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Review

Noninvasive detection of face perception characteristics in children with autism spectrum disorders[1]

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Abstract: Children with autism spectrum disorders (ASD) have delayed or deviant social interaction and communication skills. Recent neuroimaging studies have corroborated unique behaviors and patterns of facial information processing in children with ASD, such as less attention toward faces, atypical gaze pattern and face inversion effect, and difficulty in understanding facial expressions and identification of faces. The findings suggest that these specific face recognition characteristics are the result of detail-focused processing and/or a distinctive cognitive style in dealing with visual inputs. This paper reviews our recent work evaluating social perception of faces using noninvasive neuroimaging techniques in children with ASD.

Key words: autism spectrum disorders (ASD), children, noninvasive neuroimaging technique, face.

Children with autism spectrum disorders (ASD) often show difficulty in comprehending emotions and the manner of their expression (expressions, speech volume, intonation, etc.). It is believed that this is caused by an impairment of communication and social cognition. Perceptual information obtained from sensory input needs to be correctly processed for social cognition to occur effortlessly. Some children with ASD are hypersensitive or unresponsive to auditory, somatosensory, or visual stimuli. A paradox is also likely to coexist in this unresponsiveness; for example, some cases have been reported in which, despite being uncomfortable with loud noises, the child will want to listen to a particular loud sound repeatedly. Recently, noninvasive neuroimaging techniques have identified specific responses in the brains of children with ASD who show such perceptual characteristics. However, neurophysiological evidence has been reported more in relation to visual inputs than to auditory inputs.

Noninvasive neuroimaging techniques can visualize brain responses reflecting waking mental activities, in addition to the structural abnormalities and dysfunctions of the brain determined during surgery. For example, functional magnetic resonance imaging (fMRI) has demonstrated the probable brain regions involved in human behaviors and mental activities, although it reveals little about the temporal

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relationships of an activity in different brain regions. Moreover, magnetoencephalography (MEG) has some theoretical advantages, relative to electroencephalography (EEG), in identifying the localization of cortical dipoles with high spatial resolution and with a temporal resolution in the order of milliseconds. On the other hand, near infrared spectroscopy (NIRS) and EEG have the advantage of not needing to fix the participant's body to the recording instrument, although the spatial and temporal resolutions to detect brain activities are lower than those with fMRI and MEG, respectively. Therefore, these may be the most appropriate methods for children and patients. In fact, many EEG studies have revealed atypical patterns of brain responses in several mental activities, including social cognition. These were often confirmed by experiments using visual rather than auditory stimuli, whereas clinical observations have focused more on auditory inputs/outputs in the early stage of development. Experiments using visual stimuli are suitable for the investigation of social recognition excluding the use of language and it is also easy to obtain children's cooperation to maintain attention during these experiments. Progress in the development of noninvasive neuroimaging techniques has made it possible to understand brain function in ASD and has provided us with information that can be correlated with the findings of many observational studies.

Social services and supports for children with ASD seek an understanding of the functional status of cognition resulting from social cues during communication to make an appropriate assessment and choose therapeutic approaches. For instance, the Diagnostic and Statistical Manual of Mental Disorders (DSM) -IV-TR (American Psychiatric Association, 1994), which is often used for operational diagnosis of psychiatric conditions, includes a chapter on pervasive developmental disorder (PDD) that details the evaluation of the cognitive state underlying communication and detailed descriptions of impairments of nonverbal communication based on visual information, such as eye contact and gestures. There is also a chapter on impaired nonverbal communication in the modified checklist for autism in toddlers (M-CHAT) (Robins, Fein, Barton, & Green, 2001), which is used in the assessment of children aged 18 months to 2 years, that includes a large number of items concerning face perception and recognition, such as facial expressions, eye contact, response to gaze, and imitation of expressions. Indeed, many parents of children with ASD notice that something is not right with their babies' face recognition in this period, and this often prompts them to consult experts. Moreover, many recent neuroimaging studies have revealed atypical activities in the brain regions related to face perception in individuals with ASD.

