The functional neuroanatomy of social behaviour
Changes in cerebral blood flow when people with autistic disorder process facial expressions

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Summary
Although high-functioning individuals with autistic disorder (i.e. autism and Asperger syndrome) are of normal intelligence, they have life-long abnormalities in social communication and emotional behaviour. However, the biological basis of social difficulties in autism is poorly understood. Facial expressions help shape behaviour, and we investigated if high-functioning people with autistic disorder show neurobiological differences from controls when processing emotional facial expressions. We used functional MRI to investigate brain activity in nine adults with autistic disorder (mean age ± standard deviation 37 ± 7 years; IQ 102 ± 15) and nine controls (27 ± 7 years; IQ 116 ± 10) when explicitly (consciously) and implicitly (unconsciously) processing emotional facial expressions. Subjects with autistic disorder differed significantly from controls in the activity of cerebellar, mesolimbic and temporal lobe cortical regions of the brain when processing facial expressions. Notably, they did not activate a cortical ‘face area’ when explicitly appraising expressions, or the left amygdala region and left cerebellum when implicitly processing emotional facial expressions. High-functioning people with autistic disorder have biological differences from controls when consciously and unconsciously processing facial emotions, and these differences are most likely to be neurodevelopmental in origin. This may account for some of the abnormalities in social behaviour associated with autism.

Keywords: Asperger syndrome; attention; autism; facial expression; fMRI

Abbreviations: BOLD = blood oxygenation level-dependent; fMRI = functional MRI; FPQ = fundamental power quotient; ICD = International Classification of Disease; WAIS-R = Wechsler Adult Intelligence Scale—Revised

Introduction
Autism is characterized by pervasive developmental abnormalities in social and emotional behaviour, associated with stereotyped and obsessional behaviours (World Health Organization, 1993; Wing, 1997; Gillberg, 1998). Qualitative impairments in reciprocal social interaction include inadequate appreciation of social–emotional cues (as shown by a lack of responses to others’ emotions), poor use of social signals, and a lack of socio-emotional reciprocity.

Individuals with classic Kanner-type autism (Wing, 1997; Gillberg, 1998) also have delayed language development, and many have learning disability (mental impairment). However, ~20% are classified as high-functioning because they are of normal or superior general intellectual skills, despite having a history of early language delay. Individuals with Asperger syndrome have no history of language delay and have normal or superior intellectual abilities, but also show the characteristic impairments of reciprocal social interaction. Although, by definition [International Classification of Disease—Revision 10 (World Health Organization, 1993)] there is always a disparity between social understanding and cognitive skills in autism, this disparity is particularly marked in high-functioning individuals with autism/Asperger syndrome. However, the biological associates of abnormal social behaviour in autism are poorly understood.

The neuropathological basis of autism has not been
determined, and much of the work has focused on classic Kanner-type autism. However, a number of anatomical substrates have been suggested. Damasio and Maurer proposed that autism is due to dysfunction of mesolimbic (dopaminergic) brain areas (ventromedial prefrontal cortex, medial temporal lobe, striatum and limbic thalamus) because damage to these brain regions can cause features of autism (impaired social and emotional functioning, stereotyped behaviours, mannerisms and obsessivity) (Damasio and Maurer, 1978). This hypothesis is supported by studies which have reported that (i) in animals, social deficits and stereotypical behaviour are associated with damage to the medial temporal lobe in infancy (Bachevalier, 1994); (ii) in humans, autistic-type patterns of behaviour are associated with abnormalities in the temporal lobe caused by other neurodevelopmental disorders (e.g. tuberous sclerosis) (Bolton and Griffiths, 1997); and (iii) individuals with autism are impaired on ‘frontal’ executive tasks (Ozonoff et al., 1991; Hughes et al., 1994). Non-limbic areas such as the parietal lobe have also been suggested as important in aetiology because the inattention of children with autism to salient social cues resembles inattention and neglect following parietal lobe damage (Bryson et al., 1990). Some children with autism are also impaired on neurological tests sensitive to parietal dysfunction (Haas et al., 1996). Other investigators have proposed that developmental abnormalities of the cerebellum (Courchesne et al., 1988) or dysfunction of cerebellar–cortical serotonergic pathways are patho-aetiological factors for autism (Chugani et al., 1997).

