

Emotional Attribution in High-Functioning Individuals With Autistic Spectrum Disorder: A Functional Imaging Study

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ABSTRACT

Objective: To determine whether expertise in the attribution of emotion from basic facial expressions in high-functioning individuals with autistic spectrum disorder (ASD) is supported by the amygdala, fusiform, and prefrontal regions of interest (ROI) and is comparable to that of typically developing individuals. **Method:** Functional magnetic resonance imaging scans were acquired from 14 males with ASD and 10 matched adolescent controls while performing emotion match (EM) (perceptual), emotion label (EL) (linguistic), and control tasks. Accuracy, response time, and average activation were measured for each ROI. **Results:** There was no significant difference in accuracy, response time, or ROI activation between groups performing the EL task. The ASD group was as accurate as the control group performing the EM task but had a significantly longer response time and lower average fusiform activation. **Conclusions:** Expertise in the attribution of emotion from basic facial expressions was task-dependent in the high-functioning ASD group. The hypothesis that the high-functioning ASD group would be less expert and would have reduced fusiform activation was supported in the perceptual task but not the linguistic task. The reduced fusiform activation in the perceptual task was not explained by reduced expertise; it is therefore concluded that reduced fusiform activation is associated with the diagnosis of ASD. *J. Am. Acad. Child Adolesc. Psychiatry*, 2004;43(4):473–480. **Key Words:** autism spectrum disorders, emotion, functional magnetic resonance imaging.

Autism spectrum disorders (ASD) are pervasive neurodevelopmental disorders characterized by deficits in social cognition and communication and repetitive stereotyped behaviors. High-functioning ASD include Asperger's syndrome and high-functioning autism; these

conditions are differentiated by the respective presence or absence of phrased language by 3 years of age (American Psychiatric Association, 1994).

Despite normal intelligence, high-functioning individuals with ASD have marked deficits in social understanding (Heavey et al., 2000). Although individuals with high-functioning ASD are able to attribute emotion from basic facial expressions (Adolphs et al., 2001; Baron-Cohen et al., 1993; Grossman et al., 2000; Ozonoff et al., 1990; Prior et al., 1990), many of the deficits in social cognition are consistent with reduced expertise in the attribution of emotion (Braverman et al., 1989). Individuals with ASD have particular difficulty attributing emotion from more subtle facial expressions (Baron-Cohen et al., 1997; Kleinman et al., 2001) and multiple facial expressions in actual social situations (MacDonald et al., 1989).

Typically developing individuals have an innate predisposition to engage in social interactions, and human faces are of particular salience from an early age (Ellis,

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1990; Valenza et al., 1996). Typically developing individuals accumulate experience and by their second year have developed the expertise to competently attribute emotion from basic facial expressions (Nelson, 1987). In contrast, individuals with ASD have a reduced innate predisposition to engage in social interactions (Dawson et al., 1998) and are less attentive to faces (Klin et al., 2002; Osterling and Dawson, 1994). Some suggest that individuals with ASD are less expert in attributing emotion from facial expressions because faces are less salient to them (Weeks and Hobson, 1987), and they consequently accumulate less experience (for review see Grelotti et al., 2002).

The attribution of emotion from basic facial expressions has been studied in typically developing individuals by Hariri et al. using an emotion match (perceptual) (EM) task and an emotion label (linguistic) (EL) task. The EM task involves the attribution of emotion from three basic facial expressions and a visual match of emotion, whereas the EL task involves the attribution of emotion from one basic facial expression and affective labeling of the emotion. These tasks offer an opportunity to relate task demand and expertise in the attribution of emotion from basic facial expressions in high-functioning individuals with ASD. In typically developing controls, attribution of emotion has been shown to significantly activate the amygdala and fusiform regions in the EM task, and the fusiform and prefrontal regions in the EL task (Hariri et al., 2000). Accordingly, these brain regions are potentially relevant in understanding the attribution of emotion from basic facial expressions in individuals with ASD.

