Chapter 2

Social cognition and autism spectrum conditions

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2.1 Autism spectrum conditions

Autism is diagnosed when a child or adult has abnormalities in a 'triad' of behavioural domains: social development, communication, and repetitive behaviour/obsessive interests (American Psychiatric Association 1994; World Health Organization 1994). Autism can occur at any point on the IQ continuum, and IQ is a strong predictor of outcome (Rutter 1978). Autism is also invariably accompanied by language delay (no single words before 2 years old). Asperger syndrome (AS) (Asperger 1944) is a subgroup on the autistic spectrum. People with AS share many of the same features seen in autism, but with no history of language delay and with IQ in the average range or above. In this chapter we will use the term autism spectrum conditions (ASC) to describe the whole spectrum of individuals who meet diagnostic criteria for one or other of these subgroups. Because autism is a developmental condition, and because developmental psychopathology is the focus for this volume, we will at times be discussing adults with this diagnosis, even though this book has a focus on childhood conditions. Adult studies are of course relevant not only because the onset of ASC is during early childhood, but also because of how changes across the lifespan throw light on developmental outcomes.

2.2 Typical development of mindreading

In 1994 Baron-Cohen proposed a model to specify the neurocognitive mechanisms that comprise the 'mindreading system' (Baron-Cohen 1994, 1995). Mindreading is defined as the ability to interpret one's own or another agent's actions as driven by mental states. The model was proposed in order to explain (a) the ontogenesis of a theory of mind and (b) neurocognitive dissociations that are seen in children with or without autism. The model is shown in Figure 2.1 and contains four components: the Intentionality Detector (ID),

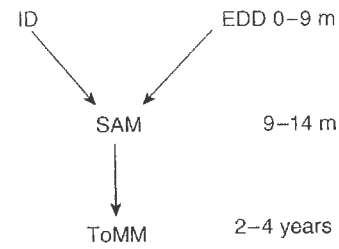

Figure 2.1 Baron-Cohen's model of mindreading (Baron-Cohen 1994): ID, Intentionality Detector; EDD, Eye Direction Detector: SAM, Shared Attention Mechanism; ToMM, Theory of Mind Mechanism.

the Eye Direction Detector (EDD), the Shared Attention Mechanism (SAM), and the Theory of Mind Mechanism (ToMM).

ID and EDD build 'dyadic' representations of simple mental states. ID automatically interprets or represents an agent's self-propelled movement as a desire or goal-directed movement, a sign of its agency, or an entity with volition (Premack 1990). For example, ID interprets an animate-like moving shape as 'it wants x' or 'it has goal y'. EDD automatically interprets or represents eye-like stimuli as 'looking at me' or 'looking at something else', i.e. EDD picks out that an entity with eyes can perceive. Both ID and EDD are developmentally prior to the other two mechanisms, and are active early in infancy.

SAM is developmentally more advanced and comes on line at the end of the first year of life. SAM automatically interprets or represents if the self and another agent are perceiving the same event. It does this by building 'triadic' representations. For example, where ID can build the dyadic representation 'Mother wants the cup' and EDD can build the dyadic representation 'Mother sees the cup', SAM can build the triadic representation 'Mother sees that I see the cup'. As is apparent, triadic representations involve embedding or recursion. (A dyadic representation—'I see a cup'—is embedded within another dyadic representation—'Mum sees the cup') to produce this triadic representation). SAM takes its input from ID and EDD, and triadic representations are made out of dyadic representations. SAM typically functions from 9to 14 months of age, and allows 'joint attention' behaviours such as protodeclarative pointing and gaze monitoring (Scaife and Bruner 1975).

ToMM allows epistemic mental states to be represented (e.g. 'Mother thinks this cup contains water' or 'Mother pretends this cup contains water'), and it integrates the full set of mental state concepts (including emotions) into a theory. ToMM develops between 2 and 4 years of age, and allows pretend play (Leslie 1987), understanding of false belief (Wimmer and Perner 1983), and understanding of the relationships between mental states (Wellman 1990).

An example of the latter is the seeing-leads-to-knowing principle (Pratt and Bryant 1990), where the typical 3-year-old can infer that if someone has seen an event, then they will know about it.

The model shows the ontogenesis of a theory of mind in the first 4 years of life, and justifies the existence of four components on the basis of developmental competence and neuropsychological dissociation. In terms of developmental competence, joint attention does not appear possible until 9–14 months of age, and joint attention appears to be a necessary but not sufficient condition for understanding epistemic mental states (Baron-Cohen 1991; Baron-Cohen and Swettenham 1996). There appears to be a developmental lag between acquiring SAM and ToMM, suggesting that these two mechanisms are dissociable. In terms of neuropsychological dissociation, congenitally blind children can ultimately develop joint (auditory or tactile) attention using the amodal ID rather than the visual EDD route. Children with autism appear able to represent the dyadic mental states of seeing and wanting, but show delays in shared attention (Baron-Cohen 1989b) and in understanding false belief (Baron-Cohen *et al.* 1985; Baron-Cohen 1989a), i.e. in acquiring SAM and ultimately ToMM. It is this specific developmental delay which suggests that SAM is dissociable from EDD.