Consistent with this, acquired cerebellar lesions have been associated with deficits in social and emotional behaviour, executive dysfunction and obsessivity (Schmahmann and Sherman, 1998). Thus the finding that lesions to discrete brain areas may result in clinical symptoms that are also present in people with autism suggests a neurobiological basis and implicates dysfunction of the mesolimbic areas, parietal cortex and cerebellum. However, lesion studies only provide partial insight into the biological basis of autistic disorder.

There is direct evidence for neurobiological abnormalities in autism. Although there have been very few post-mortem studies of people with autism, these have shown megencephaly (Bailey et al., 1998) and abnormal distribution of neurones in both limbic and non-limbic areas (Bauman and Kemper, 1985; Bailey et al., 1998). In vivo brain imaging studies of brain anatomy in autism have also reported megencephaly (Piven et al., 1995), as well as abnormal gyriﬁcation of cortical regions (including the parietal lobe) (Piven et al., 1990; Courchesne et al., 1993), hypoplasia of the cerebellar vermal lobules (Courchesne et al., 1988; Hashimoto et al., 1995) and decreased volume of the corpus callosum (Piven et al., 1997), the anterior cingulate (Hazneder et al., 1997; Abell et al., 1999) and the left inferior frontal gyrus and occipitotemporal junction (Abell et al., 1999).

Contrary to animal models (Bachevalier, 1994), in human autism the hippocampal complex is reported to be of normal size (Piven et al., 1998), and one study reported an increase in volume of the (left) amygdala, bilateral anterior cerebellar lobes and vermis, and the lateral temporal lobe visual cortex (Abell et al., 1999). Thus, imaging studies of autism suggest regionally distributed differences in brain anatomy.

PET studies, although not always consistent in their findings, have reported delayed metabolic maturation of the prefrontal cortex in autistic children (Zilbovicius et al., 1995), and in adults reduced: (i) functional associations between frontal and parietal regions at rest (Horwitz et al., 1988); (ii) prefrontal and anterior cingulate metabolism during attentional and verbal learning tasks (Seigel et al., 1995; Haznedar et al., 1997); and (iii) medial prefrontal blood flow during ‘theory of mind’ tasks (Happe et al., 1996). A functional MRI (fMRI) study reported reduced amygdala activation in high-functioning adults with autism when they were explicitly appraising mood from pictures of eyes (Baron-Cohen et al., 1999).

Thus, in vivo anatomical studies suggest that individuals with autism have diffuse abnormalities in brain development, and functional imaging studies have highlighted dysfunction of neuronal pathways involving the frontal lobe and perhaps the amygdala.

Facial expressions of emotion are important and culturally universal social signals (Ekman, 1998) and can be processed both explicitly (consciously) and implicitly (unconsciously). The rules and skills guiding normal social interactions are complex, but include the appreciation and understanding of other people’s thoughts and intentions (‘theory of mind’) and the explicit and implicit processing of emotional expression.

Normal children acquire theory of mind skills in the first 3–4 years of life, and process non-verbal social cues implicitly unless circumstances are exceptional. Many of the social impairments in people with autism are consistent with a deficit in theory of mind and/or differences in the processing of other people’s emotions (Baron-Cohen et al., 1994). For example, children or less able adults with autism are frequently impaired on theory of mind tests and when interpreting people’s feelings from emotional facial expressions. In contrast, many high-functioning adults can score normally on tests of theory of mind (Bowler, 1992) and the explicit identification of facial emotion, and may learn to guide their everyday social interactions by consciously (explicitly) applying intellectual strategies (e.g. understanding that someone will behave positively because their mouth is turned up at the corners, i.e. they are smiling). Nonetheless, they still exhibit signiﬁcant social impairment. Thus, people with autism may not simply have a deﬁcit in theory of mind, or in the ability to process explicitly emotion per se; rather, they may have abnormalities in the normal functional interaction between the use of explicit and implicit strategies that people without autism use to guide social behaviour.

