has been associated with the early perception of facial features (Haxby *et al.*, 2000).

In children we did detect a signal peaking at approximately 135 ms after stimulus onset. The main evidence for some form of face sensitivity in this response (over right inferior occipito-temporal regions) comes from the timing difference between the responses to faces and motorbikes. Differences in signal power and effects of stimulus order were less clear than for the evoked response at 100 ms. As in adults, this face sensitive response in children was consistently

(albeit not significantly) reduced in amplitude for second images, and its timing was very similar to adult data. These results seem to suggest that adult like face sensitivity has developed partially in extrastriate areas by middle childhood. In children, the 100-ms response was stronger and more discriminating between faces and motorbikes than the response at 135 ms, whereas the opposite pattern of results was true for adults. These findings suggest that in children the early visual areas may still have a central role in face perception, but that during the course of development the functional anatomy of the face processing system changes, characterized by gradually increasing involvement of the higher visual areas.

In children the timing of the apparently face sensitive response at 135 ms was different from that seen in previous ERP studies

TABLE 1. Differences between (median) locations for dipoles generating the 60 and 100 ms responses to first images in Tasks 1 and 2 in children

Category	Difference between locations (mm)		
	Δ_{L-R}	Δ_{P-A}	Δ_{I-S}
Eyes straight	-6.3	+11	+24**
Eyes closed	-4.6	+2.9	+12
Motorbike	+2.8	+26	+8.5*
Eyes left	+13	+9.5	+8.3*
Eyes right	-8.4	+9.7	+4.7

The principal directions are left-right (L-R), posterior-anterior (P-A), and inferior-superior (I-S). A positive value of Δ indicates that the generators of the 60-ms response locate more to the right, more anterior, or more superior than the generators of the 100-ms response. ** $P < 0.01$ (paired Wilcoxon test); * $P < 0.05$.

(Taylor *et al.*, 1999; Taylor *et al.*, 2001b; Henderson *et al.*, 2003), although the timing was consistent with previous MEG-data from adults (Bailey *et al.*, 2005; Swithenby *et al.*, 1998; Braeutigam *et al.*, 2001). It is likely that the disagreement between studies reflects differences in (spatial) resolution and sensitivities between the technologies used. The bilateral nature of the MEG signal at 135 ms in children is compatible with the findings of Taylor *et al.* (1999) that the face sensitive ERP was bilateral in 4–10-year-old children and that the right hemisphere dominance typically seen in adults was not apparent until 12 years of age.

In this study, another clear finding in children was that averted gaze images elicited significantly stronger activation than direct gaze (or eyes shut) at 245 ms, apparently in inferior occipital cortex and most strongly evident on the right. There was no equivalent response to motorbikes at this latency and this gaze sensitive response was not seen in adults, in keeping with previous ERP-studies in adults. There is, however, some evidence from psychological and imaging studies in adults that the right hemisphere is involved in perception of gaze direction. For example, Ricciardelli *et al.* (2002) found a left visual field (right hemisphere) bias in processing of gaze direction. Also, Pelphrey *et al.* (2003) found a larger haemodynamic response (fMRI) to gaze shift conditions in the right hemisphere (including fusiform gyrus) than in the left hemisphere and Watanabe *et al.* (2002) reported larger ERP-responses (at a latency of 190 ms) to averted than to straight gaze conditions in the right hemisphere. The most parsimonious explanation of our data is that hemispheric specialization for averted gaze processing may precede the lateralization of functions subsumed by the fusiform gyrus and surrounding regions. Nevertheless, this hypothesis needs further exploration given reports that visual attention modulates neurophysiological responses (see, e.g. Hoffman, & Haxby, 2000; Näätänen *et al.*, 2002) and in this study attention was not directed towards the eyes. It should also be noted that all the boys whose pictures were presented in Task 2 (eyes left or right) had been seen before in Task 1 (eyes open or shut). Thus, it is conceivable that priming related to some form of familiarity might have affected the neural responses at this latency. Nevertheless, no such effect was observed in Task 1, where second (same) images should have evoked a similar response if (short-term) memory was a relevant factor.

Contrary to our expectations, we did not find any evidence that the eyes are a salient feature for information processing in a short latency pathway in children. Indeed, in children responses at approximately 60 ms were qualitatively different from those seen in adults (cf. Seeck *et al.*, 1997; Braeutigam *et al.*, 2001; Bailey *et al.*, 2005), with no detectable evidence for stimulus specificity. In children the source of

the relatively strong activity at approximately 60 ms is clearly different from the generator of the 100-ms response, but its precise location is currently unclear. Overall the findings raise the possibility that the face specific short latency activity seen in adults may, at least in part be a consequence of face processing expertise.

This explanation of our findings assumes comparability between the responses in children and adults at both approximately 100 ms and at approximately 135 ms, implying that development impacts on signal specificity rather than signal latency. A more radical interpretation of our findings would equate the responses at 60 and 100 ms in children to the responses at approximately 100 and 135 ms in adults (see rms-curves in Fig. 2). This alternative view would suggest that the responses in children are faster than in adults, but reflect similar functionality (i.e. primary visual processes at 60 ms and face-sensitive processes at 100 ms in children). This would suggest, based on the signal topographies and dipole locations presented above, that primary visual processes would shift significantly posteriorly and face-sensitive processes migrate almost completely from striate to extra-striate cortices between the age of 8–11 and adulthood.

In summary, our results are difficult to reconcile with the central findings from previous electrophysiological studies suggesting that the latency of the responses evoked by faces decreases through infancy and childhood. Our findings do indicate, however, that there are qualitative changes in the neural processing of faces and eye gaze between childhood and adult life. Such changes in the neural processes may involve other brain areas in addition to those observed here, as a recent study has found developmental differences in neural activity in anterior cingulate, orbito-frontal cortices and the amygdala when adolescents and adults evaluate emotional expressions (Monk *et al.*, 2003). Finally, our findings further support the postulated role of primary visual and inferior occipital gyri in face specificity.

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Abbreviations

ECD, equivalent current dipole; ERP, event-related potential; MEG, magnetoencephalography; rms, root-mean-square.

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Face- and gaze-sensitive neural responses in children with autism: a magnetoencephalographic study

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Abstract

Face and gaze processing were studied using magnetoencephalography in 10 children with autism and 10 normally developing children, aged between 7 and 12 years. The children performed two tasks in which they had to discriminate whether images of faces presented sequentially in pairs were identical. The images showed four different categories of gaze: direct gaze, eyes averted (left or right) and closed eyes but there was no instruction to focus on the direction of gaze. Images of motorbikes were used as control stimuli. Faces evoked strong activity over posterior brain regions at about 100 ms in both groups of children. A response at 140 ms to faces observed over extrastriate cortices, thought to be homologous to the N170 in adults, was weak and bilateral in both groups and somewhat weaker (approaching significance) in the children with autism than in the control children. The response to motorbikes differed between the groups at 100 and 140 ms. Averted eyes evoked a strong right lateralized component at 240 ms in the normally developing children that was weak in the clinical group. By contrast, direct gaze evoked a left lateralized component at 240 ms only in children with autism. The findings suggest that face and gaze processing in children with autism follows a trajectory somewhat similar to that seen in normal development but with subtle differences. There is also a possibility that other categories of object may be processed in an unusual way. The inter-relationships between these findings remain to be elucidated.