The 1994 model of the Mindreading System was revised in 2005 because of certain omissions and too narrow a focus. The key omission is that information about affective states, available to the infant perceptual system, has no dedicated neurocognitive mechanism. The revised model (Baron-Cohen 2005), which now includes a new fifth component, The Emotion Detector (TED), is shown in Figure 2.2. However, the concept of mindreading (or theory of mind) makes no reference to the affective state in the observer

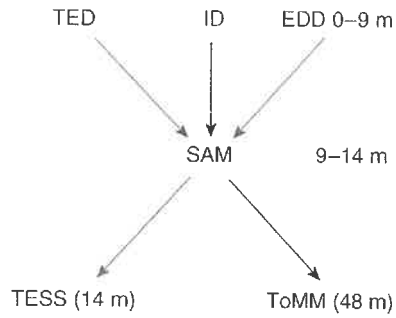

Figure 2.2 Baron-Cohen's model of empathizing (Baron-Cohen 2005): ID, Intentionality Detector; EDD, Eye Direction Detector: SAM, Shared Attention Mechanism; ToMM, Theory of Mind Mechanism; TED, The Emotion Detector; TESS, The Empathizing SyStem.

triggered by recognition of another's mental state. This is a particular problem for any account of the distinction between autism and psychopathy (see also Blair, Chapter 7, this volume). For this reason, the model is no longer of 'mindreading' but is of 'empathizing', and the revised model also includes a new sixth component–The Empathizing SyStem (TESS). Where the 1994 Mindreading System was a model of a passive observer (because all the components had simple decoding functions), the 2005 Empathizing System is a model of an observer impelled towards action (because an emotion is triggered in the observer which typically motivates the observer to respond to the other person).

Like the other infancy perceptual input mechanisms of ID and EDD, the new component of TED can build dyadic representations of a special kind, namely it can represent affective states. An example would be 'Mother – is unhappy', or even 'Mother – is angry – with me'. Formally, we can describe this as an agent-affective state-proposition. We know that infants can represent affective states from as early as 3 months of age (Walker 1982). As with ID, TED is amodal, in that affective information can be picked up from facial expression, or vocal intonation; 'motherese' is a particularly rich source of the latter (Field 1979). Another's affective state is presumably also detectable from their touch (e.g. tense versus relaxed), which implies that congenitally blind infants should find affective information accessible through both auditory and tactile modalities. TED allows the detection of the basic emotions (Ekman and Friesen 1969). The development of TED is probably aided by the simple imitation that is typical of infants (e.g. imitating caregiver's expressions), which in itself would facilitate emotional contagion (Meltzoff and Decety 2003).

When SAM becomes available, at 9–14 months of age, it can receive inputs from any of the three infancy mechanisms, ID, EDD, or TED. Here, we focus on how a dyadic representation of an affective state can be converted into a triadic representation by SAM. An example would be that the dyadic representation 'Mother is unhappy' can be converted into a triadic representation 'I am unhappy that Mother is unhappy', or 'Mother is unhappy that I am unhappy', etc. Again, as with perceptual or volitional states, SAM's triadic representations of affective states have this special embedded, or recursive, property. The phenomenon of social referencing, in which toddlers approach objects towards which their caregiver looks approvingly or avoid those objects towards which the caregiver shows alarm or disapproval, is one index of SAM (Klinnert 1984).

ToMM has been celebrated for the last 20 years in research in developmental psychology (Leslie 1987; Wimmer *et al.* 1988; Whiten 1991). ToMM is of major importance in allowing the child to represent the full range of mental states,

including epistemic ones (such as false belief), and is important in allowing the child to pull mentalistic knowledge into a useful theory with which to predict behaviour (Wellman 1990; Baron-Cohen 1995). But TESS allows more than behavioural explanation and prediction (itself a powerful achievement). TESS allows an empathic reaction to another's emotional state. However, this is not to say that these two modules do not interact. Knowledge of mental states of others made possible by ToMM could certainly influence the way in which an emotion is processed and/or expressed by TESS. TESS also allows for sympathy. It is this element of TESS that gives it the adaptive benefit of ensuring that organisms feel a drive to help each other, as seen in a toddler's early comforting behaviour towards those in distress (Harris 1989).