We have reported previously that, in healthy controls, temporal lobe regions are activated during the explicit processing of facial expression, whereas limbic/paralimbic areas are activated during implicit processing (Critchley et al., 2000). Therefore, we used fMRI to determine if there are
significant differences between high-functioning adults with autistic disorder (we use the term ‘autistic disorder’ in this paper to describe individuals who meet ICD-10 criteria for autism or Asperger syndrome and who are of normal intelligence, i.e. IQ > 70) and healthy controls when explicitly and implicitly processing facial expressions. Because some high-functioning adults with autistic disorder report that they use explicit mechanisms to guide social behaviour but still display abnormal social behaviour, it was hypothesized that there are significant differences between people with autistic disorder and controls in the comparison of explicit versus implicit processing of facial expressions (as reflected by a significant diagnosis × experiment interaction). In addition, it was hypothesized that individuals with autistic disorder would show less activity than controls in brain areas associated with the implicit processing of facial expressions.

Methods

Subjects
We studied nine high-functioning adult male volunteers [mean age ± standard deviation, 37 ± 7 years; FSIQ (full-scale IQ) 102 ± 15] clinically diagnosed, using ICD-10, as having Asperger syndrome (seven subjects) or autism (two subjects) (Table 1). Diagnosis was confirmed where possible with the Autism Diagnostic Interview (Lord et al., 1994), a structured interview of parental informants to aid the diagnosis of autism. We also studied nine right-handed adult male controls (27 ± 7 years; FSIQ 116 ± 10). Intelligence was measured using the Wechsler Adult Intelligence Scale—Revised (WAISR) (Wechsler, 1981), and subjects with autistic disorder were tested outside the scanner on their ability to recognize faces, using the Warrington recognition memory task for faces (Warrington, 1984). There were no significant differences between groups in age or intelligence. All subjects were screened to exclude co-morbid psychiatric illness (e.g. schizophrenia, depression) and neurological and extracerebral disorders that might affect brain function (e.g. epilepsy or hypertension), and they gave informed consent, in accordance with the Declaration of Helsinki, for a protocol passed by the local research ethics committee (Bethlem and Maudsley Hospitals). The subjects were familiarized with the stimuli and task procedure before scanning.

Experimental tasks
In two separate experiments, facial stimuli from a standard series (Ekman and Friesen, 1975) were presented to subjects pseudorandomly in alternating (on/off) 30 s conditions. Each face was presented for 3 s with an interstimulus interval of 0.75 s. In the ‘on’ condition, subjects viewed mixed high-emotion facial expressions (four happy, four angry), whereas in the ‘off’ (control) condition the subjects viewed neutral facial expressions. In Experiment 1 (explicit task) subjects were asked to attend to and judge the facial expression of each stimulus, and signalled their judgement by pressing one of two buttons of a hand-held response pad with the right thumb. The direction of the response was indicated by a legend beneath the stimuli (HAPPY/ANGRY – NEUTRAL). In Experiment 2 (implicit task), subjects attended to and judged the gender of each face (which was counterbalanced across both phases of the task), responding according to the legend: MALE – FEMALE. Thus, both experiments examined the processing of happy and angry faces relative to neutral faces, and required the subjects to attend to each face stimulus. Only in Experiment 1 (explicit task) did the subjects consciously attend to the emotional expression depicted on each face (Fig. 1). The order of the experiments was counterbalanced pseudorandomly across subjects to control for session effects that might otherwise introduce bias from time-dependent differences in the cognitive set or physiology of the subjects or from technical artefacts such as scanner drift, which may affect the signal-to-noise ratio.