In this paper, we outline the communicative behavior associated with the specificity of face perception in children with ASD without intellectual disability on the basis of evidence obtained using noninvasive neuroimaging techniques. The diagnostic terms used in earlier studies include PDD, the subtypes of autism disorders (AD), and Asperger's syndrome (AS). Based on the concept that PDD, AD, and AS can be viewed as part of a continuum, we use the umbrella term autism spectrum disorders (ASD).

Face detection in visual search

In general, the accuracy of interpreting other people's expressions or behaviors based on peripheral vision is substantially decreased, compared to the use of cues presented in the center of the visual field (Weymouth, 1958). Thus, to make a more detailed observation, the image of the other person is captured in the center of the visual field, where it is easily discernible. In children, the effective visual field for identifying an image is smaller (Shoji & Ozaki, 2007), and as a result, gaze and attention behaviors increased to focus on specific targets. However, because children with ASD have few opportunities to spontaneously direct attention to social cues (Dawson et al., 2004), observation of the face, which is an important social cue, is drastically decreased. Klin, Jones, Schultz, Volkmar, and Cohen (2002) analyzed the gaze domain of subjects viewing a video of a social scene, and reported that the gaze duration for images of objects (but not people's faces) was longer in children/adults with ASD than in typically developing children/adults. We recently analyzed the head orientation of children who were building something or playing games, and confirmed that children with ASD tended not to pay attention to other people's faces (Sakuma et al., 2012). However, after learning communicative behavior through individual coaching, i.e., using techniques such as modeling or rehearsal (not training to focus specifically on each face), children with ASD started to pay attention to the other person and increasingly approached other children in response to communication or for support. Therefore, even if gaze and attention behavior toward people are not inherent in children with ASD, therapeutic interventions using social skills training (SST) may improve visual search skills to social cues.

What is the primary difference in face detection in visual search between individuals with and without ASD? Individuals with ASD often show an interest in nonhuman objects, which is hypothesized to refer to a kind of attentional bias in global processing brought about by a distinctive cognitive style. Furthermore, they often prefer detail-focused processing in visual search. Its characteristics were suggested by the weak cortical coherence (WCC) theory, which proposed that in ASD there is a bias toward local rather than global information processing during perception (Happé & Frith, 2006). Thus, the sensitivity of face detection in visual search may influence a decreased experience of visual inputs, which might reflect the bias. This suggests that increasing the experience of visual inputs may partly improve the characteristic cognitive style in ASD, which would be expected following an intervention such as SST.

On the other hand, the sensitivity of face detection may be reduced by impairments of visual input rather than by the bias in local information processing. This could occur at any stage of visual perception. Visual information is input into the primary visual cortex (V1) through the retina and lateral geniculate nucleus (LGN), and evoked potentials (EP) captured by EEG can visualize this nervous system in relation to an artificial visual stimuli. A few reports have described the hyperactivity of subcortical responses from the periphery to V1 (Belmonte et al., 2004; Gauthier, Klaiman, & Schultz, 2009), which exhibited an impairment of structural encoding to detect facial patterns in many previous studies of ASD.

Processes occurring after the transmission of visual information to V1 have mainly been studied in people through measurements of oscillatory brain changes and event-related cortical potentials/magnetic fields (ERP/ERF) using EEG/MEG, brain blood flow changes using fMRI and NIRS, and glucose metabolism and neuroreceptor status using PET and SPECT. Following the spatial and temporal frequency processing to analyze texture, contrast, and visual orientation in V1, holistic/configural processing in the primary visual cortex and particularly in the extrastriate visual cortical areas involves the extraction of a meaningful pattern from the perceived visual inputs and its encoding for recognition, even when the information is of low resolution. Thus, visual inputs encoded at a higher resolution create patterns different from those derived from encoding at low resolution (Nakashima et al., 2008). Consequently, high-resolution pattern extraction focused on each part of the face would attenuate the face-inversion effect, which results from holistic/configural processing, as compared with the extraction of low-resolution information about the entire face. In individuals with ASD, it is still unclear whether a difference in visuospatial frequency leads to specificity of cognitive bias (Leonard, Annaz, Karmiloff-Smith, & Johnson, 2011). Indeed, because of the attention and interest bias in ASD, a localized bias would occur in facial feature extraction depending on the frequency of perceptual experiences, which might be interpreted as an impairment of holistic/configural processing of visual inputs.