The amygdala has been associated with the assessment of the emotional salience of facial expressions (Adolphs et al., 1998; Anderson and Phelps, 2001; Hamann et al., 1996; Prather et al., 2001). Hypotheses implicating amygdala dysfunction in autism propose that reduced activation of this region is associated with reduced emotional salience of facial expressions and the social understanding deficit observed in individuals with ASD (Adolphs, 2001; Baron-Cohen et al., 1999; 2000). Previous functional magnetic resonance imaging (fMRI) studies found reduced amygdala activation in tasks that require the individuals with ASD to attribute the gender from neutral faces (Pierce et al., 2001) and from basic facial expressions (Critchley et al., 2000b). Reduced amygdala activation also was seen in high-functioning individuals with ASD in tasks that

required the attribution of complex emotions from only the eyes region of the face (Baron-Cohen et al., 1999). However, a recent study found that high-functioning individuals with ASD who were less accurate in the explicit attribution of emotion from basic facial expressions showed relatively preserved amygdala activation (Critchley et al., 2000b).

In typically developing individuals, the fusiform area (FA) has been associated with the perceptual processing of faces (Clark et al., 1996; Kanwisher et al., 1997; McCarthy et al., 1997; Puce et al., 1996; Tarr and Gauthier, 2000) and with the attribution of emotion from basic facial expressions (Critchley et al., 2000a). The FA, often termed the fusiform "face" area, is considered a key area for processing faces and other visual percepts for which there is expertise (Gauthier et al., 2000). The development of expertise is associated with reduced response time and the progression from feature-based visual processing supported in the inferior temporal gyrus (ITG) to global visual processing supported in the FA (Tarr and Gauthier, 2000).

In contrast, individuals with ASD have been shown to have reduced FA activation when processing facial stimuli (Pierce et al., 2001; Schultz et al., 2000) and when attributing emotion from basic facial expressions (Critchley et al., 2000b). Individuals with ASD also have been shown to activate the ITG, an area normally associated with feature-based analysis of objects, during the processing of facial stimuli (Schultz et al., 2000). These findings suggest that the FA is not specialized for the global processing of facial stimuli in high-functioning individuals with ASD and that expertise in the attribution of emotion is supported outside the FA.

In typically developing individuals, the prefrontal cortex has been associated with the attribution of a mental state or "theory of mind" to another person (Shallice, 2001; Stuss et al., 2001). Individuals with ASD have been found to have mental state or "theory of mind" deficit (Baron-Cohen et al., 1994) associated with reduced activation in the prefrontal cortex (Happé et al., 1996). However, in a recent study high-functioning individuals with ASD, who were less accurate than controls, did not have significantly different prefrontal activations when asked to explicitly attribute emotion from basic facial expressions (Critchley et al., 2000b).

In summary, previous studies support the hypothesis that high-functioning individuals with ASD are less

expert in the attribution of emotion, and suggest that expertise in this cognitive domain may not be supported by the FA. Accordingly, we hypothesized that high-functioning individuals with ASD would demonstrate reduced activation in the FA during the attribution of emotion from basic facial expressions in the perceptual (EM) and the linguistic (EL) tasks. We further hypothesized that amygdala activation in the EM task and prefrontal activation in the EL task would not be significantly different between high-functioning individuals with ASD and typically developing controls.

In this study, high-functioning individuals with ASD and controls attributed emotion from basic facial expressions in two tasks (the EM task and the EL task) while fMRI scans were acquired. Accuracy and response time were measured as indicators of expertise during both tasks.