Data acquisition and analysis
Subjects were scanned while performing these tasks using a 1.5 Tesla GE Signa System (General Electric, Milwaukee,
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Fig. 1 Stimuli used in the experimental tasks. In two experiments with a repeated on/off block design, subjects were shown pictures from a standard series. In both experiments, subjects were presented with a mixture of four happy and four angry faces in the on condition and eight neutral faces in the off condition. The stimuli were pseudorandomized and counterbalanced for gender in each phase. Stimuli were presented for 3 s with an interstimulus interval of 0.75 s. There were five repetitions of the on/off phases, over 5 min. In Experiment 1 (explicit task), subjects attended to and judged the facial expressions. In Experiment 2 (implicit task), subjects attended to and judged the facial gender.

Wis., USA) fitted with ANMR hardware and software (ANMR, Woburn, Mass., USA) at the Institute of Psychiatry, London. A quadrature birdcage headcoil was used for RF (radio frequency) transmission and reception. One hundred T2*-weighted images depicting blood oxygenation level-dependent (BOLD) contrast were acquired [TE (echo time) 40 ms, TR (repetition time) 3000 ms] over 14 non-contiguous slices parallel to the intercommissural line (in-plane resolution 3.1 mm, slice thickness 5 mm, slice skip 0.5 mm), and a high-resolution inversion recovery echoplanar image of the whole brain was acquired during the same session for the purpose of spatial registration [TE 73 ms, TR 16 000 ms, 43 slices, in-plane resolution 1.5 mm, slice thickness 3 mm). The subjects were secured during scanning to prevent head movement, and standard methods were used to correct for residual movement (Friston et al., 1996). Generic brain activation mapping software (Brammer et al., 1997) was used to calculate the power of the BOLD signal changes at the frequency of alternation between the on and off conditions. This was expressed for each voxel as the fundamental power quotient (FPQ; power of frequency-related signal change divided by its standard error) and was represented in a parametric map, registered to standard coordinates (Talairach and Tournoux, 1988). The significance of BOLD signal changes was computed from the median value of FPQ at each voxel of the observed parametric maps after comparison with a null distribution of median FPQs from randomized parametric maps. Post hoc analysis of the time-course of regional increases in BOLD signal was applied in the analyses to determine the relationship between regional signal changes in the on and off conditions. We used a factorial design to examine significant regional BOLD activity in the brain due to the main effect of diagnosis (autistic disorder versus control) and the diagnosis × experiment interaction. ANOVA (analysis of variance) of voxel-wide BOLD signal changes was constrained to brain areas that showed significant activation (P < 0.001) in at least one of the four conditions. The total search volume for ANOVA was 355 voxels, and the expected number of false-positive activations at P < 0.01 was 4 voxels. We report voxel clusters of ≥3 showing significant (P < 0.01) diagnosis × task interaction. Where there was a significant interaction, we plotted the mean power (FPQ) of the BOLD signal change (from a 3 × 3 voxel volume) for each individual performing each experiment, in order to determine whether the significant interaction at that location
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Fig. 2 Patterns of significant \((P < 0.001)\) activations of nine subjects with autistic disorder during explicit and implicit processing of emotional facial expressions. Group data in-phase with the processing of happy and angry faces (versus neutral expressions) are plotted in red on axial slices of a normalized template brain derived from the structural scan of one subject. Vertical distances of axial sections are given above in millimetres, corresponding to Talairach \(z\)-coordinates. Experiment 1 tested the explicit processing of facial expressions: subjects judged the emotional content of visually presented facial stimuli by signalling with a button-press response if the face depicted a happy, angry or neutral expression. Experiment 2 tested the implicit processing of facial expression: subjects judged the gender of facial stimuli by signalling with a button-press response if the face was male or female. Brain regions indicated are (1) right amygdal hippocampal junction; (2) right fusiform gyrus; (3) anterior cingulate cortex; (4) left dorsolateral prefrontal cortex; (5) left superior/middle temporal gyrus; and (6) posterior cingulate/precuneus.

was due to differences unique to one task (e.g. underactivity during implicit processing in individuals with autistic disorder).