To see the difference between TESS and ToMM, consider this example: 'I see you are in pain'. Here, ToMM is needed to interpret your facial expressions and writhing body movements in terms of your underlying mental state (pain). But now consider this further example: 'I am devastated – that you are in pain'. Here, TESS is needed, since an appropriate affective state has been triggered in the observer by the emotional state identified in the other person. And where ToMM employs M-representations (Leslie 1995) of the form agent–attitude–proposition (e.g. Mother – believes – Johnny – took– the – cookie), TESS employs a new class of representations, which we can call E-representations of the form self-affective state-[self-affective state-proposition] (e.g 'I feel sorry that – Mum feels sad about – the news in the letter') (Baron-Cohen 2003). The critical feature of this E-representation is that the self's affective state is appropriate to and triggered by the other person's affective state. Thus TESS can represent [I am horrified – that you are in pain], or [I am concerned – that you are in pain], or [I want to alleviate – that you are in pain], but it cannot represent [I am happy – that you are in pain]. At least, it cannot do so if TESS is functioning normally. One could imagine an abnormality in TESS leading to such inappropriate emotional states being triggered, or one could imagine them arising from other systems (such as a competition system or a sibling rivalry system), but these would not be evidence of TESS *per se*.

Before moving to review the development of mindreading in autism spectrum conditions, we should mention the literature documenting typical sex differences in empathizing, with females showing greater attention to faces at birth (Connellan *et al.* 2001), more eye contact as toddlers (Lutchmaya *et al.* 2002), greater sensitivity to *faux pas* in childhood (Baron-Cohen *et al.* 1999a), and better ability to decode subtle mental states from facial expressions (Baron-Cohen *et al.* 1997b). Such sex differences are one clear source of evidence for individual differences in empathy. Taking a dimensional approach

to empathy as a normally distributed trait in the population leads to the view that autism spectrum conditions may simply be at one end of a spectrum that runs throughout the population. We do not suppose that this is the only relevant dimension along which individuals with autism differ, another one being in 'systemizing', but that literature is reviewed elsewhere (Baron-Cohen 2002, 2006; Goldenfeld *et al.* 2007).

2.3 Mindreading in autism spectrum conditions

Since the first test of mindblindness in children with autism (Baron-Cohen *et al.* 1985), there have been more than 30 experimental tests. The vast majority of these have revealed profound impairments in the development of their empathizing ability. These are reviewed elsewhere (Baron-Cohen *et al.* 1993b; Baron-Cohen 1995). Some children and adults with AS only show their empathizing deficits on age-appropriate tests (Baron-Cohen *et al.* 1997a,b, 2001a). This deficit in their empathizing is thought to underlie the difficulties that such children have in social and communicative development (Baron-Cohen 1988; Tager-Flusberg 1993), and in the imagination of others' minds (Baron-Cohen 1987; Leslie 1987).

The majority of studies of emotion recognition have focused on the face, and tested recognition of six emotions (happiness, sadness, fear, anger, surprise, and disgust). These 'basic emotions' are expressed and recognized universally (Ekman and Friesen 1971; Ekman 1993). Some studies reveal emotion recognition deficits among individuals with ASC, compared with typical or clinical control groups, using both static (MacDonald *et al.* 1989; Celani *et al.* 1999; Deruelle *et al.* 2004) and dynamic (Hobson 1986a,b; Yirmiya *et al.* 1992) stimuli. Other studies have found that children and adults with high-functioning autism (HFA) or AS have no difficulties in recognizing these basic emotions from pictures (Grossman *et al.* 2000; Adolphs *et al.* 2001) or films (Loveland *et al.* 1997). Possible reasons for this apparent lack of consistency are the heterogeneity of symptom severity within the ASC population and the fact that accuracy measures for emotion recognition tasks might not be fine-tuned to pick up subtle differences in measures of perceived task difficulty (e.g. reaction time). It is hoped that correlative designs in future experiments, with quantitative dimensions of 'symptom' severity such as the ADI-R (Lord *et al.* 1994) or AQ (Baron-Cohen *et al.* 2001b), should resolve this issue. The observed deficit in accuracy measures of emotion recognition becomes much more apparent when testing recognition of more 'complex' emotions (such as embarrassment, insincerity, intimacy, etc.) in both adults and children with ASC (Baron-Cohen *et al.* 1997b, 2001a; Golan *et al.* 2006a). These findings suggest that recognition of basic emotions is relatively preserved among

high-functioning individuals with ASC, and that they show greater difficulties in recognizing more complex emotional and mental states.

Emotion recognition from voices has been studied less frequently. Here too there are contradictory findings in relation to recognition of basic emotions (Loveland *et al.* 1995, 1997; Boucher *et al.* 2000). Regarding recognition of complex emotions from voices, several studies report a deficit in performance in high-functioning adults with ASC compared with controls (Kleinman *et al.* 2001; Rutherford *et al.* 2002; Golan *et al.* 2006a, 2007).