Introduction

The face is an important source of social information for humans under normal conditions. Infants preferentially orientate to face-like stimuli immediately after birth (for a review, see Maurer, 1985) and face processing plays an important role in normal social development. Furthermore, infants' orientation to faces may support language development and facilitates complex interactions with other people (e.g. Johnson, 1997). Children with autism, who have impairments in reciprocal social interaction and communication, spontaneously look less at the face and eyes than do normally developing individuals (e.g. Hutt & Ounsted, 1966; Volkmar & Mayes, 1990; Phillips *et al.*, 1992; Osterling & Dawson, 1994). They also show a range of deficits in face processing, e.g. in recognizing facial identity (e.g. Boucher & Lewis, 1992; Hauck *et al.*, 1998; Klin *et al.*, 1999), facial gender and age (Hobson, 1987; Hobson *et al.*, 1988) and facial emotional expressions (e.g. Hobson, 1986; Braverman *et al.*, 1989; Celani *et al.*, 1999; Howard *et al.*, 2000).

Some data suggest that individuals with autism use unusual cognitive strategies when processing faces. For instance, there may be a particular reliance on processing local features of the face (Langdell, 1978; Joseph & Tanaka, 2003) rather than the more typical pattern of processing configural or holistic information (e.g. Tanaka & Farah, 1993) observed even in infants (de Haan & Nelson, 1998). It has also been argued that the face-processing abnormalities found in

autism are due to general difficulties in processing affective states and that these problems lead to a lack of attention to faces (Hobson *et al.*, 1988).

Numerous neurophysiological (e.g. Bentin *et al.*, 1996; George *et al.*, 1996; Swithenby *et al.*, 1998; Braeutigam *et al.*, 2001; Xu *et al.*, 2005) and neuroimaging (e.g. Haxby *et al.*, 1994; Clark *et al.*, 1996; Kanwisher *et al.*, 1997; McCarthy *et al.*, 1997) studies of healthy adults have found that viewing human faces selectively activates regions of ventral occipito-temporal cortex around fusiform gyrus, particularly in the right hemisphere. More recently, brain activity in adults with autism has been measured whilst viewing faces with neutral (Schultz *et al.*, 2000; Pierce *et al.*, 2001; Hadjikhani *et al.*, 2004; McPartland *et al.*, 2004; Bailey *et al.*, 2005; Dalton *et al.*, 2005; O'Connor *et al.*, 2005) and emotional expressions (Baron-Cohen *et al.*, 1999; Critchley *et al.*, 2000; Hubl *et al.*, 2003; Wang *et al.*, 2004; Dalton *et al.*, 2005). Most of these studies have reported either weak or absent face-specific activation in the fusiform area in adults with autism compared with control groups of healthy adults. Event-related potential (ERP) studies (McPartland *et al.*, 2004; O'Connor *et al.*, 2005) have reported that adults with autism spectrum disorders show delayed responses to faces compared with control adults. There is, however, no consensus about how the underlying neural processing of faces differs in autism, i.e. whether adults with autism all use the same alternative regions of cortex to process faces and objects (Schultz *et al.*, 2000) or whether each individual might use unique neural circuitry (Pierce *et al.*, 2001; Bailey *et al.*, 2005).

In typically developing children, an adult level of face expertise is reached relatively late in development, with performance still

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improving during adolescence (for reviews, see Chung & Thomson, 1995; Want *et al.*, 2003). This long developmental time course is also observed in studies investigating the neural basis of face processing during development. Imaging studies have shown a more distributed pattern of brain activation in infants (Tzourio-Mazoyer *et al.*, 2002) and children than in adults (Passarotti *et al.*, 2003). Face-sensitive ERPs are bilateral and of longer latency in infants (e.g. de Haan *et al.*, 2002; Halit *et al.*, 2003) and children (Taylor *et al.*, 1999, 2001; Henderson *et al.*, 2003) compared with the responses observed in adults (e.g. Bentin *et al.*, 1996; George *et al.*, 1996). The magnetic counterparts of ERP have been found to be of equal latency in children and adults but in children the magnetic responses are bilateral (Kylliäinen *et al.*, 2006) whereas they are right lateralized in adults (Sams *et al.*, 1997; Swithenby *et al.*, 1998; Braeutigam *et al.*, 2001; Xu *et al.*, 2005). Thus, it remains unresolved whether the neural development of face-processing expertise simply reflects increased processing speed (cf. Taylor *et al.*, 1999, 2001) or whether there are more fundamental developmental changes in the neural mechanisms of the face processing (cf. Halit *et al.*, 2003; Kylliäinen *et al.*, 2006).

The developmental time course of face processing in autism is largely unknown. Previous neuroimaging studies of children and adolescents with autism have mainly investigated facial emotion processing and found reduced fusiform area activation compared with control individuals (Piggot *et al.*, 2004; Wang *et al.*, 2004). Differences in late ERP responses (around 400 ms) have been found between 3- to 4-year-old children with autism and typically developing children in the processing of neutral vs. fearful facial expressions (Dawson *et al.*, 2004) and familiar vs. unfamiliar faces (Dawson *et al.*, 2002). An ERP study of children with Asperger's syndrome and control children did not find any differences, however, in the processing of happy, sad, scared and neutral faces at latencies around 200 ms (O'Connor *et al.*, 2005).

Some of the deficits in face processing in autism possibly relate to processing of the eyes. This conjecture is supported by the observation that individuals with autism avoid eye contact (e.g. Hutt & Ounsted, 1966; Volkmar & Mayes, 1990) and that, unlike normally developing individuals, they do not prefer to look at the eye region when looking at faces (Klin *et al.*, 2002; Pelphrey *et al.*, 2002; Dalton *et al.*, 2005), recognizing facial identity (Langdell, 1978; Joseph & Tanaka, 2003), and judging other people's complex mental states and intentions (Baron-Cohen *et al.*, 1995, 1997, 2001). When required to pay attention to the eyes, however, children with autism show basic knowledge about eyes and seeing (Tan & Harris, 1991), and they are able to make overt discriminations about where another person is looking (Baron-Cohen *et al.*, 1995; Leekam *et al.*, 1997; Kylliäinen & Hietanen, 2004). Seeing another person's averted gaze and/or head also shifts visual attention automatically in children with autism (Swettenham *et al.*, 2003; Kylliäinen & Hietanen, 2004; Senju *et al.*, 2004).

The purpose of this study was to investigate the neural bases of face and gaze processing in children with autism using magnetoencephalography (MEG) (e.g. Hämäläinen *et al.*, 1993). We investigated (i) whether we could identify differences between normally developing children and those with autism in the neural activity evoked by viewing faces with direct gaze similar to the differences observed between normally developing adults and those with autism spectrum disorder (Bailey *et al.*, 2005); (ii) whether the neural responses to straight and averted gaze in children with autism differed from those seen in normally developing children, and (iii) at which stage of visual processing, as reflected in the magnetic responses, differences between children with autism and typically developing children could first be detected.

The 7- to 12-year-old children in the clinical and control groups performed two tasks in which they had to discriminate whether images presented very briefly (200 ms) and sequentially in pairs were the same or different. In Task 1, the participants viewed pairs of face images with neutral expression. In this task, the eyes were either open (straight gaze) or shut. Pairs of motorbikes were used as control images. In Task 2, participants saw pairs of faces, in which gaze was averted to the left or right. This type of task design requires attention to be paid to the face and allows the identification of face-sensitive neural activity as early as 30–60 ms after stimulus onset (Seeck *et al.*, 1997; Braeutigam *et al.*, 2001; Bailey *et al.*, 2005). The results in normally developing children compared with healthy adults have been reported previously (Kylliäinen *et al.*, 2006).

Materials and methods

This study closely follows Kylliäinen *et al.* (2006) and the reader is referred to that article for more details.