Results

Behavioural performance

Subjects with autistic disorder and controls were debriefed after scanning, and both groups reported no difficulties in viewing or judging the face stimuli. However, although the subjects with autistic disorder performed well above chance, performance data showed that they made more errors than controls during the explicit processing of facial expressions (Experiment 1, controls 97% correct, subjects with autistic disorder 82% correct). The number of errors made by subjects with autistic disorder during this task correlated (Pearson) significantly with deficits in performance of the Warrington face recognition memory task \((r = 0.915, P < 0.05)\). Thus, subjects with autistic disorder may have had different subjective experiences of task difficulty compared with controls, which were not elicited at debriefing. These may have contributed to the differences in brain activity described below.

Brain activity associated with task performance

When subjects with autistic disorder performed the experiments, explicit processing of emotional facial expressions was associated with significantly \((P < 0.001)\) increased activation of the right amygdal hippocampal junction (Talairach coordinates of cluster centroid, \(x, y, z: 35, -3, -13\)), right fusiform gyrus \((-29, -50, -10)\), anterior cingulate/medial prefrontal cortex \((-6, 34, 14)\), left dorsolateral prefrontal cortex \((-25, 36, 9)\), left superior temporal gyrus \((-48, -28, 12)\) and posterior cingulate/precuneus \((-4, -53, 28)\). Implicit processing of facial expressions in subjects with autistic disorder was associated with significant activation in the left superior and middle temporal gyrus \((-52, -28, 4)\), cerebellar vermis \((-3, -72, -18)\) and left anterior insula \((-23, 17, 4)\), extending to the left dorsolateral prefrontal cortex (Fig. 2).

To explore the differences between controls and subjects with autistic disorder when processing facial expressions explicitly and implicitly, we used a \(2 \times 2\) factorial design to determine the main effect of experiment (explicit versus implicit processing), the main effect of diagnosis, and the diagnosis \(\times\) experiment interaction. In the main effect of experiment, activity in the left fusiform gyrus was greater during the explicit processing of the expressions than during the implicit processing. Activity in the left insula and left anterior hippocampus was greater during the implicit task than during the explicit task (Table 2).

Group differences during explicit and implicit processing of facial expressions

In the main effect of diagnosis, individuals with autistic disorder had significantly greater activity than controls in the left superior temporal gyrus (auditory cortex) and left peristriate visual cortex, whereas controls had significantly more activity in the right fusiform cortex (Table 2).

It was hypothesized that adults with autistic disorder, compared with controls, would show greater abnormalities during the implicit processing of expressions than when they
attended explicitly to facial emotion. This was tested by examining the diagnosis × experiment interaction, to identify brain areas that differed significantly between groups in relative activity during explicit versus implicit processing of expressions. The cerebellar vermis, left lateral cerebellum, striatum (left globus pallidus and putamen), paralimbic and limbic areas (left insula and the amygdalohippocampal junction) and left middle temporal gyrus showed a significant diagnosis × experiment interaction (Table 2).

To interpret these findings further, we determined the task-related activity in each of these brain areas for each subject. In keeping with the hypothesis that subjects with autistic disorder would show less activity than controls during the implicit processing of expressions, the left cerebellum and left amygdalohippocampal region were activated in controls but not in subjects with autistic disorder (Fig. 3). However, during the explicit processing of expressions, the left middle temporal gyrus was activated in controls but not in subjects with autistic disorder. Task-dependent differences in the other brain areas where a significant diagnosis × condition interaction was expressed (i.e. the cerebellar vermis, left pallidum and left insula) were not readily interpretable (e.g. activity in the cerebellar vermis was increased in the explicit task in controls but increased in the implicit task in the subjects with autistic disorder). It is possible that these regions may reflect the differential recruitment of separate neural systems by the two groups when explicitly and implicitly processing facial expression, but this remains speculative.