METHOD

Subject Recruitment

Fourteen high-functioning males with ASD (mean age 13.1 [SD 2.5]; range 9–17 years) and 10 male control subjects (mean age 14.4 [SD 3.3]; range 10–18 years) were recruited. Individuals with ASD were recruited through the Stanford Autism Clinic, professionals working with high-functioning individuals with ASD in the local community, parent networks, and media advertisement. These high-functioning individuals with ASD all had a documented clinical diagnosis of autism or Asperger's syndrome (AS) using *DSM-IV* (American Psychiatric Association, 1994) and a Full Scale IQ of greater than 70. All high-functioning individuals with ASD fulfilled the Autism Diagnostic Observation Schedule-Generic (ADOS-G) (Lord et al., 2000) criteria for the broader ASD, and those with a clinical diagnosis of autism also fulfilled criteria for autism using the Autism Diagnostic Interview-Revised (ADI-R) (Lord et al., 1994). The ADI-R was administered by two trained assessors who had obtained reliability during formal training with the instrument. The assessors conducted interrater reliability on one third of the ADI-R assessments performed and had an interrater agreement of 100% for diagnosis. The ADOS-G was administered by one trained assessor who had obtained reliability during formal training with the instrument. The high-functioning ASD group consisted of seven individuals with autism and seven individuals with AS.

High-functioning individuals with ASD and anxiety or attention-deficit disorder and individuals taking medication for these symptoms were included in the study. Individuals with major psychiatric or neurological disorders or a known etiology for their diagnosis (fragile X, tuberous sclerosis, rubella) were excluded. The control individuals were recruited through media advertisement. Individuals with major psychiatric or neurological disorders were also excluded from the control group. Psychiatric diagnoses were excluded using the Child Behavior Checklist (CBCL) (Achenbach, 1991) and the Symptom Check List (SCL-90) (Derogatis, 1997). Individuals who did not have English as their first language were excluded from both groups. The Stanford Human Subjects Committee approved all protocols, and informed consent was obtained

from all subjects and their parents prior to participation in the study.

Subject Characteristics

Full Scale IQ (FSIQ), Verbal IQ (VIQ), and Performance IQ (PIQ) were assessed for each participant using the Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999). The ASD group (FSIQ = 112 [SD 15.9], VIQ = 104 [SD 20.3], PIQ = 118 [SD 13.6]) and the control group (FSIQ = 116 [SD 10.5], VIQ = 114 [SD 14.2], PIQ = 114 [SD 6.3]) had average to above-average cognitive function. All subjects were right-handed (ASD = 87 [SD 17.0]; control = 82.3 [SD 15.3]) as assessed by the Edinburgh Inventory (Oldfield, 1971). The ethnicity of the ASD group was nine Caucasian, three Asian, and two Hispanic individuals; the control group was seven Caucasian, one Asian, and two Hispanic individuals. There was no significant difference in the socioeconomic status between groups. Two individuals had anxiety disorder and were receiving serotonin reuptake inhibitors, two individuals had attention-deficit disorder and were receiving methylphenidate, and one individual who had both diagnoses was receiving both of these medications in the ASD group.

Design and Procedure

Accuracy and response time were measured as indicators of expertise on two tasks that investigated the attribution of emotion from basic facial expressions. In the EM (perceptual) task (Fig. 1A), the subjects matched the facial expression presented on a target face with the same facial expression present on one of two other faces simultaneously presented below. In the EL (linguistic) task (Fig. 1B), the subjects matched the facial expression presented on the target face with one of two affective labels presented below. A standard set of 18 pictures was used for the experimental tasks and included photographs of faces with fearful, surprised, and angry facial expressions (Ekman and Friesen, 1976). In the control task (Fig. 1C), the subjects matched one of six oval target forms to one of two oval forms presented simultaneously below. Oval target forms were used to control for the visual processing of three percepts. Neutral faces were not used in the control task as adolescents have been shown to attribute emotional salience to neutral faces (Thomas et al., 2001). Each subject performed each of the three tasks.

The experiment consisted of a total of nine blocks: four experimental blocks (two blocks of the EM task and two blocks of the EL task) alternated with five blocks of a control task. Faces were presented in a random order for 5 seconds each, in blocks that contained six photographs. Each 30-second experimental block was presented twice, once with male and once with female faces. Oval forms were presented in a random order for 5 seconds in blocks that contained six oval forms; a 30-second control block was presented five times alternating with the experimental tasks.