Participants

Ten school-aged children with autism took part in this study. The children's clinical diagnoses were confirmed by a clinical psychologist experienced in the diagnosis of autism. The presentation of the children, their past histories and subsequent development were entirely typical of high-functioning autism. Additionally, the parents were administered the Autism Diagnostic Interview-Revised (Lord *et al.*, 1994) and all the children met the Autism Diagnostic Interview algorithm criteria for autism. Table 1 shows the algorithm scores of the clinical group for the three domains of the Autism Diagnostic Interview-Revised. The findings from the 10 children who served as gender- and mental-age-matched controls for the children with autism have been reported previously (Kylliäinen *et al.*, 2006). The control

TABLE 1. Participant characteristics

	Group	
	Clinical (<i>n</i> = 10)	Control (<i>n</i> = 10)
Chronological age (years, months)		
Mean ± SD	9, 10 ± 1, 5	9, 1 ± 1, 2
(Range)	(7, 8–12, 1)	(7, 10–10, 11)
Full IQ		
Mean ± SD	91 ± 17	103 ± 6
(Range)	(63–117)	(93–113)
Verbal IQ		
Mean ± SD	93 ± 16	104 ± 10
(Range)	(69–118)	(91–120)
Performance IQ		
Mean ± SD	92 ± 20	101 ± 7
(Range)	(51–117)	(86–111)
ADI-R		
Social domain (cut-off 10)		
Mean ± SD	20.0 ± 4.2	
(Range)	(14–24)	
Communication domain (cut-off 8)		
Mean ± SD	15.3 ± 3.7	
(Range)	(9–23)	
Stereotypy domain (cut-off 3)		
Mean ± SD	7.0 ± 2.3	
(Range)	(3–11)	

IQ, intelligence quotient; ADI-R, Autism Diagnostic Interview-Revised.

children had no history of mental or neurological disorders as reported by their parents. The children and their parents gave informed consent (Helsinki Declaration) before experimentation. The experiment was approved by the Ethical Committee of Pirkanmaa Hospital District. Children in the two groups were individually matched for intelligence (WISC-R or WISC-III). Three subtests were used to estimate both verbal intelligence quotient (IQ) (information, similarity and arithmetic) and performance IQ (picture completion, object assembly and coding). There were no significant differences between the clinical and control groups in chronological age, full scale IQ, verbal IQ and performance IQ (see Table 1).

Stimuli

The children viewed static, grey-scale images of faces of adolescent boys (without eye glasses, facial hair or ear rings) and images of motorbikes (all motorbikes pointed to the left) (see Fig. 1). Motorbikes were chosen as a complex comparison stimulus likely to be of interest to boys which also have some symmetry, are rich in details and have spatial frequencies similar to faces. (A representative sample of images

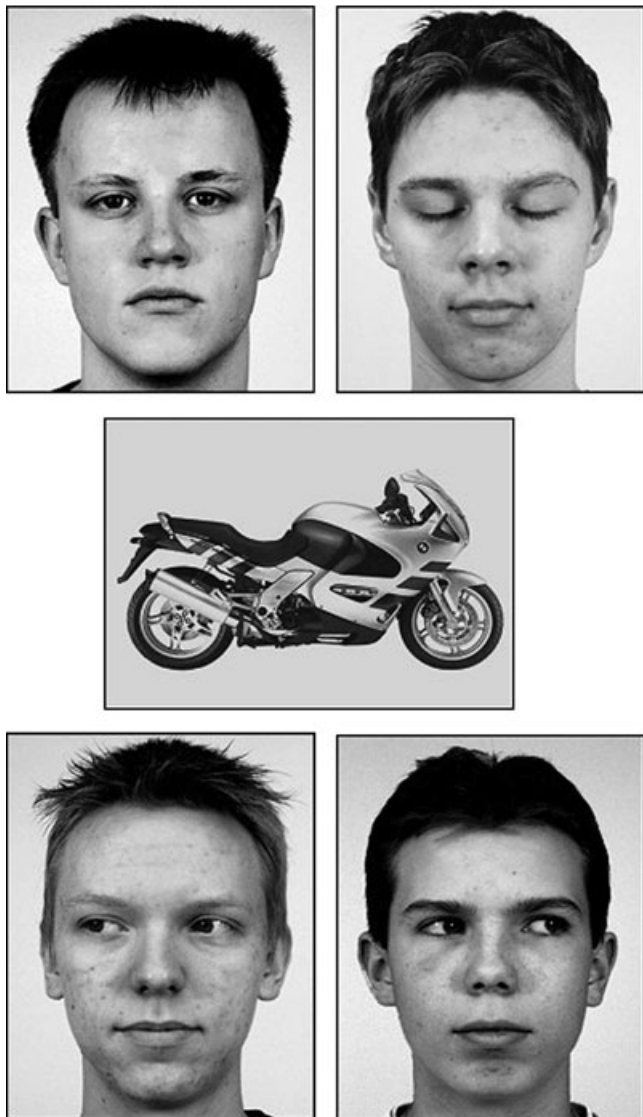


FIG. 1. Examples of the visual stimulus categories used.

was analysed using a two-dimensional FFT periodogram method.) Typically, the face and motorbike images had the same spectral power for frequencies up to about 15 cycles/image. Frequency components above 15 cycles/image have relative powers of -30 dB or less (see also Swithenby *et al.*, 1998.) The images were projected onto a screen placed 90 cm in front of participants' eyes whilst they sat under the MEG helmet. The images were displayed for 200 ms and were standardized for luminosity (42 ± 8 cd/m²) and size (subtended $10^\circ \times 8^\circ$ at the eye).

Design and procedure

The tasks involved sequential presentation of pairs of images of the same type. The second image followed the first after a delay of 1000 ± 100 ms. The second image was followed after 1400 ± 100 ms by a visual prompt to respond, which was displayed for 400 ms. The visual prompt was a drawn picture of a hand on which the response fingers (buttons) were marked with different colours to cue the children to respond by pressing a key under the right index finger if the second image was a repetition of the first image and a key under the middle finger if it was different. A red fixation point was displayed during the interstimulus interval of 1600 ± 200 ms. An optical-fibre feedback system was used to measure the exact onset of stimulus presentation with reference to the computer trigger (delayed by 32 ms in this study).

In Task 1, the image pairs comprised adolescent boys with either straight gaze (50 image pairs) or eyes shut (50 image pairs) and pairs of motorbikes viewed in profile (50 image pairs). In half of the trials the second image was a repetition of the first image and in half of the trials it was different. The task was completed in two runs with balanced content.

In Task 2, the procedure was exactly the same as in Task 1. Children viewed pairs of images of adolescent boys' faces in which the eyes were directed either to the left (50 image pairs) or the right (50 image pairs). In this task direction of gaze was always the same within a pair of images but the identities of the individuals were different in half of the image pairs. The boys were the same as those seen in Task 1. The task was completed in two balanced runs.

During each experiment a progress bar was displayed for a few seconds after blocks of 20–25 trials. After each run the children were rewarded with a token (a plastic toy animal) that they had selected before the experiment. During the measurements a researcher sat on each side of the child.

Training

All the participating children were first seen in the Human Information Processing Laboratory at the Department of Psychology, University of Tampere, accompanied by their parents. The purpose of the visit was to inform the child of the study procedure, to familiarize them with the stimuli, tasks, helmet, and electrode environment, to train them when to respond with a button press, to suppress blinking when an image was presented and finally to stress the importance of remaining as still as possible in the scanner. The interest in face processing, the purpose of the study and the training procedure were explained to the child and their parent(s), who were shown photographs of the scanner, the physical environment and the MEG preparation procedures. The training procedure was illustrated using picture cards with the youngest children. The children were also told that they could withdraw from the study at any time without explanation. A laptop was used for presentation of the practice tasks and the buttons of the

laptop were used as response buttons. Each child was trained to press a response button and to blink, if needed, only after a visual prompt (a drawn hand) appeared on the computer screen. The child was taken through the MEG study preparation procedure by attaching electrode leads to the face and wrist (as if recording the electro-oculogram and electro-cardiogram, respectively). Practice trials for each task were then presented whilst the child sat under an outer casing of the MEG helmet array. The main emphasis during this practice session was upon teaching the child to press and blink only after the visual prompt. Children took away a card showing the hand cue to remind them when to press the response buttons and not to blink before this cue.