Discussion
Facial expressions are an outward display of emotional state, and are important cues in social communication (Ekman, 1998). Significant differences between subjects with autistic disorder and controls were found during the processing of facial expressions in the activity of early visual and auditory cortices (main effect of diagnosis), despite the fact that the groups were matched on the basis of age, IQ, education and occupational level. There were also significant differences in the relative patterns of activity during the explicit and implicit processing of facial expressions in the cerebellum, mesolimbic areas (insula, amygdalohippocampal junction and putamen) and lateral temporal lobe. Thus, high-functioning individuals with autistic disorder appear to have significant biological differences from controls in the function of brain areas that have previously been implicated in the aetiology of autism (e.g. Damasio and Maurer, 1978), particularly when shifting from explicit to implicit processing of facial expressions. However, caution is required in the interpretation of these results for a number of reasons. First, we could not address the developmental time course of these impairments in the autism group. Secondly, although subjects with autism were able to perform well above chance in the experimental
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The differences in brain function we observed in this study provide some support for the hypothesis that autism is associated with cerebellar abnormalities, and other research has reported significant differences in the anatomy of the cerebellum (Courchesne et al., 1988; Hashimoto et al., 1995). However, macroscopic cerebellar abnormalities may occur in the absence of autistic symptoms, and are not apparent in everyone with autism (Kleiman et al., 1992; Ciesielski and Knight, 1994). Moreover, oculomotor tests for cerebellar dysfunction are normal in adolescents and adults with autism (Minshew et al., 1999). Nonetheless, our study suggests that people with autistic disorder differ from controls in the activity of two cerebellar regions during the implicit, but not the explicit, processing of facial expressions. In adults without autism, cerebellar damage may give rise to clinical symptoms that resemble features of autism (impaired executive skills, flattening of affect and abnormal social behaviour). It has been suggested that these cognitive/affective symptoms arise from dysfunction of the pathways connecting the cerebellum to the prefrontal, limbic and striatal regions of the brain (Schmahmann and Sherman, 1998). Also, abnormal 5-hydroxytryptamine (serotonin) neurochemistry within one such cerebellar-thalamocortical pathway has been reported in children with autism (Chugani et al., 1997). Thus, some of the functional abnormalities observed in the present study may reflect abnormal cerebellar structure, and perhaps abnormal serotoninergic function.

Our finding that people with autistic disorder have abnormal activity within the medial temporal lobe, striatum and insula when processing facial emotion are broadly consistent with Damasio and Maurer’s mesolimbic model of autism (Damasio and Maurer, 1978), and previous studies have implicated these brain areas in the processing of facial expressions (e.g. Sprengelmeyer et al., 1996; Phillips et al., 1997). Because high-functioning people with autism have social deficits despite the preservation of explicit intellectual skills, we explored which brain areas could have influenced the between-group differences in patterns of activation. Further studies are required to address these issues.

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abnormalities and autism-like behaviours (e.g. stereotypies) (Bachevalier, 1994; Bolton and Griffiths, 1997). Also, studies of people with autism have reported: (i) abnormalities in the distribution of pyramidal cells in the medial temporal lobe (Bauman and Kemper, 1985); (ii) (left) amygdala enlargement (Abell et al., 1999); and (iii) functional abnormalities in amygdala activity during a theory of mind task (Baron-Cohen et al., 1999). Thus, the amygdala region may form an important part of the pathogenic substrate of autism. However, our findings also suggest that people with autistic disorder have functional abnormalities in other brain regions when processing facial expressions, including the right fusiform gyrus, early sensory cortices, insula and cerebellum.

