Annotation: The neural basis of social impairments in autism: the role of the dorsal medial-frontal cortex and anterior cingulate system

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Background: The fundamental social disturbance of autism is characterized, in part, by problems in the acquisition of joint attention skills in the first years of life, followed by impairments in the development of social cognition, as assessed on theory of mind (ToM) measures. Recently, studies have indicated that a system involving the dorsal medial-frontal cortex (DMFC), and the anterior cingulate (AC), may contribute to the development of the tendency to initiate joint attention in infancy. Similarly, research has implicated the DMFC/AC system in ToM performance in typical and atypical individuals. These data suggest it may be useful to consider the functions associated with this system in the developmental psychopathology of autism. Method: A review of the studies of the connections between the DMFC/AC system, joint attention and ToM task performance. Results and conclusions: This review raises the hypothesis that the DMFC/AC may be involved in the basic disturbance in social orienting in autism. The DMFC/AC may also play a role in the capacity to monitor proprioceptive information concerning self-action and integrate this self-related information with exteroceptive perceptual information about the behavior of other people. A disturbance in these functions of the DMFC/AC may contribute to the atypical development of intersubjectivity, joint attention and social cognition that may impair the lives of people with autism. Thus, impairment in the development of this system may constitute a neural substrate for socio-cognitive deficits in autism. Keywords: Brain imaging, frontal cortex, anterior cingulate, joint attention, social orienting, social cognition, autism. Abbreviations: IJA: Initiates Joint Attention; RJA: Responds to Joint Attention; IBR: Initiates Behavior Regulation/Requests; ToM: Theory of Mind; DMFC: dorsal medial-frontal cortex; AC: anterior cingulate.

Social impairments, along with disturbances in communication and restricted or repetitive patterns of behavior, constitute a pathognomonic symptom cluster of autism (APA, 2000). Therefore, one of the longstanding challenges of research on autism has been to describe the neural systems involved in these social-communication impairments. In this regard, at least three complementary approaches have emerged in the contemporary literature. One approach has been to identify anomalies in the neural functions and neural morphometrics of people with autism and, then, to attempt to relate these anomalies to social behavior impairment. Work on orienting difficulties and related cerebellar cell atypicalities in autism provides a seminal example of this approach (Carper & Courschesne, 2000; Courschesne et al., 1994; Townsend et al., 2001).

Another approach focuses on the brain systems involved in a variety of social perceptual processes, such as face perception and recognition (Elgar & Cambell, 2001), the perception of emotional or motivation-related information (Wantanabe, 1999; Le-Doux, 1989), and the perception of the direction of gaze of a social partner (Kawashima et al., 1999). Social perception may be supported by a complex ventromedial ‘social brain’ circuit involving the orbito-frontal cortex, temporal cortical areas including the superior temporal sulcus (STS) as well as superior temporal gyrus (STG), and subcortical areas such as the amygdala (Adolphs, 2001; Brothers, 1990; Baron-Cohen et al., 1999). Since behavioral deficits in social perception have long been recognized in autism (e.g., Hobson, 1993; Sigman, Kasari, Kwon, & Yirmiya, 1992), it has been a logical step for researchers to begin to examine the hypothesis that deficits in ventral ‘social brain’ systems give rise to fundamental impairments in the social perception and social behavior of children with autism (e.g., Baron-Cohen et al., 1999; Critchley et al., 2000).