Data acquisition

All measurements were performed in the Brain Research Unit of the Low Temperature Laboratory, Helsinki University of Technology, using a Vectorview™ neuromagnetometer. The system provides a helmet-shaped array of 102 pairs of orthogonal, first-order planar gradiometers. This system also has 102 magnetometers, whose output has not been analysed for this study. The outputs of each pair of sensors are most sensitive to tangential current flow in the region directly below the detectors. The local root-mean-square (rms) signal summed over the two readings is a measure of the current strength.

The data were sampled at 600 Hz (0.01–200 Hz anti-alias filter). Artefacts were identified by recording the electro-oculogram and electro-cardiogram. Foam inlays were used to compensate for a helmet that was slightly oversized for the children. Head movement was monitored by measuring head position before and after each experimental run and, if necessary, head position was adjusted between runs to maintain an overall head-position accuracy of ± 5 mm across runs for each child. Individual pre-auricular-nasion coordinates were coregistered with the device system in order to verify that all the children's heads had the same relative position with respect to the helmet.

Time-series analysis

For each participant, average evoked responses based on all runs were calculated for latencies from 0 to 800 ms after stimulus onset, according to task condition, stimulus type and image position within a pair. An unreported analysis did not reveal differences when further subdividing the data according to second-same vs. second-different images. Thus, the data were pooled for statistical robustness, yielding 10 types of evoked responses: straight gaze, closed, left, right, motorbikes; first and second image for each stimulus category. The average signals were then filtered between 0.2 and 30 Hz (roll-off 0.5 Hz), and normalized to the signal variance within the baseline interval 0–200 ms before stimulus display.

Significant differences between evoked responses were sought using a previously described (Braeutigam *et al.*, 2001) time-dependent measure $P(t)$, which takes into account the data from all detectors and does not require the prior identification of peaks in the evoked responses:

$$P(t) = \text{probability}(\chi^2), \text{ with } \chi^2 = -2 \sum_{i=1}^N \ln[n_i(t)]$$

where n denotes the number of channels. For each channel, $n_i(t)$ is an appropriately chosen local, non-parametric measure of the significance of differences between matched evoked responses across participants within a participant group. Then, $P(t)$ describes the

significance across the entire helmet of the channel differences (as a function of time). In this study, intervals with $P(t) < 0.01$ were considered significant, where n_i denotes a Friedman analysis of variance (f_i) used to compare the responses to the five types of stimuli in Tasks 1 and 2 (separately for first and second images). A Wilcoxon post-hoc test (w_i) was employed for pair-wise comparisons when $P(t)$ indicated significant variation. In the case of comparisons between responses to first and second images, n_i denotes a Wilcoxon test (w_i) applied to images of the same type. For each such interval with $P(t) < 0.01$, the set of all values n_i (Friedman and/or Wilcoxon) provided the spatial distribution of significance of differences between evoked responses. Those distributions were used to identify significant regions at the group level as well as individually. For each latency of interest, spatial maps of local rms signals (amplitude maps) as a measure of neuronal activity were calculated. Occasionally, the restriction to matched samples was relaxed using a Mann–Whitney U -test (n_i) to allow for direct comparisons of data from the clinical and control group.

Source estimation

Equivalent current dipole (ECD) estimation was performed using Curry™ software utilizing a homogeneous sphere as the volume conductor. For each participant, the sphere was centred on the base of the perpendicular from the nasion to the line joining the pre-auricular points (pre-auricular-nasion head co-ordinate system). Source analysis was carried out for first images in both tasks, where an ECD was calculated for each individual and each time slice. A fitted ECD was considered acceptable if: the goodness-of-fit parameter was greater than 0.7, the located position was stable to within 5 mm in each co-ordinate over at least three consecutive time slices, and the confidence volume did not exceed 1 cm³. Multiple current dipole and distributed source estimates were not considered, as these are inherently unstable without anatomical (magnetic resonance imaging) constraints.

Results

Some of the results from the normally developing children have been reported previously (Kylliäinen *et al.*, 2006). In what follows, these previously reported findings are repeated, together with unreported data, in order to facilitate a direct comparison with the children with autism.

All the children completed both runs of Task 1. Two children in the control group and one child in the clinical group did not perform Task 2 because of technical problems. Task performance was good in both groups and on both tasks. Overall accuracies for the control children were $95 \pm 1\%$ (faces in Task 1; straight $96 \pm 1\%$, closed $95 \pm 2\%$); $86 \pm 2\%$ (motorbikes in Task 1) and $93 \pm 2\%$ (faces in Task 2; left $94 \pm 2\%$, right $93 \pm 2\%$) and for the children with autism $87 \pm 2\%$ (faces in Task 1; straight $84 \pm 3\%$, closed $89 \pm 2\%$); $80 \pm 3\%$ (motorbikes in Task 1) and $87 \pm 2\%$ (faces in Task 2; left $86 \pm 2\%$, right $89 \pm 3\%$). In Task 1, the performance for faces was better in the control group than in the clinical group (Mann–Whitney, $U = 15$, $P = 0.005$) whereas there was no difference between groups in performance for motorbikes ($U = 39$, $P = 0.258$). Nevertheless, for both the control (Wilcoxon, $z = 2.7$, $P = 0.007$) and the clinical ($z = 2.0$, $P = 0.046$) groups, performance was better for faces than motorbikes. In Task 2 the difference in performance accuracy between the groups was also statistically significant ($U = 15$, $P = 0.026$). The unpooled data for straight, left and right gaze, and closed eyes were consistent with these results.

Premature (before the prompt) key presses occurred in 10% of all trials but these all occurred relatively late after stimulus onset (1215 ± 50 ms) and did not interfere with analysis of the MEG data. Significantly more premature key presses occurred in the group of children with autism compared with controls. However, no correlation was found between the number of premature presses and task, stimulus category or accuracy. The total number of epochs associated with both incorrect and premature key presses was insufficient for a separate MEG analysis of averaged signals and excluding those epochs did not alter the observations presented. A small number of epochs ($< 0.9\%$) had to be excluded from the analysis due to eye blink or other artefacts.

The results of the MEG analysis are reported in the remainder of this section, beginning with a brief overview of evoked responses to all stimuli in both normally developing children and the children with autism. A detailed description of significant effects and other noteworthy observations (within and between groups) follows, ordered according to latency within the interval 0–400 ms after stimulus onset. For ease of presentation only, the data are shown as grand-mean evoked responses. All reported significant effects were also identifiable at the individual level in at least six out of 10 children in each group. All differential effects were identified using the measure $P(t)$ and the criterion $P(t) < 0.01$.

Evoked signals – overview

In all the children, averaged evoked field patterns elicited by all stimuli involved a complex sequence of neural activity (see Fig. 2). Despite some marked variations in the evoked responses across tasks, stimuli and participant groups, the neural responses exhibited broadly the same pattern, with the first maximum of evoked activity identified in posterior regions approximately 60 ms after stimulus onset. This short latency response was followed by a strong maximum at 100 ms, localized predominantly over posterior regions. The responses at 100 ms were the strongest overall. Slightly later and to varying degrees, responses were observed at around 135 ms after stimulus onset, corresponding in time but not in strength to the strong signal maxima evoked by faces in adults performing similar tasks (Switkenby *et al.*, 1998; Braeutigam *et al.*, 2001; Bailey *et al.*, 2005; Kylliäinen *et al.*, 2006). Although the 135-ms responses exhibited characteristic features, as reported below, in the children they did not appear as local maxima in the global rms signals.

The next, albeit in these data non-specific, maxima in the evoked responses were observed about 200 ms after stimulus onset over posterior brain regions; these responses became weaker between about 220 and 270 ms but more specific with respect to eye condition, as detailed below. Subsequently, neural responses were observed over parietal and temporal regions approximately 300 ms after stimulus onset. At longer latency, widespread evoked responses could be observed for latencies up to about 700 ms (data not shown in Fig. 2). These late responses, however, were too varied across participants for a meaningful analysis.