The scan started and ended with a 30.5-second rest period. Each of the nine blocks was prefixed by a 2.5-second instruction set. Nine 32.5-second blocks were presented, equating to a total scan time of 5:53 minutes. Functional images were acquired on a 3-Tesla GE Signa scanner using a standard GE whole head coil. A custom-built head stabilization system prevented head movement. The entire brain was imaged in 28 axial slices (4 mm thick, 0.5 mm skip) parallel to the AC-PC line. A shimming procedure was used before acquiring functional MRI scans (Kim et al., 2000). fMRI images were acquired using a T2*-weighted gradient-echo spiral pulse sequence (repetition time [TR] = 200 ms, echo time [TE] = 30 ms,

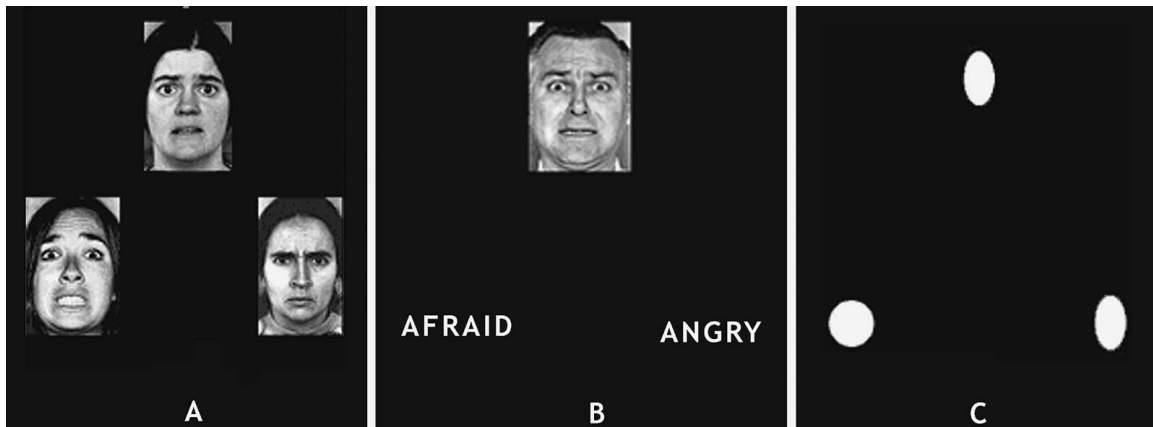


Fig. 1 Example of the stimuli used in the emotion match task (A), the emotion label task (B), and the control task (C).

flip angle = 89° and interleave; field of view = $200 \times 200 \text{ mm}^2$; matrix = 64×64 ; in-plane resolution = 3.125 mm (Glover and Lai, 1998). A high-resolution T1-weighted spoiled gradient recalled (SPGR) three-dimensional anatomical image was acquired during the same scan session (TR = 35 ms; TE = 6 ms; flip angle = 45° ; 24 cm field of view; 124 slices in the sagittal plane; 56×192 matrix; acquired resolution = $1.5 \times 0.9 \times 1.2 \text{ mm}$).

Image Preprocessing

fMRI data analysis has been described in detail previously (Adleman et al., 2002). Briefly, images were reconstructed by inverse Fourier transformation into $64 \times 64 \times 18$ image matrices (voxel size $3.75 \times 3.75 \times 7 \text{ mm}$) using Statistical Parametric Mapping software (SPM99, Wellcome Department of Cognitive Neurology, London, UK). Images were corrected for motion, normalized, and spatially smoothed (full-width/half-maximum = 4 mm). Data were high pass-filtered and temporally smoothed. Voxel-wise t scores were normalized to z scores. For each subject, increases and decreases in activation were recorded by contrasting the experimental and control conditions.

Regions of Interest Processing

The three regions of interest (ROIs), designated a priori, were identified using BrainImage software (Reiss, 2002), and anatomical ROIs were drawn on normalized high-resolution coronal anatomical images by individuals blinded to diagnosis as follows.

The prefrontal ROI was designated using AC-PC stacks; each was oriented along the AC-PC axis on the Talairach grid and resliced. All brain tissue anterior to the slice in which the corpus callosum first appears, and bridges the left and right hemispheres, was included.