Studies assessing the ability of individuals with ASC to identify emotions and mental states from context have also shown deficits relative to the general population or to other clinical control groups (Baron-Cohen *et al.* 1986; Fein *et al.* 1992). For example, adolescents and adults with ASC have difficulties in answering questions on the Strange Stories Test (Happé 1994; Jolliffe and Baron-Cohen 1999). This test assesses the ability to provide context-appropriate mental state explanations for non-literal statements made by story characters (e.g. ironic or sarcastic statements).

Studies assessing complex emotion and mental state recognition from ecologically rich social situations containing multimodal sources of information show a deficit in individuals with ASC compared with controls (Heavey *et al.* 2000; Klin *et al.* 2002; Golan *et al.* 2006b). These difficulties may be related to a failure to attend to the right emotional cues, and/or to a failure in integrating them, explained by weak central coherence in the cognitive level (Frith 1989) and under-connectivity between brain regions in the neurobiological level (Belmonte *et al.* 2004a,b; Courchesne and Pierce 2005; McAlonan *et al.* 2005).

To summarize, although emotion recognition deficits in ASC are lifelong, some high-functioning individuals develop compensatory strategies which allow them to recognize basic emotions. However, when recognition of more complex emotions and mental states is required from faces, voices, context, or the integration of these, many find them hard to interpret. It would appear that in autism TED may function, although this may be delayed (Hobson 1986a; Baron-Cohen *et al.* 1993a, 1997b), at least in terms of detecting basic emotions. Even high-functioning people with autism or AS have difficulties in both ToMM (when measured with mental-age-appropriate tests) (Happé 1994; Baron-Cohen *et al.* 1997a, 2001a) and TESS (Attwood 1997; Baron-Cohen *et al.* 1999b, 2003; Baron-Cohen and Wheelwright 2004; Dapretto *et al.* 2006). This suggests that TED and TESS may be fractionated.

In contrast, the psychiatric condition of psychopathy may entail an intact TED and ToMM alongside an impaired TESS. The psychopath (or sociopath) can represent that you are in pain, or that you believe that he is the gas-man so that he can gain access to your house or your credit card. The psychopath can

go on to hurt you or cheat you without having the appropriate affective reaction to your affective state. In other words, he or she does not care about your affective state (Mealey 1995; Blair *et al.* 1997). Lack of guilt or shame or compassion in the presence of another's distress is diagnostic of psychopathy (Cleckley 1977; Hare *et al.* 1990). Thus separating TESS and ToMM allows a functional distinction to be drawn between the neurocognitive causes of autism and psychopathy.

2.4 Causes

We can think of causes of the social cognitive deficits in ASC in terms of the brain basis of empathy and mindreading in the typical brain. This is reviewed first.

Neuroimaging experiments have implicated the following different brain areas for performing tasks that tap empathy. Traditional 'theory of mind' (cognitive empathy) tasks have consistently shown activity in medial prefrontal cortex, superior temporal gyrus, and the temporo-parietal junction (Frith and Frith 2003; Saxe *et al.* 2004). This could be equated to the brain basis of ToMM. Studies of emotional contagion have demonstrated involuntary facial mimicry (Dimberg *et al.* 2000) as well as activity in regions of the brain where the existence of 'mirror' neurons has been suggested (Wicker *et al.* 2003; Decety and Jackson 2004; Keysers and Perrett 2004). Sympathy has been relatively less investigated, with one study implicating the left inferior frontal gyrus, among a network of other structures (Decety and Chaminade 2003).

ID has been tested in a PET study in a task involving attribution of intentions to cartoon characters (Brunet *et al.* 2000). Reported activation clusters included the right medial prefrontal (BA 9) and inferior frontal (BA 47) cortices, the superior temporal gyrus (BA 42), and the bilateral anterior cingulate cortex. In an elegant set of experiments that required participants to attribute intentions to animations of simple geometric shapes, it was found that the 'intentionality' score attributed by the participants to individual animations was positively correlated to the activity in superior temporal sulcus, the temporo-parietal junction, and the medial prefrontal cortex (Castelli *et al.* 2000). A subsequent study (Castelli *et al.* 2002) demonstrated a group difference in activity in the same set of structures between people with autism/AS and neurotypical controls.

EDD has been studied in several neuroimaging studies on gaze direction perception (Calder *et al.* 2002; Pelphrey *et al.* 2003), which have implicated the posterior superior temporal sulcus bilaterally. This evidence, taken together with similar findings from primate literature (Perrett and Emery 1994), suggests this area to be a strong candidate for the anatomical equivalent of the EDD.