Evoked signals – 60 ms

Relatively strong and localized short latency activity was present in response to all stimuli in normally developing children and children with autism. There was no significant dependence of these responses on participant group, stimulus type or task. Some neural activity above baseline was observed in all children before 60 ms but the signals varied too much across children to permit meaningful analysis.

Evoked signals – 100 ms

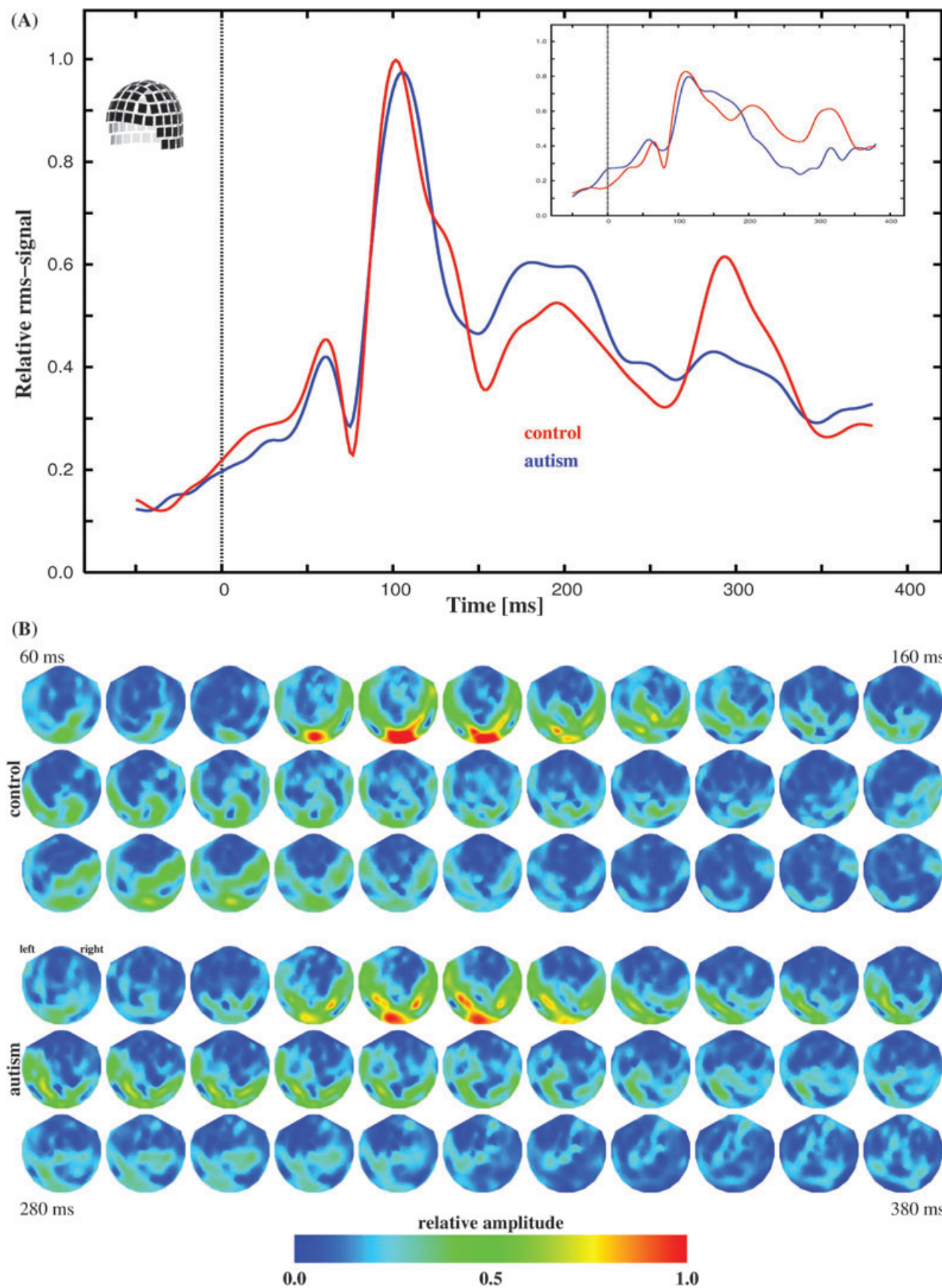
In normally developing children, the neural responses at 100 ms after stimulus onset were the same for all types of first faces (eyes straight, closed, left and right) but non-significantly weaker and significantly later ($P < 0.01$) by about 10 ms for first motorbikes. From 100 ms onwards, in normally developing children all responses evoked by motorbikes were significantly delayed by 10–30 ms compared with those evoked by faces, although the signal topographies elicited by motorbikes were broadly similar to those evoked by faces (see Fig. 3, left rms curves). At 100 ms (110 ms for motorbikes), second images of faces with straight, closed and left (but not right) eyes, and second images of motorbikes elicited lower signal amplitudes than corresponding first images but the differences were only significant for faces with closed eyes [$P(t) < 0.01$ between 95 and 115 ms].

In children with autism, the neural responses to first faces at 100 ms were very similar to those observed in the normally developing children. The responses to first motorbikes were weaker and delayed compared with first face images, as in controls, but these effects did not reach significance (Fig. 3, right rms signals). Unexpectedly, the responses to motorbikes at 100 ms in children with autism were more right lateralized than the responses to faces; this lateralization reached significance in the case of first images [$P(t) < 0.01$ between 80 and 95 ms; Friedman test across image categories within the clinical group]. The responses to motorbikes were also significantly more right lateralized in the group of children with autism compared with the control children [$P(t) < 0.01$ between 90 and 115 ms; Mann–Whitney U -test; see Fig. 3]. In children with autism there was a non-significant trend for all categories of second images to evoke stronger signals than first images at latencies around 100 ms [faces: $P(t) < 0.1$ between 90 and 105 ms; motorbikes: $P(t) < 0.1$ between 95 and 110 ms].

Evoked signals – 135 ms

At 130–140 ms after stimulus onset, the evoked responses were bilateral in normally developing children. There were responses over right inferior occipito-temporal cortices detectable for all image types (Fig. 4). The responses were similar in amplitude for faces and motorbikes, although they were later for motorbikes than faces (by about 10 ms; see above). There were no significant differences between the responses following first or second images, although the former were stronger over right inferior occipito-temporal cortices for straight eyes, averted gaze and motorbike stimuli. Individual peaks in the waveforms at around 130 ms were identified in eight control children.

In general, the evoked responses at 130–140 ms in children with autism were similar to the responses seen in normally developing children. Neural activity was observed over bilateral posterior regions, including responses over right inferior occipito-temporal cortices detectable for all image types (Fig. 4). In contrast to the control children, however, in the children with autism the responses to first motorbikes over right inferior occipito-temporal cortices were significantly stronger than the responses to first faces [$P(t) < 0.01$ between 125 and 155 ms]. There was no evidence for a delay in the responses to motorbikes compared with faces, as observed in the control group. There were no significant differences between the responses following the first or second images, although the former were stronger over right inferior occipito-temporal cortices for all stimuli. Individual peaks in the waveforms at around 130 ms were identified in eight children with autism. The responses to all face images in children with autism were consistently but insignificantly [$P(t) < 0.1$] of smaller