Of course, autism is marked not only by social-perceptual or social input system impairments but also by impairments in social output systems that mediate the spontaneous organization, generation and expression of social attention, behavior and cognition (Klin, Jones, Schultz, & Volkmar, 2003; Minshew, Meyer, & Goldstein, in press; Mundy, 1995; Mundy & Neal, 2001; Leslie, 1987). Hence, a third approach has emerged which involves the study of the neural output systems involved in the self-initiation of social attention and behavior. Exemplifying this research approach are studies of the neural systems involved in infant joint attention skills, as well as the later emerging, but theoretically related, facility for generating social cognition on Theory of Mind tasks (Dawson et al., 2002; Frith & Frith, 1999, 2001; Henderson, Yoder, Yale, & McDuffie, 2002; Mundy, Card, & Fox, 2000). An intriguing set of observations to emerge from this
research is that, in addition to ventral social brain systems, activity in the dorsal medial-frontal cortex (Brodmann’s areas 8/9) and the anterior cingulate (Brodmann’s area 24; Martin, 1996) may be a common correlate of both joint attention skills in infants (Henderson et al., 2002; Mundy et al., 2000), and theory of mind task performance in children and adults with typical and atypical development (e.g., Frith & Frith, 1999, 2001). The dorsal medial-frontal cortex (DMFC) and the anterior cingulate (AC), along with components of the ‘social brain’ are illustrated in Figure 1.

The potential contribution of the dorsal medial-frontal cortex and anterior cingulate has been acknowledged, but not well described in recent discussions of the neurobiology of typical social behavior development (e.g., Adolphs, 2001), or atypical social behavior in autism (e.g., Baron-Cohen et al., 1999). To address this gap in the literature this paper will present a review of the literature on the neurophysiological and neuro-imaging studies of joint attention and theory of mind skills. Following this, several hypotheses concerning the specific social-executive, as well as non-social-executive functions of the DMFC/AC system will be described. The points of intersection between new theory and research on the social contributions of the DMFC/AC, and hypotheses about the nature of the neuropsychological disturbance of autism will be emphasized.

Joint attention

Brain-behavior studies of joint attention may be critical to understanding autism (Dawson et al., 2002; Mundy et al., 2000) because the early social-communication disturbance of autism is exemplified by a robust developmental failure in this domain (Mundy & Sigman, 1989). Joint attention skills refer to the capacity of individuals to coordinate attention with a social partner in relation to some object or event. In the first years of life this may only involve the social coordination of overt aspects of visual attention, such as when a toddler shows a toy to a parent. Theoretically, though, this capacity eventually becomes elaborated and integral to the social coordination of covert aspects of attention, as when social partners coordinate attention to psychological phenomena, such as ideas, intentions or emotions (Tomasello, 1995).

This capacity begins to emerge by at least 6 months of age (Scaife & Bruner, 1975) and takes several different forms. One behavior involves an infant’s ability to follow the direction of gaze, head turn and/or pointing gesture of another person (Scaife & Bruner, 1975). This behavior may be referred to as Responding to Joint Attention skill (RJA: Seibert, Hogan, & Mundy, 1982; Mundy, Hogan, & Doehring, 1996). Another type of skill involves the infant’s use of eye contact and/or deictic gestures (e.g., pointing or showing) to spontaneously initiate coordinated attention with a social partner. The latter type of protodeclarative act (Bates, 1976) may be referred to as Initiating Joint Attention skill (IJA; Seibert et al., 1982; Mundy et al., 1996). These behaviors, and especially IJA, appear to serve social functions. That is, the goal and reinforcement of these behaviors has been interpreted to revolve around the sharing experience with others and the positive valence such early sharing has for the young child (Bates, 1976; Mundy, 1995). Alternatively, social attention coordination may also be used for less social but more instrumental purposes (Bates, 1976). So, for example, infants and young children may use eye contact and gestures to initiate attention coordination with another person to elicit aid in obtaining an object or event. This may be referred to as a protoimperative act (Bates, 1976) or Initiating Behavior Requests (IBR; Mundy et al., 1996).