In the main effect of group, subjects with autistic disorder had reduced activity of the right fusiform gyrus, an area implicated in the general processing of faces (e.g. Kanwisher et al., 1999). Moreover, it was hypothesized that people with autistic disorder would not be impaired in the explicit processing of facial expressions; however, they made significantly more errors than controls and had reduced activity in left middle temporal gyrus during the explicit processing of facial features and emotional expressions. The deficits in performance on the task were significantly correlated with deficits for memory for faces (Warrington face recognition memory task), and so may reflect a more generalized deficit in processing facial features. The middle temporal gyrus is a visual cortical area that is important in the processing of facial features (Puce et al., 1998), and is activated during the explicit processing of facial expressions (Critchley et al., 2000). The fusiform and middle temporal gyri are both strongly modulated by ‘top-down’ attentional mechanisms, and it is therefore unclear whether the observed group differences in the activity of these regions reflect a primary deficit in facial processing or result from different attentional mechanisms operating with respect to faces in individuals with autistic disorder. Nevertheless, our findings suggest that the cortical representation of facial features may be abnormal in people with autism, and this may be the basis of the observed errors in the explicit task and in the Warrington face recognition memory task. Moreover, although explicit cognitive strategies may assist people with autistic disorder in some aspects of social behaviour, some individuals may have abnormalities in the representation of facial features within cortical visual areas, which impair these strategies and affect behaviour.

Although we only examined adults, autism is neurodevelopmental in origin, and therefore our observations may have arisen from differences present during brain development. The core deficits of autism (lack of social reciprocity and circumscribed behavioural repertoires) are apparent in early childhood, and can be modelled experimentally in non-human primates by damage to medial temporal lobe structures (amygdalohippocampal complex) in infancy (Bachevalier, 1994). The amygdala has an important role in learning and representing the motivational meaning of stimuli (Gaffan, 1992). We speculate that abnormalities in these mechanisms during development may provide a basis for understanding the development of some behavioural features of autism. For example, in infancy, if social stimuli (e.g. faces, voices and touch) cannot be associated with internal states of comfort/discomfort, then they would not acquire special meaning (salience), preferential attention or the development of specialized processing streams (e.g. cortical language or face areas). Thus, a failure in associative learning of salience may arise from local lesions or abnormal neuronal architecture in the medial temporal lobe (e.g. Bauman and Kemper, 1985) or from abnormal connectivity with other regions. In the normal development of the human brain, different regions undergo dynamic maturation processes at different regionally specific times. However, in autism, evidence suggests diffuse abnormalities in brain development (e.g. Piven et al., 1990; Bailey et al., 1998; Abell et al., 1999) which may impair interregional connectivity (Horwitz et al., 1988) and result in transient metabolic abnormalities in specific association regions (Zilbovicius et al., 1995). We hypothesize that the functional abnormalities we observed, and the social deficits of autism, may arise from impaired learning and representation of the motivational meaning of social stimuli during a critical period of early brain development. Moreover, if such mechanisms contribute fundamentally to autism, it is probable that, in the majority of people with autism, this would result from abnormal connectivity due to widespread anomalies in regional brain maturation rather than simply focal lesions of medial temporal lobe structures (Piven et al., 1998; Abell et al., 1999). However, more detailed studies of the neural mechanisms contributing to the development of emotional skills in children are needed to enhance understanding of the patho-aetiology of autism and to aid the interpretation of studies of adults with autism.

In summary, high-functioning adults with autistic disorder, compared with controls, have abnormalities in regional brain activity during the explicit and implicit processing of emotional facial expressions, indicating dysfunction of pathways between limbic and paralimbic regions, the cerebellum and the extrastriate visual cortices. These findings may partly explain the social impairments of people with autism, but further studies are required to elucidate how these abnormalities arise and change with age.

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