This fits in with the Haxby model of face-processing, where he suggested a role for this region in processing 'variable' aspects of faces (in contrast with non-varying aspects such as identity) (Haxby *et al.* 2000). In a recent imaging study, Williams *et al.* (2005) investigated the neural correlates of SAM and reported bilateral activation in anterior cingulate (BA 32,24) and medial prefrontal cortex (BA 9,10) and the body of caudate nucleus in a joint attention task, when compared with a control task involving non-joint attention (Frith and Frith 2003).

We can now turn to neuroimaging studies of processing facial expressions of emotion in people with ASC. These show less activation in brain regions central to face-processing, such as the fusiform gyrus (Critchley *et al.* 2000; Pierce *et al.* 2001; Schultz *et al.* 2003). Behavioural studies show that children and adults with ASC process faces differently compared with controls: Participants with ASC tend to process faces in a feature-based approach, whereas controls process faces configurally (Hobson *et al.* 1988; Teunisse and De Gelder 1994; Young and Bruce 1998; Schultz *et al.* 2003). There is also evidence of reduced activation in brain areas that play a major role in processing of emotion, such as the amygdala, when individuals with ASC process social-emotional information (Baron-Cohen *et al.* 1999c; McAlonan *et al.* 2005; Ashwin *et al.* 2007).

However, a recent study (Dalton *et al.* 2005) shows that the observed hypoactivation of the amygdala and the fusiform gyrus in response to facial expressions of emotion is related to the lack of fixation on the eye region of the face. In light of this new result, it is essential to re-evaluate existing results from studies that involve emotional stimuli in a non-visual domain. One study measured brain activity of participants with ASC and matched controls whilst listening to theory of mind stories. Activation in the medial frontal area of the brain, whilst judging others' mental states, was less intensive and extensive in the AS group compared with controls (Neiminen-von Wendt *et al.* 2003). When using a verbal ToM task in a neuroimaging study, reduced activation of the left medial prefrontal cortex was found in people with ASC compared with matched controls (Happé and Frith 1996).

Anatomical abnormalities have been identified in many brain areas in autism. These include the cerebellum (Murakami *et al.* 1989; Courchesne *et al.* 1994b,c,d; Hashimoto *et al.* 1995), the brainstem (Hashimoto *et al.* 1995; Rodier *et al.* 1996), the frontal lobes (Carper and Courchesne 2000; Courchesne *et al.* 2001; Aylward *et al.* 2002; Sparks *et al.* 2002), the parietal lobes (Courchesne *et al.* 1993), the hippocampus (Aylward *et al.* 1999; Saitoh *et al.* 2001), and the amygdala (Aylward *et al.* 1999). Volume deficits have been shown in the cerebellum (Murakami *et al.* 1989; Courchesne *et al.* 1988, 1994d;

Hashimoto *et al.* 1995). However, there has been a report of a subgroup of children with ASC who have an increased cerebellar volume (Courchesne *et al.* 1994a). Epilepsy also occurs commonly, at least in classic autism (Ballaban-Gil and Tuchman 2000).

In terms of neuropathology, the number of Purkinje cells in the cerebellar cortex is abnormally low (Williams *et al.* 1980; Bauman and Kemper 1985, 1994; Ritvo *et al.* 1986). This has been postulated to lead to disinhibition of the cerebellar deep nuclei and consequent over-excitement of the thalamus and cerebral cortex (Courchesne *et al.* 1994b,c). The brainstem (Hashimoto *et al.* 1995) and posterior corpus callosum (Egaas *et al.* 1995) have also been shown to have lower volumes in people with ASC when compared with neurotypical controls. A volume deficit has also been reported in the parietal lobe (Courchesne *et al.* 1993). Neuropsychology suggests that this is associated with a narrowed spatial focus of attention (Townsend and Courchesne 1994). The results of either MRI volumetric analysis or measures of head circumference show that the autistic brain appears to involve transient postnatal macrocephaly (Courchesne 2002). Neonates later diagnosed with autism or PDD-NOS (pervasive developmental disorder-not otherwise specified) have normal head circumference, but by 2–4 years of age 90 per cent of these have larger than average MRI-based brain volumes (Carper and Courchesne 2000; Courchesne *et al.* 2001; Aylward *et al.* 2002; Sparks *et al.* 2002). This reflects an enlargement of cerebellar and cerebral white matter, and cerebral grey matter (Courchesne *et al.* 2001; Herbert *et al.* 2003). Enlargement of superficial white matter tracts containing cortico-cortical fibres may persist abnormally late into development, whilst the internal capsule and corpus callosum are smaller (Herbert *et al.* 2002). Cerebellar and cerebral white matter volumes, and cerebellar vermis size, can distinguish 95 per cent of toddlers with autism from normal controls, and predict if the child with autism will be high or low functioning (Courchesne *et al.* 2001). The overgrowth is anterior to posterior (frontal lobes are the largest). This increase in volume of cortical grey matter may reflect a failure of synaptic pruning, an excess of synaptogenesis, or an excess of neurones (Belmonte *et al.* 2004a).