Figure 1  Lateral (top) and medial (bottom) illustrations of Brodmann’s cytoarchitectonic areas of the cerebral cortex (adapted from Gazzagnia, Ivry, & Mangun, 1998). The dorsal medial-frontal cortex (DMFC) includes areas 8 and 9. The anterior cingulate is depicted as area 24. The ventral ‘social brain’ includes the orbitofrontal cortex (area 11), the amygdala (area 34) and the superior temporal gyrus (area 22) and the superior temporal sulcus (the division between area 22 and 21)
Joint attention skills are a critical milestone of early development and social learning (Bakeman & Adamson, 1984; Baldwin, 1995). In language learning, for example, much of early lexical acquisition in the second year takes place in unstructured or incidental social-learning situations where: a) the parent provides a learning opportunity by referring to a new object or event in the environment but b) the infant may need to discriminate among a number of stimuli in the environment in order to focus on the correct object/event to acquire the appropriate new word association. Thus, the infant is confronted with the possibility of referential mapping errors (Baldwin, 1995). To deal with this problem infants may utilize the direction of gaze of the parent (i.e., use RJA skill) to limit the number of potential stimuli to attend to and increase the likelihood of a correct word learning experience (Baldwin, 1995). Similarly, when an infant initiates bids for joint attention, the responsive caregiver may follow the child’s line of regard and take advantage of the child’s focus of attention to provide a new word in a context that maximizes the opportunity to learn (cf. Tomasello, 1995). Hence, joint attention may be regarded as an early developing self-organizing facility that is critical to much of subsequent social and cognitive development (e.g., Baldwin, 1995; Mundy & Neal, 2001).

**Joint attention impairment in autism**

Children with autism, unfortunately, display robust levels of impairments in joint attention development from as early on as 12 to 18 months of age (Osterling, Dawson, & Munson, 2002; Swettenham et al., 1998). This impairment may be associated with a disruption of the early self-organizing process in social learning that contributes to the subsequent behavioral, and even neural development of children with autism (Mundy & Crowson, 1997; Mundy & Neal, 2001).

While young children with autism display deficits in both IJA and RJA skills, they display less pronounced deficits in IBR or social attention coordination for instrumental purposes (Mundy, Sigman, Unronger, & Sherman, 1986). Moreover, the impairment in RJA appears to remit to a significant degree with development (Mundy, Sigman, & Kasari, 1994; Leekam & Moore, 2001). The impairment in IJA, however, remains robust even in older children (Mundy et al., 1994; Sigman & Ruskin, 1999). In a related vein, research suggests that symptom intensity and course, such as the capacity to establish peer relations in adolescence, are related to the degree of IJA, but not RJA, impairment displayed by young children with autism (Mundy et al., 1994; Sigman & Ruskin, 1999). A dissociated pattern of IJA and RJA development is also observed in typical development and may occur because IJA and RJA reflect different integrations of social-cognitive and social-emotional processes (Mundy et al., 2000).

IJA reflects the tendency to spontaneously initiate social attention coordination behavior, whereas RJA is a measure of the tendency to respond to another person’s signal to shift attention. Hence, IJA may be more affected by executive and social-motivation processes involved in the generation and self-initiation of behavioral goals than RJA (Mundy, 1995; Mundy et al., 2000). In particular, IJA appears to involve the tendency to spontaneously initiate episodes of sharing the affective experience of an object or an event with a social partner (Mundy, Kasari, & Sigman, 1992). Indeed, a significant component of IJA disturbance in autism may be explained in terms of an attenuation of the tendency to initiate episodes of shared positive affect with a social partner (Kasari, Sigman, Mundy, & Yirmiya, 1990).

This literature has led to the instantiation of joint attention disturbance, and especially IJA disturbance, as a central symptom of autism. For example, a ‘lack of spontaneous seeking to share enjoyment, interests, or achievements with other people (e.g., by a lack of showing, bringing or pointing out objects of interest)’ is now one of four cardinal symptoms of the social impairment of autism in a current nosology (APA, 2000, p. 75). Thus, many of the current autism diagnostic and screening instruments include measures of joint attention (Baron-Cohen et al., 1996; Lord et al., 1999). The ‘gold standard’ Autism Diagnostic Observation Schedule (Lord et al., 1999) even reflects the notion of a developmental dissociation in joint attention. Measures used for diagnosis with the youngest children (Module 1) include both IJA and RJA assessments. Module 2 is designed for developmentally more advanced children and although it includes measure of both IJA and RJA, only the former is included in the diagnostic scoring.