The structural encoding of the face also elicits the N170 component of the ERP originating in the fusiform gyrus and superior temporal sulcus (STS), which appears in both healthy adults and those with ASD (Pierce, Haist, Sedaghat, & Courchesne, 2004; Schultz et al., 2000). Similar to the observation in typically developed children, its amplitude is also greater in children with ASD when looking at a face than at another object (e.g., a plant); thus, compared with other visual information, the N170 component significantly reflects the processing of facial patterns even in children with ASD (Gunji, Inagaki, Inoue, Takeshima, & Kaga, 2009). However, compared with typically developed children/adults, face-inversion effects are not readily reflected in the N170 component in ASD (McPartland, Dawson, Webb, Panagiotides, & Carver, 2004). Moreover, decreased activation in the fusiform gyrus, which is the main source of N170, indicates specificity of structural encoding of face perception (Suzuki et al., 2011). These findings would support the hypothesis that the distinctive cognitive style and/or detail-focused processing in individuals with ASD might be clouded not only by unstable processing of texture and contrast in the primary visual cortex but also by impairments of neural connectivity between the extrastriate visual cortical areas, including the fusiform gyrus (Bertone, Mottron, Jelenic, & Faubert, 2005).

Orientating responses toward eyes and mouth

In healthy adults, N170 latency is significantly delayed when looking only at the mouth and nose compared with looking at the whole face (Bentin, Allison, Puce, Perez, & McCarthy, 1996; Watanabe, Kakigi, Koyama, & Kirino, 1999). However, there was no difference in N170 latencies between looking at the eyes and the whole face (Bentin et al., 1996; Watanabe et al., 1999). That is, our visual orientation when looking at someone might be directed to the eyes (Walker-Smith, Gale, & Findlay, 1977). It has also been reported that more time was spent fixating on the eye area of familiar faces than that of unfamiliar faces (Althoff & Cohen, 1999), which implies the existence of local scanning strategies for face identification to extract semantic information. The above findings suggest that the N170 recorded in fusiform gyrus might be equally activated by looking at the eyes and the whole face, although brain activity in the fusiform gyrus was modulated by the scanning strategy (Morris & McCarthy, 2007; Toyoda et al., 2008).

We tried to identify the part of the face to which children with ASD direct their gaze. Klin et al. (2002) reported that, while the duration of gaze at the eye region was considerably shorter in children/adults with ASD than in healthy children/adults, the duration of gaze at the mouth region was significantly longer in the ASD group than in control group. This characteristic behavior has been reported to appear by one year of age (Osterling & Dawson, 1994). Moreover, because the focus of the gaze outside the face was minimized, even when only the face was presented, little gaze was directed toward the eye region in children with ASD (Pelphrey et al., 2002). In addition, in these children, the gaze was directed at the mouth rather than the eyes when identifying expressions (Spezio, Adolphs, Hurley, & Piven, 2007). In general, importance is placed on the eyes as social cues in communication; however, in children with ASD, there is a tendency to focus on the mouth, which is likely to provide specific communication information such as speech, and has movements that are more evident than those in the eyes.

Although children/adults with ASD tended to look at the mouth region or the background outside the face (Klin et al., 2002; Pelphrey et al., 2002), their N170 latency was not delayed compared with typically developing children/adults. Even when comparing N170 latency for spatial arrangements using upright and inverted faces, there was no difference between individuals with and without ASD. That is, the N170 elicited in the temporo-parietal area does not show any advantage in response to the perception of the eyes and the whole face in individuals with ASD. If difficulty in discerning an inverted face is due to deviation from a cognitive pattern acquired by perceiving the upright face in its entirety, specificity for recognition of an inverted face in ASD may suggest that these individuals do not select the cognitive style of perceiving the entire face.