Abnormalities in the density of packing of neurons in the hippocampus, amygdala, and other parts of the limbic system have also been reported (Bauman and Kemper 1985, 1994; Raymond *et al.*1996). An abnormally low degree of dendritic branching was also found in a Golgi analysis of the hippocampus of two autistic brains (Raymond *et al.* 1996), although it remains to be seen if such an abnormality is confirmed in a larger sample. A separate report suggests a reduction in the size of cortical minicolumns and an increase in cell dispersion within these minicolumns. These might indicate

an increase in the number of and connectivity between minicolumns (Casanova *et al.* 2002a,b).

Abnormal levels of arousal have been inferred from physiological and endocrine indices (Tordjman *et al.* 1997; Hirstein *et al.* 2001). Functional studies suggest that sensory inputs evoke hyperactivation, resulting in decreased ability to select amongst competing inputs. Thus, on the Embedded Figures Task, people with autism show unusually high activation in ventral occipital areas and abnormally low activation in prefrontal and parietal areas (Ring *et al.* 1999).

Regarding event-related potential results, the P1 evoked potential is either abnormally heightened in response to stimuli that are the target of attention, or abnormally generalized to stimuli that are outside the target of attention (Townsend and Courchesne 1994). The visual N2 to novel stimuli is also heightened to irrelevant stimuli (Kemner *et al.* 1994). The P3 in response to auditory stimuli is abnormally generalized to occipital sites in visual cortex (Kemner *et al.* 1995). Both hemispheres show abnormal activation, indiscriminately, during shifts of attention into either hemifield (Belmonte 2000; Belmonte and Yurgelun-Todd 2003). Regarding attentional research, a deficit has been found in rapid shifting of attention between modalities (Courchesne *et al.* 1994b,c), between spatial locations (Wainwright-Sharp and Bryson 1993, 1996; Townsend *et al.* 1996a,b, 1999; Harris *et al.* 1999; Belmonte 2000), and between object features (Courchesne *et al.* 1994b,c; Rinehart *et al.* 2001).

A neural basis of empathy has built on a model first proposed by Brothers (1990). She suggested from animal lesion studies (Kling and Brothers 1992), single-cell recording studies (Brothers *et al.* 1990), and neurological studies that social intelligence was a function of three regions: the amygdala, the orbito-frontal and medial frontal cortex, and the superior temporal sulcus and gyrus. Together, she called these the 'social brain'. Abnormalities in autism have been found in the amygdala, the orbito-frontal cortex, and the medial frontal cortex.

There is converging evidence from several lines of research on the abnormalities of these 'social brain' structures in ASC. There is evidence for amygdala hypoactivation in an emotion recognition task in autism (Baron-Cohen *et al.* 2000). We have reported significantly less amygdala activation in adults with HFA/AS during a mentalizing task (Reading the Mind in the Eyes Task) compared with normal subjects (Baron-Cohen *et al.* 1999c). Reduced activity in these 'social brain' structures has been reported in the left medial frontal cortex (Happé *et al.* 1996) during an empathizing (theory of mind) task, and also in the orbito-frontal cortex (Baron-Cohen *et al.* 1994). A neuroanatomical study of autism at post-mortem found microscopic pathology (in the form

of increased cell density) in the amygdala in the presence of normal amygdala volume (Bauman and Kemper 1994; Rapin and Katzman 1998). Secondly, patients with autism tend to show a similar pattern of deficits to those seen in patients with amygdala lesions (Adolphs *et al.* 2001). Thirdly, several structural MRI studies of autism have revealed abnormal development of the amygdala (reviewed by Baron-Cohen *et al.* 2005). A recent larger structural study suggests more generalized structural abnormalities in the social brain (McAlonan *et al.* 2005). We have also recently reported a functional dysconnectivity of the amygdala with other brain structures (Welchew *et al.* 2005).