**Joint attention and brain-behavior research**

Given the foregoing literature it is reasonable to assume that understanding the brain systems involved in various types of joint attention skill development may provide clues with respect to critical aspects of the neurobehavioral pathology of autism (Mundy et al., 2000; Mundy & Neal, 2001). In this regard, several studies have been conducted. Caplan et al. (1993) studied the behavioral outcome of 13 infants who underwent hemispherectomies in an attempt to treat their intractable seizure disorders. The Early Social Communication Scales (ESCS; Seibert et al., 1982; Mundy et al., 1996) were used to assess the post-surgical development of joint attention and related behaviors among these children. Positron Emission Tomography (PET) data were gathered prior to surgical intervention. These data indicated that metabolic activity in the frontal hemispheres, and especially the left frontal hemisphere, predicted the development of Initiating Joint Attention (IJA).
skill in this sample. However, the capacity of these children to respond to the joint attention bids, or initiate requesting bids, was not observed to relate to any of the PET indexes of cortical activity. Moreover, metabolic activity recorded from other brain regions (e.g., orbital, temporal, parietal and occipital) was not significantly associated with joint attention or other social-communication skills in this study. Thus, frontal activity appeared to be specifically related to the development of the tendency to spontaneously initiate social attention coordination with others to share experience.

A post-hoc explanation of this frontal connection to IJA was offered in a later paper (Mundy, 1995). By about 10 months of age, a frontal and left lateralized system may emerge that plays a role in the executive and emotional processes associated with approach tendencies involved in positive social affiliative behaviors (Fox, 1991). Mundy (1995) suggested that the IJA impairment in autism may reflect a disturbance in the emergence of this left frontal ‘social-approach’ system. Based on earlier work (Panksepp, 1979), the specific notion here was that a primary path of pathology in autism was the early onset of a disturbance in frontally mediated sensitivity to the reward value of social stimuli. This insensitivity hypothetically creates an affective, social-motivation imbalance that results in a robust decrease in the tendency to direct attention to social stimuli. This, in turn, leads to a dramatic reduction in the tendency of infants with autism to initiate joint attention bids and a related reduction in social information input to the child that results in a marginalization of subsequent social-cognitive and social behavior development (Mundy, 1995; Mundy & Neal, 2001).

**EEG studies**

To begin to test aspects of this model, Mundy et al. (2000) examined the hypothesis that EEG activity in a left-lateralized, frontal-cortical system would be a significant correlate of IJA development in typical infants. Baseline EEG and ESCS joint attention data were collected on 32 infants at 14 to 18 months of age. The results indicated that individual differences in 18-month IJA were predicted by a complex pattern of 14-month EEG activity in the 4–6 Hz band that included indices of left medial-frontal EEG activation, as well as indices of right central deactivation, left occipital activation and right occipital deactivation. Although the location of the generators of the EEG data could not be definitively determined in this study, the frontal correlates of IJA reflected activity from electrodes at F3 of the 10/20 placement system (Jasper, 1958). These electrodes were positioned above a point of confluence of Brodmann’s areas 8 and 9 of the medial-frontal cortex of left hemisphere (Martin, 1996). This area includes aspects of the frontal eye fields and supplementary motor cortex commonly observed to be involved in attention control (Posner & Petersen, 1990). Moreover, theory on attention development (Posner & Petersen, 1990) suggested that, in addition to medial-frontal cortical activity, data from these electrodes may have reflected activity in the anterior cingulate (Brodmann’s area 24), a subcortical structure contiguous with the ventral surface of Brodmann’s cortical areas 8/9 (Martin, 1996).

Neither RJA nor IBR measures were associated with a similar pattern of EEG activity (Mundy et al., 2000). RJA at 18 months, however, was predicted by EEG indexes of left-parietal activation and right parietal deactivation at 14 months. This observation was consistent with research that suggests parietal areas specialized for spatial orienting and attention, along with temporal systems specialized for processing gaze, may contribute to RJA-related skill development (Kingstone, Friesen, & Gazzaniga, 2000; Kawashima et al., 1999). However, eye contact with others, or at least the degree of gaze aversion displayed by pictures of faces, has also been observed to activate components of the medial-frontal cortex (Calder et al., 2002). So, a frontal contribution to RJA should not be ruled out on the basis of this one study.