The amygdala ROI was drawn from the central, thick white matter tract in the temporal lobe until that tract was intersected either by the white matter tract or CSF. The inferior border of the ROI was drawn superior to this white matter tract. The medial border was drawn along the medial aspect of the white matter tract, CSF, pons, and brain stem. The superior border was drawn following the white matter tract or CSF boundary above, and the lateral border followed the thick, central white matter tract of the temporal lobe.

The fusiform ROI was drawn from the deepest part of the occipitotemporal sulcus; this sulcus was followed posteriorly to the

end of the cortical matter. The boundary of the cortical matter was followed medially until the collateral sulcus, which divides the fusiform gyrus and the entorhinal cortex. This sulcus was followed to the deepest point where the gray matter and white matter converge.

Demographic and Neuropsychological Statistical Analysis

Independent samples t tests were undertaken for age; FSIQ, VIQ, and PIQ; and accuracy and response time in the EL and EM tasks (between-group factor: diagnosis [ASD and control]).

ROI Statistical Analysis

All voxels containing gray matter were measured, and the mean z scores of the voxels activated above $z = 1.67$ ($p < .05$) were used to measure the average activation intensity within each ROI. All average activation levels were log-transformed to normalize the distribution for each ROI. Between-group analysis of covariance (ANCOVA) was undertaken for average activation of fusiform, amygdala, and prefrontal ROIs for the EL and EM tasks (between-group factors: diagnosis [ASD and control]; covariates: accuracy and response time).

RESULTS

Demographic and Neuropsychological Results

Independent samples t tests showed no significant difference in age ($t_{22} = -0.99$; $p = .33$) or intelligence (FSIQ: $t_{22} = 0.633$; $p = .53$; VIQ: $t_{22} = -1.26$; $p = .22$; PIQ: $t_{22} = 0.897$; $p = .328$) between the two groups. There also was no significant difference in accuracy between groups in the EM task ($t_{22} = -1.626$; $p = .118$) (ASD mean = 76% [SD 25%], control mean = 90% [SD 11%]) or the EL task ($t_{22} = -1.768$; $p = .095$) (ASD mean = 69% [SD 27%], control mean = 85% [SD 12%]). There was a significant difference between groups in response time (Fig. 2) in the EM task ($t_{22} = 3.33$; $p = .003$; ASD mean = 2,531 sec [SD 393]; control mean = 2,047 sec [SD 272]). There was no sig-

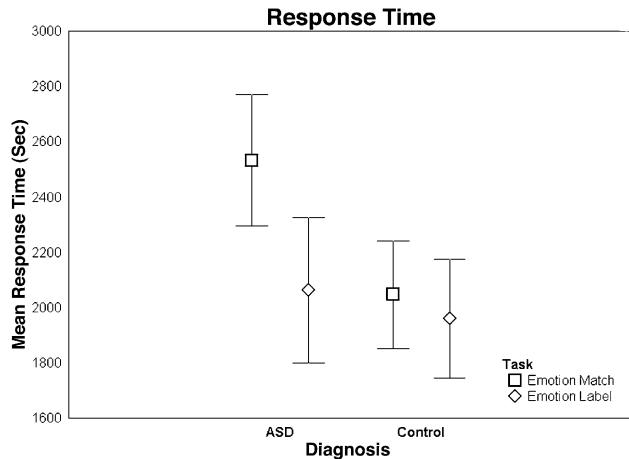


Fig. 2 There was a significant difference ($F_{1,22} = 3.33$; $p = .003$) in the mean average response time between the autism spectrum disorder (ASD) group and the control group in the emotion match task. Standard deviations are shown.

nificant response time difference between groups in the EL task ($t_{22} = 0.623$; $p = .539$; ASD mean = 2,141sec [SD 363]; control mean = 1,960 sec [SD 300]). Accuracy and response time were incorporated as covariates into the ANCOVA model to remove the variance attributable to expertise and to ascertain the average activation attributable to diagnostic group (Fig. 2).