On the other hand, the unique face recognition strategies of individuals with ASD may reflect their distinctive cognitive style for each of face parts such as eyes, a nose, and mouth, rather than an impairment of holistic/configural processing represented in the face-inversion effect (Joseph & Tanaka, 2003; Lahaie et al., 2006; Teunisse & de Gelder, 2003). Joseph and Tanaka (2003) indicated that the accuracy of identifying eyes was higher than that for other face parts in children with ASD, as well as in typically developing children, in priming tasks using partial faces, where there was no difference in reaction time (RT) related to holistic/configural processing. In other words, holistic/configural processing of the faces seems to be intact in individuals with ASD, but the processing may be influenced by the position of their attentional cues for face perception. An inventive approach has reported that expression identification was influenced by differences in initial fixation position on the face (Kliemann, Dziobek, Hatri, Baudewig, & Heekeren, 2012). The scanning strategy for face identification changes between fixation on the eyes and mouth as an initial position in individuals with ASD, but not in healthy adults, which showed an interaction with changes of blood oxygen level-dependent (BOLD) in the amygdala. This suggests that the inexperienced face recognition scanning strategy in individuals with ASD may be reflected by an abnormal processing profile in the amygdala.

Joint attention

The act of looking at another person's eyes, i.e., eye contact, creates joint attention through understanding the gaze direction of the other person as well as through mutual understanding and sympathy. Both of these qualities develop during early childhood as social recognition and are important cues in communication (Butterworth & Jarrett, 1991; Naoi, Tsuchiya, Yamamoto, & Nakamura, 2008). In ASD, relatively early identification of behaviors such as "not meeting someone's gaze" or "avoiding eye contact" can be often be interpreted as atypical gaze recognition responses (Senju & Johnson, 2009).

Although it has been reported that children with ASD have difficulty understanding gaze direction, which is an opportunity for joint attention, many of them have difficulty in controlling the direction of their own gaze to draw the attention of the other person to themselves or to another target (signaling with their eyes) (Whalen & Schreibman, 2003). Actually, children with ASD acquire the act of searching for the gaze direction of other people. However, typically developing children also predominantly direct their gaze at other items, such as the direction of an arrow, whereas children with ASD do not (Senju, Tojo, Dairoku, & Hasegawa, 2004; Vlamings, Stauder, van Son, & Mottron, 2005). Furthermore, Senju, Tojo, Yaguchi, and Hasegawa (2005) studied ERP in children with or without ASD looking at a picture of a face whose eyes looked straight or in another direction. They reported that children without ASD showed significantly more activity when eye contact was established with the person in the photo than when it was not established, whereas such an effect was not observed in children with ASD. This finding can be interpreted as a cognitive characteristic of averting the direction of the other person's gaze as a distinct manner of gaze detection in children with ASD.

Expression recognition

Eye contact is established when we become aware of someone's gaze, or when looking at someone who notices our gaze. Simply by looking at someone else's eyes we sometimes know what that person is feeling; however, it has been reported this is difficult in individuals with ASD (Hobson, 1986a,b; Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001). In general, visual information encoded as facial structure involves the temporal processing not only of the eyes but also of the entire face in the form of expressions that signify particular emotions (Ekman & Friesen, 1975). Individuals with ASD often demonstrate a difficulty in understanding emotions, and it has therefore been suggested that they have an impairment of expression recognition.

As mentioned earlier, individuals with ASD show specificity in the encoding of facial structure, and this process has been strongly associated with a decrease in fusiform gyrus activity (Suzuki et al., 2011). In individuals with ASD, low activation of the fusiform gyrus during expression recognition has been observed in fMRI studies (Bölte et al., 2006; Piggot et al., 2004; Serra et al., 2003; Wang, Dapretto, Hariri, Sigman, & Bookheimer, 2004). The specificity of facial structure recognition in ASD, such as not using a distinct attentional bias in visual search, may therefore be linked with a difficulty in understanding emotions.

At this point we will discuss how the understanding of emotions is influenced by the process of recognizing changes in expression associated with human movements. The type of emotion expressed changes according to the speed of change in expression (Kamachi et al., 2001). Therefore, understanding expressions may depend to a great extent on responsiveness to temporal changes in facial pattern. The process used to selectively detect human movement, i.e., biological motion (BM), involves activation of the superior temporal sulcus (STS) as well as motion perception related to the MT/V5 visual association area (Downing, Jiang, Shuman, & Kanwisher, 2001). The STS is activated in relation to perception of body movement, such as walking or dancing, and other body movements, such as gaze or the expressions expected from such movements (Grossman & Blake, 2002; Hirai, Kaneoke, Nakata, & Kakigi, 2008; Jastorff & Orban, 2009; Watanabe, Miki, & Kakigi, 2005). However, right hemisphere STS activity was attenuated during BM perception in children with ASD, as compared to typically developing children (Kaiser et al., 2010). In other words, the process of detecting the pattern of movement of other people's facial structure as well as the process of understanding visual information in patterns of facial structure may be dysfunctional in children with ASD (Blake, Turner, Smoski, Pozdol, & Stone, 2003; Klin, Lin, Gorrindo, Ramsay, & Jones, 2009; Koldewyn, Whitney, & Rivera, 2010). This may be a factor inhibiting the understanding of expressions.