Even with this proviso in mind, Mundy et al. (2000) suggested that a dual process, or multiple systems neurodevelopmental model of joint attention disturbance in autism may be useful to consider. A dual parietal and frontal model of joint attention is consistent with theory that emphasizes the initial contribution of parietal systems to less volitional attention control. This is followed by the advent of frontal contributions for more volitional control in the typical path of early attention development (Posner & Petersen, 1990). Similarly, researchers have noted both parietal and frontal contributions to orienting impairments in autism (Townsend et al., 2001). Moreover, a dual process model of joint attention is consistent with observations of a dissociation between IJA and RJA impairments in the development of children with autism (Leekam & Moore, 2001; Mundy et al., 1994).

The dual process model may also have implications for neuropsychological research on joint attention in autism. Some of the best work of this kind has recently been presented by Dawson et al. (2002) who have reported that joint attention ability in children with autism appears to be significantly correlated with neuropsychological measures associated with a temporal-ventromedial-frontal circuit, rather than a dorsolateral frontal system. This important observation is consistent with EEG and imaging findings on RJA (Kawashima et al., 1999; Mundy et al., 2000). Indeed, the latent variable reflecting joint attention used in structural equation modeling by Dawson et al. was composed of two measures of RJA to one measure of IJA. Consequently, though, it may be that observations derived from this dependent variable are more applicable to
systems involved in RJA than to systems involved in IJA. Indeed, other studies that used separate IJA and RJA measures have observed that IJA skill in children with autism was correlated with task performance that presumably also taps into dorsolateral frontal processes, such as response inhibition, memory and planning (Griffith, Pennington, Wehner, & Rogers, 1999; McEvoy, Rogers, & Pennington, 1993). A dual process model of joint attention may assist in better understanding these inconsistencies among studies. In the final analysis, though, it may be that both dorsal and more ventral brain systems contribute to joint attention and its impairment in autism.

Such a possibility is consonant with recent data provided by Henderson et al. (2002) which also employed the ESCS to examine the baseline EEG correlates of joint attention in 27 typically developing infants at 14 and 18 months of age. However, to improve the spatial resolution of their data, this group used a high density array of 64 electrodes. Moreover, they reasoned that, since the total ESCS scores for measures of IJA and other domains used in Mundy et al. (2000) were composites of several items, the exact nature of the behaviors involved in associations with EEG activity were unclear. Therefore, Henderson et al. compared the EEG correlates of only two behaviors, self-initiated pointing to share attention with respect to an active mechanical toy (IJA pointing) and self-initiated pointing to elicit aid in obtaining an out-of-reach object (IBR pointing).

No significant correlations were observed between any of the 14-month EEG data and IBR-pointing at 18 months. However, in the 3–6 Hz band there were four significant, negative correlations of 14-month EEG power and IJA-pointing at 18 months (r = −.55 to −.62). The nature of EEG power data is such that lower power is considered to be indicative of greater brain activity. These correlations indicated that higher bilateral activity recorded above frontal medial cortical sites at 14 months was associated with more IJA-pointing at 18 months. The correlations involved electrodes that were placed above cortical regions corresponding to Brodmann’s areas 8, 9, and 6. Henderson et al. (2002) also analyzed data from the 6–9 Hz band. This revealed 15 significant negative correlations with IJA-pointing (r = −.60 to −.78). Again, higher bilateral activity corresponding to the previously identified medial-frontal sites was among the strongest predictors of IJA-pointing at 18 months. In addition, though, IJA pointing at 18 months was also predicted by activity in this bandwidth from circumspect regions of the orbito-frontal, temporal and dorsolateral frontal cortical regions. The latter data were consistent with the findings of Dawson et al. (2002), as well as the observations of Griffith et al. (1999) and McEvoy et al. (1993).