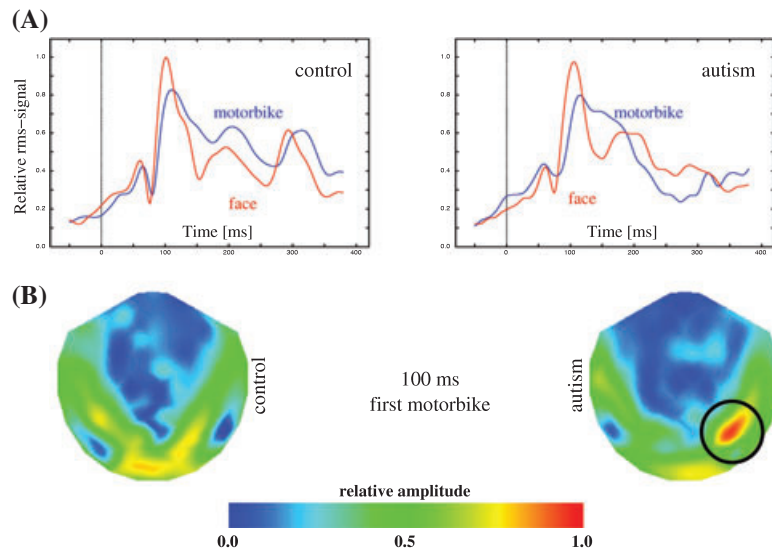


FIG. 3. (A) Children's grand root-mean-square (rms) signals following first face (eyes straight) and motorbike images in Task 1. In normally developing children the responses evoked by face and motorbike images are broadly similar in terms of signal amplitude and topography. For latencies longer than about 100 ms, responses elicited by motorbikes are delayed by 10–30 ms compared with faces. Such a delay might also be present in children with autism but it was not significant in these data. (B) Local rms signals at 100 ms following first motorbikes in control children and children with autism. In the latter group, responses to motorbikes are more right lateralized at this latency (solid circle).

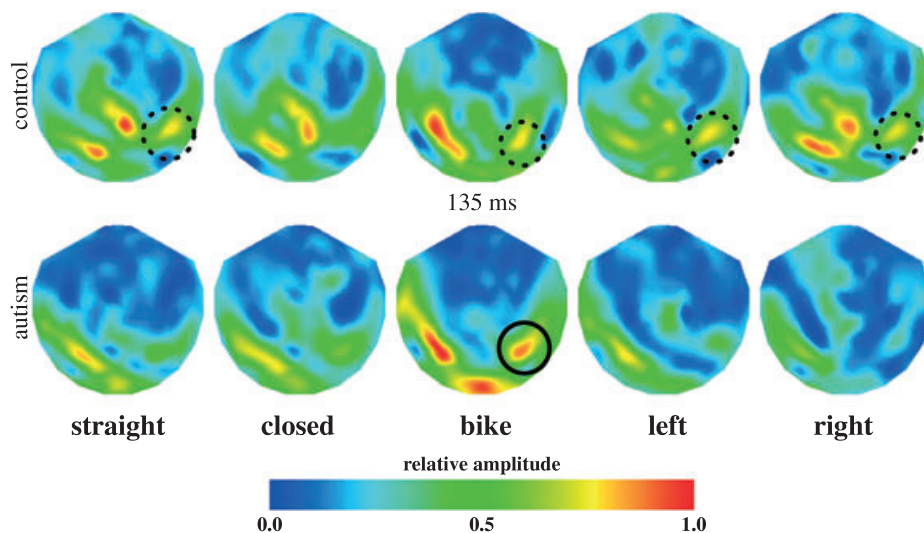


FIG. 4. Root-mean-square signal distribution of neuronal activity in children at about 135 ms after stimulus onset. At this latency, a relatively weak response can be observed over right inferior occipito-temporal regions. The latency and topography of this response in children are similar to responses typically associated with face-specific processes in adults at fusiform area. In normally developing children, however, this activity is not stronger following face images compared with non-face images. This response is consistently reduced in amplitude for second images but the difference did not reach significance (dotted circles are for visualization only and refer to first vs. second image comparisons within the group of normally developing children; see text). A similar response was observed in children with autism at this latency. In contrast to the control children, the responses to first motorbikes over right inferior occipito-temporal cortices were significantly stronger than response to first faces in children with autism (solid circle denotes face vs. motorbike comparisons within the clinical group). As in control children, there were no significant differences between the responses following first or second images, although the former were stronger over right inferior occipito-temporal cortices for all stimuli.

FIG. 2. (A) Grand root-mean-square (rms) signals following first face (eyes straight) images in Task 1. The curves have been obtained by summation over all participants within a participant group (red, control children; blue, children with autism; stimulus onset is at 0) and channels. The inset on the left shows the helmet-shaped array of detectors used to record neural responses to static images. Each black plate represents two first-order gradiometers (channels) measuring two orthogonal spatial gradients of the magnetic field. These detectors are most sensitive to the tangential neuronal currents in the region below the detectors. The inset on the right shows grand rms signals following first motorbike images in Task 1 (red, control; blue, autism). (B) Spatial distribution of local rms signals to first faces in Task 1. The maps have been obtained by summation over all children (upper rows, control; lower row, autism) and the two detectors at each site. For presentation of data, the detectors have been projected into two dimensions (right ear on the right, front at the top). The maps show neuronal activity at latencies between 60 and 380 ms after stimulus onset, where 10 ms elapse from one map to the next. The responses in normally developing children and children with autism are broadly similar in terms of absolute signal strength and signal topography. In this and the following figures, all global rms curves were normalized to 3.5 fT/cm. Local rms maps were normalized to 7 fT/cm in this figure.

amplitude at 130–140 ms over right inferior occipito-temporal cortices compared with typically developing children (see Fig. 4).

Evoked signals – 240 ms

After 200 ms, two differential effects were observed in the neural responses, one in each group of children. For ease of presentation these effects have been labelled ‘responses at 240 ms’, although the precise peak latencies as well as intervals of significance vary, as described below.

In normally developing children, the first images of faces with averted gaze (both left and right) in Task 2 evoked significant responses over right inferior occipito-temporal regions [peak amplitude at 245 ms, $P(t) < 0.01$ between 240 and 260 ms; Fig. 5 top row] that were weak or absent in response to straight eyes, eyes closed and motorbikes in Task 1; this response was independent of whether gaze was averted to left or right. The 245-ms response to faces with averted gaze was also observed following second images but it was weaker and did not reach significance.

In the children with autism the response at 245 ms over right inferior occipito-temporal cortices following faces with averted gaze was strongly reduced, but not absent, compared with normally developing children. This reduction was significant for gaze directed to the left (between 250 and 260 ms) but not for gaze directed to the right (probably due to a lack of statistical power), although the topographies of the two signals were very similar. Slightly earlier, however, a component over left superior temporal, parietal and inferior occipito-temporal cortices was enhanced in children with autism compared with normally developing children (peak amplitude at 235 ms; Fig. 5 bottom row). Between groups, this increase was not significant but within the children with autism it was strongest for first straight eyes compared with other images [$P(t) < 0.01$ between 200 and 245 ms]. The response to straight eyes in the children with autism was also observed for second images but it was weaker and did not reach significance.

Evoked signals – 300 ms

In normally developing children, neural activity over occipital, mid-parietal and right temporal regions was significantly stronger for first compared with second face images [$P(t) < 0.01$ between about 285 and 345 ms, exact interval differed slightly across the different stimulus types; responses to faces with eyes straight and motorbikes are shown in Fig. 6]. At this latency the children with autism showed topographically similar but consistently weaker responses. This difference in signal amplitude between subject groups reached significance only for images of motorbikes; responses to first images over occipital regions were significantly reduced in children with autism compared with the control children [$P(t) < 0.01$ between 290 and 305 ms; Fig. 6]. In children with autism, no significant reduction in amplitude between the first and second images was observed.