Klin et al. (2009) found that typically developing two-year-old children spent a long time looking at the point-light displays of BM that moved like a human, whereas such behavior was not seen in children with ASD. Children with ASD aged 8–10 years also showed difficulties in detecting BM but not in detecting a figure made up of short lines (e.g., a circle) with random motion (Blake et al., 2003). This difficulty remains present in adolescents with ASD (Freitag et al., 2008). However, a few studies have reported typical BM perception in adults with ASD (Cook, Saygin, Swain, & Blakemore, 2009; Murphy, Brady, Fitzgerald, & Troje, 2009). The impairments in children and adolescents are believed to be caused by a developmental delay in BM perception.

The specificity of identification of BM in individuals with ASD has been discussed in relation to the dysfunctional activity in the STS and to developmental validity. The repeated perception of BM through social experiences may facilitate the identification of BM because primary motion perception is intact (Blake et al., 2003). Unfortunately, there have been few neurophysiological and clinical studies of BM perception, and further evidence is urgently needed.

The STS is activated more when viewing meaningful movements than random body movements (Castelli, Frith, Happé, & Frith, 2002; Frith, 2001; Pelphrey et al., 2003; Pelphrey, Morris, & McCarthy, 2004). In addition, temporal processing of other aspects of social cognition, such as voice, phoneme, and language, involves brain regions adjacent to the STS (Boddaert et al., 2004; Gervais et al., 2004; Redcay, 2008). The amygdala is another important region associated with emotion processing, which is activated by the perception of emotions (Takahashi et al., 2010; Williams et al., 2006). The amygdala has been reported to have a weak connection with the fusiform gyrus, which detects amygdala volume and facial structure (Dziobek, Bahnemann, Convit, & Heekeren, 2010; Grelotti et al., 2005; Inoue et al., 2010; Schultz, 2005). Thus, the difficulty in understanding emotions from expressions in ASD may involve impairment in the integration of visual information as well as impairments of social cognition and emotion.

Person identity

In addition to emotions, the semantic processing of a face reflects an individual's identity, as well as interpersonal relationships, such as familiarity and shyness toward other people. The semantic processing is achieved by comparing visual information with images stored in the face recognition unit (Bruce & Young, 1986), and structural encoding of repeatedly learned facial patterns (in terms of familiarity) are reflected – and thus detected – as changes in the activity of the fusiform gyrus. Increased familiarity with faces has also been found to increase activity of the fusiform gyrus in individuals with ASD (Pierce et al., 2004); however, no difference between familiar and unfamiliar faces was found in ERP components in the temporo-occipital area (Gunji et al., 2009). These interpretational discrepancies may be due to differences in study procedures, such as definitions of a familiar face, and similar results were obtained in studies that included typically developing children/adults. However, fMRI studies suggest that the precuneus, medial prefrontal area, and fusiform gyrus are the brain areas related to recognition of facial familiarity and that the activity of these areas have been shown to be attenuated in ASD (Pierce et al., 2004). Person identity is determined by the facial structure encoded in the fusiform gyrus as an image in the facial recognition unit. In general, this process involves detection of the face presented, which corresponds to the ERP component (P300/P3b) appearing in the parietal region with a peak latency of 300 ms or later; however, it has been reported that recognition of familiar faces is not reflected in this ERP component in children with ASD (Dawson et al., 2002; Gunji et al., 2009).