Ultimately, the cognitive and neural abnormalities in autism spectrum conditions are likely to be strongly linked to genetic factors. The sibling risk-rate for autism is approximately 4.5 per cent, or a tenfold increase over general population rates (Jorde *et al.* 1991). Regarding twin studies, in an epidemiological study of same-sex autistic twins, it was found that 60 per cent of monozygotic (MZ) pairs were concordant for autism compared with no dizygotic (DZ) pairs (Bailey *et al.* 1995). When these authors considered a broader phenotype (of related cognitive or social abnormalities), 92 per cent of MZ pairs were concordant compared with 10 per cent of DZ pairs. The high concordance in MZ twins indicated a high degree of genetic influence, and the risk to a co-MZ-twin can be estimated at over 200 times the general population rate. However, genetics cannot be the whole story, since concordance is not 100 per cent and gene–environment interactions can render monozygotic twins strongly discordant for the level of severity of ASC (Belmonte and Carper 2006).

The past few years have seen rapid progress in molecular genetic understanding of autism (O'Roak and State 2008; Abrahams and Geschwind 2008), although there remains a great deal of work to be done in discerning the metabolic and developmental pathways by which identified genetic variants contribute to autistic development. Recent discoveries seem to segregate into four overarching and interacting themes (Belmonte and Bourgeron 2006): (1) anomalies in synaptic formation, maintenance, or signal transduction, (2) imbalance between excitatory and inhibitory tone, (3) abnormal cell number, and (4) abnormal neuromodulation.

Evidence for abnormalities at the synapse comes from rare variants associated with familial autism, as well as from more common variants associated with comorbid syndromes. Autism is comorbid with Fragile X syndrome, caused by transcriptional silencing of FMR1. FMR1 encodes FMRP, an mRNA-binding protein that negatively regulates activity-dependent synaptic modification in response to activation of Group I metabotropic glutamate receptors (Bear *et al.* 2004). Absence of FMRP thus results in runaway synaptic plasticity.

Also relevant to synaptic function, familial variants of the neuroligin genes NLGN3 and NLGN4 segregate with autism (Jamain *et al.* 2003; Laumonnier *et al.* 2004), as do variants of the neuroligin binding partner genes neurexin-1 (NRXN1) (Kim *et al.* 2008) and SHANK3 (Durand *et al.* 2007; Moessner *et al.* 2007), and the neurexin superfamily member contactin-associated protein-like 2 (CNTNAP2) (Alarcón *et al.* 2008; Arking *et al.* 2008). Among other functions, the balance between excitatory and inhibitory synapses is regulated by neuroligins (Chih *et al.* 2005).

Further to excitatory-inhibitory balance, autism has been associated with the ionotropic NMDA receptor gene GRIN2A (Barnby *et al.* 2005) and the ionotropic kainate receptor gene GRIK2 (Jamain *et al.* 2002), and with the GABA receptor subunit gene GABRB3 (Buxbaum *et al.* 2002). GABRB3 in turn is regulated by the methyl-CpG binding protein MeCP2 (Samaco *et al.* 2005), disrupted in Rett syndrome, with which autism is again comorbid.

Regarding cell number, the tumour suppressor genes NF1 and TSC1/TSC2 code for GTPase-activating proteins with widespread effects on cell survival, cell structure and cell function. These, along with the lipid phosphatase tumour suppressor PTEN, negatively regulate the phosphoinositide-3 kinase pathway which spurs cell growth and synaptogenesis and blocks apoptosis. PTEN mutation, in particular, has been associated with cases of autism with macrocephaly (Butler *et al.* 2005), and variations in these three genes may explain autism's comorbidity with neurofibromatosis, tuberous sclerosis, and Cowden syndrome, respectively. Also recently linked to autism is a promoter polymorphism that decreases expression of the MET gene (Campbell *et al.* 2006). MET encodes a receptor tyrosine kinase active not only in brain development but also in immune and gastrointestinal functions—an association that may explain comorbidities in these domains in some cases of autism.

The major result in neuromodulaton and autism concerns the serotonin membrane transporter gene SLC6A4. The short allele of the SLC6A4 promoter is associated with increased volume of cerebral cortical and especially frontal grey matter in autism (Wassink *et al.* 2007), and the division of results between preferential transmission of long and short alleles in autism suggests a gene dosage effect or interaction with other susceptibility and resistance factors (Belmonte and Bourgeron 2006).

Many of these genetic variations may have divergent endophenotypic effects, helping to explain the partial independence of some autistic traits (Ronald *et al.* 2006) as well as the population continuum between autism spectrum conditions and normal cognitive variation (Constantino and Todd 2005), including the subclinical, broader autism phenotype found in some family members (Piven *et al.* 1997; Dawson *et al.* 2002). In addition to this locus and

allelic heterogeneity, gene dosage is likely to play a major role, as evidenced by recent findings of copy number variation as a contributing factor especially in sporadic, non-familial cases of autism (Sebat *et al.* 2007). The future of research in this field will be not only to isolate the relevant genes but also to understand the networks within which these genes function, and ultimately the relationships between these different causal levels in autism. It is hoped that during this research endeavour there will also be evaluations of the most promising treatments.