ROIs

Amygdala. ANCOVA indicated that there was no significant difference in the average amygdala activation between groups in the EM ($F_{1,22} = 3.39$; $p = .56$) or EL ($F_{1,22} = 1.81$; $p = .198$) tasks.

Fusiform Gyrus. ANCOVA indicated that there was a significant difference in average fusiform activation ($F_{1,22} = 12.02$; $p = .003$) between groups in the EM task; specifically, there was significantly less average fusiform activation in the ASD group (mean = 2.13 [SD 0.32]) than in the control group (mean = 2.61 [SD 0.31]) (effect of covariate: response time: $F_{1,22} = 8.8$; $p = .008$). There was no significant difference in average fusiform activation ($F_{1,22} = 0.111$; $p = .743$) between the ASD (mean = 2.52 [SD 0.33]) and the control (mean = 2.47 [SD 0.34]) groups in the EL task (Fig. 3).

Prefrontal Cortex. ANCOVA indicated that there was no significant difference between groups for average prefrontal activation in the EM ($F_{1,22} = 0.028$; $p = .87$) or the EL ($F_{1,22} = 0.086$; $p = .772$) tasks.

DISCUSSION

Our hypothesis that high-functioning individuals with ASD would be less expert in the attribution of emotion from basic facial expressions was supported only for the EM task. Specifically, the ASD group had a significantly longer response time than the control group in the EM task. The ASD and the control groups had comparable accuracy and response times, and thus expertise, on the EL task. Comparing different brain activations is facilitated when both groups are able to perform the tasks (Price and Friston, 1999). However, differing expertise potentially confounds the interpretation of brain activation (Fletcher et al., 1998). Therefore we covaried for differences in both accuracy and response time to determine the ROI activation attributable to diagnostic group.

Our findings support the hypothesis that activation in the amygdala and prefrontal regions of high-functioning individuals with ASD is comparable to that of typically developing individuals for both the EL and the EM tasks. The most similar study to date also found no significant differences in amygdala and prefrontal activation when high-functioning individuals with ASD were explicitly instructed to attribute emotion from basic facial expressions (Critchley et al., 2000b). One possible explanation for these findings is that high-functioning individuals with ASD, although able to attribute emotion from basic facial expression, do so only when this is a necessary and explicit aspect

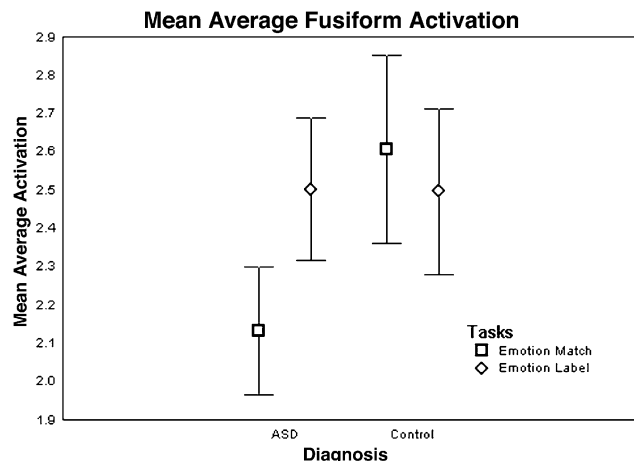


Fig. 3 There was a significant difference ($F_{1,22} = 12.02$; $p = .003$) in the mean average fusiform activation between the autism spectrum disorder (ASD) group and the control group in the emotion match task after covarying for expertise. Standard deviations are shown.

of the task. Previous studies that have shown reduced prefrontal (Happé et al., 1996) and reduced amygdala (Baron-Cohen et al., 1999; Critchley et al., 2000b; Pierce et al., 2001) activation did not involve the explicit attribution of emotion from basic facial expressions. In these studies, there were also differences in performance between groups that potentially could have confounded the interpretation of the observed profiles of activation.