When identifying one's own face, we usually access the memory of self-experience. Keenan, Nelson, O'Connor, and Pascual-Leone (2001) reported that the anterior inferior frontal lobe of the right hemisphere was remarkably activated when identifying one's own face (Pierce et al., 2004; Platek, Keenan, Gallup, & Mohamed, 2004; Platek et al., 2006; Sugiura et al., 2008; Uddin, Kaplan, Molnar-Szakacs, Zaidel, & Iacoboni, 2005). Kaplan, Aziz-Zadeh, Uddin, and Iacoboni (2008) reported that this region is remarkably activated when identifying both the face and human voice. In general, a person can distinguish the self from other people through visual, auditory, and somatosensory perceptions by around two years of age. However, while children with ASD pass the mirror rouge test to identify themselves from others (Amsterdam, 1972), they do not exhibit embarrassment, which often occurs when looking at a self-image. This suggests a failure to develop self-awareness, which may disturb the understanding of other people's thoughts and intentions (Dawson & McKissick, 1984). We found that the ERP component in the parietal region increases with identification of one's own face compared with others' faces in typically developing children (Gunji et al., 2009). However, in children with ASD, the ERP was not enhanced: there was no difference in the brain activity elicited by the meaningful identification of individuals through facial recognition. Furthermore, although the involvement of the lower right inferior anterior lobe in the process of identifying self from others was not apparent, in this study, in ERP analysis using the averaging method (Sakihara, Gunji, Furushima, & Inagaki, 2012), an involvement of this area was detected in hemodynamic studies using fMRI and NIRS. This finding suggests a dysfunction related to self-identification in the same region in children with ASD (Kita et al., 2010a, 2011; Uddin, 2011; Uddin et al., 2008).

Prospects for evaluating face perception

When thinking about support for individuals with ASD, a suitable approach should be selected after ascertaining the cognitive state of the individual involved, to determine what modality would provide appropriate communication skills. In this respect, the above-mentioned neurophysiological evidence (e.g., specificities in person identification by face) should help us not only to understand the individual's present state but also to develop a strategy for therapeutic intervention. Also, the operational diagnostic criteria, based on the knowledge and experience of the child's mother and physician, might be made more objective by application of the neurophysiological evidence. Most of the objective methods of quantitative evaluation described in the present report use noninvasive measurements, making them repeatable, and thus useful in increasing clinical understanding of children's periodic states.

For example, Bölte et al. (2006) reported neurophysiological evidence that therapeutic intervention improves the impairment of face perception in individuals with ASD. They confirmed that training in facial affect identification increased activity in the fusiform gyrus in adolescents and adults with ASD who received a computer-based intervention consisting of two hours training a week over five weeks. This suggests that there is plasticity in the structural and/or semantic encoding of face perception in individuals with ASD, which could be interpreted in terms of the neurophysiological evidence described in the earlier discussion of "Expression recognition." However, it was not mentioned whether the enhancement of fusiform gyrus activity improved communicative behaviors in the longer term.

We have also evaluated the familiarity effect on facial identity processing in children with ASD before and after SST, where a therapist helped the children to learn techniques for improving their behavioral communication problems through modeling, role-playing, and instructions. As mentioned in the earlier discussion of "Face detection in visual search," their behaviors were improved and behaviors appropriate to the occasion increased after SST sessions. Simultaneously, they often paid attention to the other person. The behaviors were proved by analyzing their head coordination during communication (Sakuma et al., 2012). Furthermore, in other children with ASD who had attended a similar SST training, it was found that familiarity effects in relation to identification of the therapist's face, involving an increased P300 amplitude in the ERP, appeared after, but not before, the SST sessions, even though the children were not trained to memorize the therapist's face during SST (Gunji et al., 2013). The P300 might reflect a difference in attentional resource allocation underlying familiarity identification rather than the accuracy of face identification itself (Polish, 2007). Considering the neurophysiological evidence mentioned earlier in the discussions of "Face detection" and "Person identity," an opportunity to meet someone, such as a SST session, may change the state of attentional resource allocation related to face identification, even in children with ASD.

However, in other children with ASD who had attended the similar SST, neurophysiological improvement associated with face detection in visual search and joint attention has not yet been proved (Kita et al., 2010b). Because appropriate methods for the evaluation of the communication skills affected by the intervention have not yet been established, we need to continue to accumulate data to develop optimal methods of evaluation.

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