Source localization

The ECD analysis of the data from both groups of children complemented the evaluation of responses at 60 and 100 ms. In the case of normally developing children, robust ECD sources were obtained in a total of seven participants for each type of first image. All ECD sources located consistently within the posterior, midline regions of the individual heads, regardless of image type. The ECD analysis did not reveal differences in either latency or strength

between the generators of the 60- and 100-ms responses evoked by faces and motorbikes, or between the generators of the 100-ms responses evoked by the two types of face images with averted gaze. A paired comparison of ECD sources showed that the generators of the 60-ms response were located consistently anterior and superior to the generators of the 100-ms response for all image types (Table 2, upper part; note some comparisons did not reach significance).

Similarly, robust ECD sources were obtained in a total of seven children with autism for each type of first image. In children with autism, all face ECD sources located consistently within the posterior, midline regions of the individual heads. As in control children, the ECD analysis did not reveal differences in either latency or strength between the generators of the 60- and 100-ms responses evoked by faces and motorbikes, or between the generators of the 100-ms responses evoked by the two types of face images with averted gaze. In the case of face images, a paired comparison of ECD sources suggested that the generators of the 60-ms response were located consistently anterior and superior to the generators of the 100-ms response (Table 2, lower part; note some comparisons did not reach significance). No such differences in location were evident in the case of motorbike images. It is currently unclear how this observation relates to the finding of a right lateralized signal following motorbikes at 100 ms reported above. At longer latency the number of robust ECD dipoles obtained in both groups was too low for statistical comparisons.

Although the two groups of children were matched for mean age and IQ, the ranges of these measures were, nevertheless, somewhat different between the groups. A systematic exploration of the effects of age and IQ on between-group differences was not possible because of limited sample size. Nevertheless, a within-group analysis of age and IQ as covariates did not reveal any significant effects on either signal latency or ECD location. This finding was taken as indicative that the between-group differences in age and IQ ranges did not influence the results.

Discussion

This study measured the neural responses to faces with different gaze direction in 7- to 12-year-old children with autism and in age- and IQ-matched normally developing children. The findings revealed that the neural responses of children with and without autism exhibited striking similarities regarding overall signal latencies, amplitudes, and topographies, as well as differences regarding the detailed nature of the stimulus dependence of evoked responses. The behavioural performance of both groups of children was good (recognition accuracy 80% or better across all tasks and stimuli). Children in both groups recognized faces more accurately than non-face objects (motorbikes) in line with previous behavioural findings (see e.g. Klin *et al.*, 1999) and the control children recognized faces significantly better than did the children with autism.

In this study children had to decide whether images presented sequentially in pairs were the same or different. Previous studies of healthy adults have shown that, in this type of task, face-sensitive neural responses can be detected as early as 30–60 ms after stimulus onset (Seeck *et al.*, 1997; Braeutigam *et al.*, 2001). In adults with autism spectrum disorder, the early neural activity to faces appears qualitatively different compared with control adults (Bailey *et al.*, 2005). The present study of children found strong activity at approximately 60 ms after stimulus onset, although this varied considerably across individuals, and there was no detectable evidence of adult-like face-sensitive early neural activity at 30–60 ms (cf. Seeck *et al.*, 1997; Braeutigam *et al.*, 2001; Bailey *et al.*, 2005). These

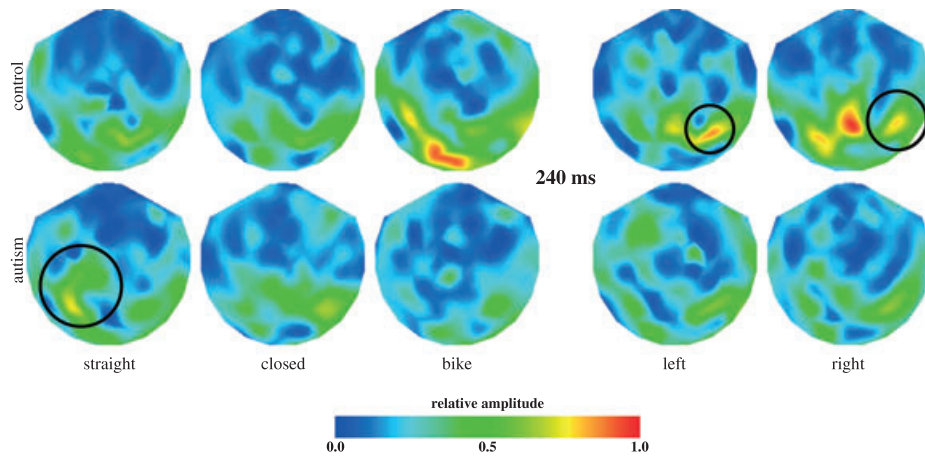


FIG. 5. Local root-mean-square signals following first images in Tasks 1 and 2. At around 245 ms after stimulus onset, averted gaze elicits a response over right occipito-temporal (the circles indicate the regions of spatial significance according to $w_i < 0.01$) in normally developing children. In these data, this response is independent of the left–right direction of the gaze. In contrast, straight eyes elicit a significantly stronger response over left superior temporal and left inferior occipito-temporal cortices than other stimulus categories in children with autism.

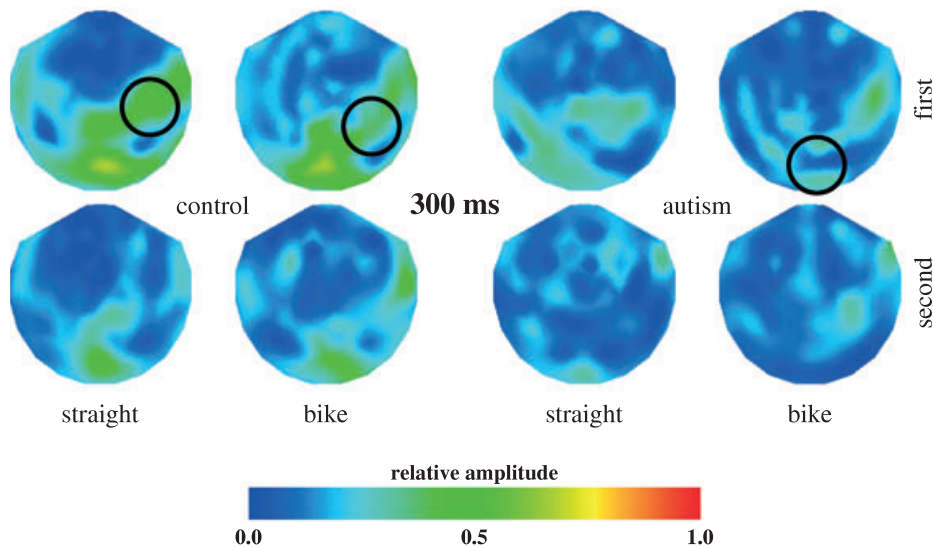


FIG. 6. At P300-like latencies, local root-mean-square signals are significantly (circles, within-group comparison) stronger for first compared with second images in normally developing children. The responses in children with autism are consistently weaker (significant for motorbikes; circle, between-subject comparison) at this latency. As in control children, first images elicited stronger responses than second images; however, the differences did not reach significance in the clinical group.

observations suggest that the early latency, face-sensitive activity may be associated with the development of face-processing expertise in late adolescence/early adulthood. Nevertheless, the suggestion that the ECD dipoles for motorbikes collate at 60 and 100 ms in children with autism means that we cannot exclude the possibility of as yet undetected short latency specificity to non-face objects in children with autism.