In the EL task, both groups were equally expert, as shown by comparable average accuracy and reaction times, and there was no significant difference in average fusiform activation. This finding was contrary to our hypothesis and supports the notion that high-functioning individuals with ASD are expert in attributing emotion when stimuli are presented in a language-based (EL) paradigm. The equivalent fusiform activation in the EL task suggests that the fusiform is involved in attributing emotion from basic facial expressions in both the ASD and the control groups. One plausible explanation is that both groups activate the fusiform to support the rapid global processing of the basic facial stimuli in the EL task. However, in the EL task, there was no control for the labeling of basic facial expressions. Therefore, the similar fusiform activation between the groups may have been related to the reading of the affective labels in the EL task.

In the EM task, the ASD group had a significantly longer response time than the control group. This finding supports the hypothesis that high-functioning individuals with ASD have less expertise in the EM task. However, covarying for response time did not explain the reduced fusiform activation in the ASD group. Individuals with ASD have been reported to have reduced fusiform activation when processing facial stimuli (Pierce et al., 2001; Schultz et al., 2000). This study supports the finding that reduced fusiform activation is associated with diagnosis.

The principal finding of this study was that the expertise in the attribution of emotion from basic facial expressions is task-dependent in individuals with ASD. Explanation of the difference in expertise in the ASD group requires consideration of the differences between task demands. The presentation of a single facial expression and affective labels may facilitate expertise in the attribution of emotion in the EL task. Individuals with ASD may have similar expertise in the EL task because they use a language-based strategy to facilitate

the attribution of emotion. Reduced expertise in the perceptual (EM) task may be explained by the absence of affective labels and/or the increased number of facial stimuli presented, constituting an increased global processing load. Individuals with ASD have been suggested to have reduced expertise in the global processing of facial stimuli (Grelotti et al., 2002) and during the processing of facial stimuli to activate the ITG, an area associated with feature-based analysis of objects (Schultz et al., 2000). The use of a feature-based strategy supported outside the fusiform offers a possible explanation for the reduced expertise and reduced fusiform activation when individuals with ASD attribute emotion from basic facial expressions in the perceptual (EM) task.

Limitations

The sample size used in this study was relatively small, reducing the power of the study to detect significant differences between groups. This is of particular relevance when considering the null findings for amygdala and prefrontal regions. The sample size was, however, comparable to, or greater than, samples reported in other studies of face and emotion processing in autism (Critchley et al., 2000b; Pierce et al., 2001; Schultz et al., 2000).

Future fMRI studies with larger sample sizes are required to replicate the findings of this study. These studies should exclude individuals taking medication as it is difficult to predict the implications of medication on functional imaging findings. Future fMRI studies should also include females and lower-functioning individuals with ASD to determine whether the findings of this study can be generalized across different populations with ASD. Further fMRI studies should also determine whether the clinical interventions that increase experience actually facilitate the development of expertise in the attribution of emotion from facial expressions, and identify the brain regions that support expertise in individuals with ASD.

Clinical Implications

The finding that expertise in the attribution of emotion from basic facial expressions was task-dependent in high-functioning individuals with ASD has potentially important clinical implications. First, there are many anecdotal accounts of high-functioning individuals with ASD who are able to attribute emotion from basic

facial expressions but have difficulty in actual social situations involving the rapid attribution of emotion from multiple facial expressions. This study provides research evidence to support this anecdotal finding and offers a possible explanation for this phenomenon. Second, our findings have clinical implications when assessing emotional attribution in high-functioning individuals with ASD. In comparison to typically developing controls, assessment of expertise in the attribution of emotion is task-dependent. Therefore, expertise should not be generalized across emotion attribution tasks in high-functioning individuals with ASD. Third, this study suggests that social skills interventions should explicitly instruct individuals with ASD to attribute emotion to each facial expression when presented with more than one facial expression, and process information from the whole face, especially when the task can be accomplished by matching facial characteristics. Social skills interventions also should train high-functioning individuals with ASD for speed, as well as accuracy, when attributing emotion from basic facial expressions, as both are required for expertise in actual social situations.

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