2.5 Clinical implications

Past attempts to teach emotion recognition to adults and children with ASC have either focused on the basic emotions (Hadwin *et al.* 1996; Howlin *et al.* 1999) or have been part of social skills training courses, usually run in groups (Howlin *et al.* 1999; Rydin *et al.* 1999; Barry *et al.* 2003). Typically, these training programmes do not focus specifically on systematically teaching emotion recognition, but instead address other issues, such as conversation, reducing socially inappropriate behaviour, personal hygiene, etc. In such groups it is difficult to target the individual's specific pace of learning. Finally, such groups are socially demanding and therefore might deter more socially anxious participants.

Other attempts to teach individuals with ASC social skills have used computer-based training (Swettenham 1996; Rajendran and Mitchell 2000; Bernard-Opitz *et al.* 2001; Silver and Oakes 2001; Bolte *et al.* 2002; Hetzroni and Tannous 2004). The use of computer software for individuals with autism spectrum conditions has several advantages: First, individuals with ASC favour the computerized environment since it is predictable, consistent, and free from social demands, which they may find stressful. Secondly, users can work at their own pace and level of understanding. Thirdly, lessons can be repeated over and over again until mastery is achieved. Fourthly, interest and motivation can be maintained through different and individually selected computerized rewards (Moore *et al.* 2000; Parsons and Mitchell 2002; Bishop 2003). Previous studies have found that the use of computers can help individuals with autism pass false-belief tasks (Swettenham 1996), recognize basic emotions from cartoons and still photographs (Silver and Oakes 2001; Bolte *et al.* 2002), and solve problems in illustrated social situations (Bernard-Opitz *et al.* 2001). However, participants find it hard to generalize their knowledge from learnt material to related tasks.

The computer-based interventions above used drawings or photographs for training, rather than more life-like stimuli. This might have made generalization harder than if more ecologically valid stimuli were used. In addition, the programs teaching emotion recognition focused on basic emotions, and only on facial expressions. No reported program to date has systematically trained

complex emotion recognition in both visual and auditory channels, with life-like faces and voices.

We have recently evaluated *Mind Reading* (Baron-Cohen *et al.* 2004), an interactive guide to emotions and mental states, and its value as a tailored teaching tool for emotion recognition for learners on the autistic spectrum. *Mind Reading* is based on a taxonomic system of 412 emotions and mental states, grouped into 24 emotion groups and six developmental levels (from age 4 to adulthood). The emotions and mental states are organized systematically, according to the emotion groups and developmental levels. Each emotion group is introduced and demonstrated by a short video clip giving some clues for later analysis of the emotions in this group. Each emotion is defined and demonstrated in six silent films of faces, six voice recordings, and six written examples of situations that evoke this emotion. The resulting library of emotional 'assets' (video clips, audio clips, or brief stories) comprises $412 \times 18 = 7416$ units of emotion information to learn to recognize or understand. Therefore this is a rich and systematically organized set of educational material. The software was created for the use of children and adults of various levels of functioning. Vocal and animated helpers give instructions on every screen.

We tested for any improvement in *adults* with HFA/AS in emotion recognition skills following *independent* use of the software, and the extent to which these users can generalize their acquired knowledge. The intervention took place over a period of 10–15 weeks to ensure a meaningful period for training, recognizing that a longer duration might lead to individuals dropping out. Participants were tested before and after the intervention. A no-computer-intervention control group of adults with HFA/AS was matched to the intervention group. This HFA/AS control group was also tested before and after a similar period of time, but had no intervention. The need for a no-intervention HFA/AS group was to assess whether any improvement was related to the intervention or was merely due to taking the tasks twice or to time passing. A third typical control group from the general population was matched to the intervention groups. This group was only tested once, to obtain baseline measures.

Results showed that following 10–20 hours of using the software over a period of 10–15 weeks, users with ASC significantly improved in their ability to recognize complex emotions and mental states from both faces and voices, compared with their performance before the intervention, relative to the control group. This finding is interesting, considering the short usage time and the large number of emotions included in the software, and since participants were not asked to study these particular emotions (Golan and Baron-Cohen 2006).

The above study illustrates one practical teaching method focused on improving mindreading in ASC, but it should be recognized that other approaches (such as preverbal intervention to encourage the development of shared attention) are also being explored.

2.6 Future directions

The area of social cognition in ASC remains important, and in this chapter we have necessarily reviewed research in a range of separate areas (cognitive development, neuroimaging, neuroanatomy, genetics, intervention). The hope is that, in the future, interdisciplinary science will take place so that we can integrate these currently disparate areas and discover which brain regions change as a result of intervention, or are under the control of which genetic mechanisms, in which subgroup on the autistic spectrum.

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