Neural activation at around 100 ms was the strongest recorded signal in this study and was stronger to faces than to motorbikes in both groups of children. Previous neurophysiological studies have found that images of faces and other objects lead to differential activation at about 100 ms in both children (Taylor *et al.*, 2001) and adults (Debruille *et al.*, 1998; Linkenkaer-Hansen *et al.*, 1998; Halgren *et al.*, 2000; Itier & Taylor, 2002; Liu *et al.*, 2002). This 100-ms response has been argued to reflect processes related to categor-

ization of a face as a face and not just processing of low-level features of visual stimuli (Linkenkaer-Hansen *et al.*, 1998; Itier & Taylor, 2002; Liu *et al.*, 2002). The findings from this study suggest that this presumed early categorization process is somewhat similar in children with and without autism. Further support for this assumption comes from the ECD source analysis indicating that the generators underlying responses to faces at early latency (60 and 100 ms) are very similar in the two groups of subjects. This putative similarity, however, is not complete as suggested by the absence of (repetition) priming in children with autism. Repetition priming refers to a reduction in signal amplitude following the second image, suggesting activation of neurones already activated by the previous image and/or increased efficiency of neural processing. That the responses at 100 ms showed differential repetition priming in children with and without autism might, in turn, indicate that the responses at this

TABLE 2. Differences between (median) locations for dipoles generating the 60- and 100-ms responses to first images in Tasks 1 and 2 in normally developing children and children with autism

	Δ_{L-R}	Δ_{P-A}	Δ_{I-S}
Normally developing children			
Eyes straight	-6.3	+11	+24**
Eyes closed	-4.6	+2.9	+12
Motorbike	+2.8	+26	+8.5*
Eyes left	+13	+9.5	+8.3*
Eyes right	-8.4	+9.7	+4.7
Children with autism			
Eyes straight	-0.12	+11	+7.2
Eyes closed	+6.2	+0.8	+20*
Motorbike	+0.11	+2.6	-19
Eyes left	+2.3	+5.1	+3.9
Eyes right	+2.9	-2.4	+28*

The principal directions are left–right (L–R), posterior–anterior (P–A) and inferior–superior (I–S), as defined by the individual pre-auricular-nasion coordinates. A positive value of Δ indicates that the generators of the 60-ms response locate more to the right, more anterior or more superior than the generators of the 100-ms response. *Significant at $P < 0.05$. **Significant at $P < 0.01$ (paired Wilcoxon test). In general, Δ -values are similar across the two participant groups.

latency are not simply reflecting simple object (i.e. face vs. non-face) categorization but could have a functional significance beyond basic categorization in the young normal brain.

An unexpected finding was that the activity evoked by motorbikes at 100 ms differed between the two groups of children. In normally developing children, the 100-ms response evoked by motorbikes apparently collocated with that evoked by faces in mid-line posterior occipital cortex but was approximately 10 ms slower than the response to faces. In children with autism the signal evoked by motorbikes at 100 ms occurred predominantly over right extrastriate cortex and was not significantly delayed compared with the response evoked by faces. This pattern of results suggests that, at 100 ms after stimulus onset, the visual system of the children with autism might process non-face objects at a presumed higher (extrastriate) level than it processes faces. Conceivably this process might start before 100 ms, as the ECD analysis did not reveal differences in generator locations at 60 and 100 ms. Whether this (possibly precocious) pattern of response to motorbikes in children with autism interferes with the normal development of face specialization by preventing natural development of face processing or is an abnormality related to more general visual processing difficulties (cf. Jemel *et al.*, 2006) is at present unclear.

The response at around 135 ms, although weaker and more bilateral in children than adults, is likely to be homologous to the N170/M170 face-sensitive, right lateralized response at about 140–180 ms reported previously in healthy adults (Sams *et al.*, 1997; Linkenkaer-Hansen *et al.*, 1998; Swithenby *et al.*, 1998; Braeutigam *et al.*, 2001; Xu *et al.*, 2005). In children the evidence for some form of face or object sensitivity in this response (over right inferior occipito-temporal regions) comes from the difference in timing (normally developing children) and signal strength (children with autism) between responses to faces and motorbikes. Also, the tendency for a reduction in signal amplitude following second images is broadly consistent with the repetition priming effects typically observed in adults at this latency (Campanella *et al.*, 2000; Braeutigam *et al.*, 2001; Bailey *et al.*, 2005). At the same latency, a weaker and less face-specific response (compared with the control adults) has been observed in adults with autism spectrum disorder (McPartland *et al.*, 2004; Bailey *et al.*, 2005), whereas an ERP study showed no difference between children

with Asperger's syndrome and control children in the N170 response to faces (O'Connor *et al.*, 2005). Thus, it is tempting to speculate that the weak responses at 135 ms over right extrastriate cortices in children with autism predict the more robust finding of lack of face-sensitive activation at this latency in adults with autism.

At about 240 ms there were also differences between the two groups of children in the responses to faces with different gaze direction. In the children with autism, but not in the normally developing children, direct gaze elicited greater responses than averted gaze. This 240-ms response is broadly consistent with a recent study reporting an anterior mid-line component at 200–260 ms which was stronger to direct gaze than to averted gaze (Grice *et al.*, 2005) and may become interpretable in the context of other findings. Eye contact elicits greater physiological arousal than averted gaze in children with autism compared with normally developing children (Kylliäinen & Hietanen, 2006) and visual fixation to eyes increases amygdala activation in adolescents with autism (Dalton *et al.*, 2005). The stronger cortical activation to straight rather than to other gaze categories in children with autism may reflect a modulatory effect of amygdala circuit activation elicited by a stimulus of perceived emotional significance (Morris *et al.*, 1998; Amaral *et al.*, 2003; Vuilleumier *et al.*, 2004) or may simply reflect amygdala processing of low level visual properties (visible sclera). This interpretation is broadly consistent with a recent model positing an early neurodevelopmental failure in autism involving an extended, possibly amygdala-modulated face-processing system (Schultz, 2005).

At about 240 ms, averted gaze elicited a response in normally developing children that was stronger than to the straight gaze or to closed eyes conditions. This finding is broadly in line with Senju *et al.* (2005) who observed right lateralized and gaze direction-sensitive ERP responses around 280 ms in typically developing children, whereas the response was not lateralized and was insensitive to gaze direction in children with autism. [Note that, in contrast to the present study, Senju *et al.* (2005) required attention to be paid to the direction of gaze.] Given that children with autism can recognize where another person is looking (Baron-Cohen *et al.*, 1995; Leekam *et al.*, 1997; Kylliäinen & Hietanen, 2004), these findings suggest that this knowledge may be mediated by alternative neural strategies (Leekam *et al.*, 1997).

Finally, the reduction in signal amplitude at about 300 ms in children with autism as compared with normally developing children is broadly consistent with previous ERP studies of visual processing in autism (e.g. Courchesne *et al.*, 1989; Ciesielski *et al.*, 1990; Hoeksma *et al.*, 2004). This finding indirectly supports the assumption that, in individuals with autism, diminished signal amplitude at this latency is related to reduced processing capacity and/or reduced task-related attention (e.g. Hoeksma *et al.*, 2004).

In conclusion, the findings from children with autism corroborate the view (Kylliäinen *et al.*, 2006) that the face-processing system undergoes qualitative changes during development, where response strength, topography and stimulus sensitivity rather than response timing are dependent on age. The responses of the children with autism resemble those of 7- to 12-year-old normally developing children, although there are subtle abnormalities associated with the perception of faces and gaze direction. Gaze-sensitive neural responses most clearly differentiated between the two groups of children, although it is unclear whether the unusual response to gaze direction is related to more general face-processing difficulties or is an independent phenomenon. Finally, it should be noted that in the present study, and many others, a clinical control group was not examined. Thus, strictly speaking, the effects observed here might not be specific to autism *per se*. We find this explanation unlikely,

however, because the current findings are consistent with converging evidence obtained from a variety of studies indicating face-processing abnormalities in autism (for a review, see Schultz, 2005). In future studies it would be helpful to determine if Autism Diagnostic Observation Schedule scores relate to the MEG findings because the algorithm scores from the Autism Diagnostic Interview derive mainly from behaviours occurring at the age of 4–5 years.

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Abbreviations

ECD, equivalent current dipole; ERP, event-related potential; IQ, intelligence quotient; MEG, magnetoencephalography; rms, root-mean-square.

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