These observations are extremely important for several reasons. First, the bilateral nature of the Henderson et al. findings suggests that Mundy’s (1995) model emphasizing only left frontal contributions to IJA and affective, social-emotional motivation processes may, at best, be incomplete. Nevertheless, these results do provide support for the hypothesis that medial-frontal cortical processes play an important role in IJA development (Mundy et al., 2000). As previously noted, the specific medial-frontal cortical areas of involvement suggested by data from Mundy et al. (2000) and some of the data from Henderson et al. (2002) correspond to aspects of both the frontal eye fields and supplementary motor cortex associated with the control of saccadic eye movement and motor movement planning (Martin, 1996). It may, therefore, be tempting to suggest that these associations simply reflect the motor control of the eye movements and/or gestural behaviors that are intrinsic to IJA behavior. However, the simple elegance of the Henderson et al. study controls for this possible interpretation. The gross motor topography of IJA-pointing and IBR-pointing are virtually identical. Therefore, a neuro-motor explanation of the different cortical correlates of IJA and IBR appears unlikely. Instead, since IJA-pointing and IBR-pointing appear to serve different social-communicative functions, it is reasonable to assume that the difference in EEG correlates of these infant behaviors also reflects differences in the neurodevelopmental substrates of these social-communicative functions.

Another important aspect of the results of the Henderson et al. (2002) study is that they indicate that baseline activity associated with other cortical areas such as dorsolateral, orbito-frontal and temporal cortex may be involved in IJA. The latter observations are especially intriguing as they suggest that IJA development may reflect an integration of dorsal cortical functions with the ventral ‘social brain’ facilities. The possible nature of this integrated activity will be discussed in the last section of this paper.

At this point, though, it is important to recognize that, because two of the studies of IJA utilized baseline EEG data, there may be a tendency to dismiss these studies because their methodology is insufficiently precise to indicate the specific cortical systems involved in joint attention. Nevertheless, an intriguing, albeit indirect path of argument may be raised in response to this important potential critique.

Recall that joint attention development has long been theoretically linked to social cognition and Theory of Mind (ToM) development (e.g., Baron-Cohen, 1995; Mundy, Sigman, & Kasari, 1993; Tomasello, 1995). As noted earlier, when brain-behavior studies on Theory of Mind task performance are examined the most consistent observation to emerge is that ToM performance is also associated with activity in the Brodmann’s areas 8/9 of the DMFC (Frith & Frith, 1999, 2001). This literature provides evidence of a potentially significant
neuro-functional linkage that lends credence to observations of a dorsal medial-frontal contribution to joint attention. A review of this research will be presented after a brief discussion of theory of mind and its relations to autism and joint attention.

Theory of Mind

One hypothesis of 'social brain' theory has been that neural systems may develop which ultimately function specifically in the regulation of social behavior (Brothers, 1990). In a related fashion, research on social cognition has often adopted a modular perspective where the capacity to understand the intentions of others is thought to follow its own proprietary developmental course, with brain mechanisms responsible for apprehending mental states separable from brain mechanisms related to non-social cognition (e.g., Leslie & Thaiss, 1992; Baron-Cohen, 1995). This dedicated social-neuro-cognitive mechanism has various descriptions (Baron-Cohen, 1995) but will be referred to here as the Theory of Mind (ToM) module (Leslie, 1987).

Hypothetically, the ToM module employs a special type of cognition called meta-representation. The development of meta-representation involves the onset of a critical 'decoupling' mechanism that enables the child to keep multiple cognitive representations organized so that representations of one's own thoughts and feelings can be 'tagged' and distinguished from representations of the thoughts and feelings of others (Leslie, 1987). This facility allows one to generate representations of the psychological status of others, such as their thoughts, beliefs or feelings, and compare them to one's own thoughts, beliefs and feelings. This enables people to interpret and even predict the behavior of others in a complex and sophisticated fashion.

According to the ToM model of autism, a disturbance in this meta-representational capacity gives rise to the social and pragmatic deficits of people with this syndrome (Baron-Cohen, 1995; Leslie, 1987). The logic here is that, if children with autism have difficulty thinking about the psychological status of others, then their ability to interpret, or predict and anticipate the behavior of others will be impaired. This impairment would, in turn, make sharing experiences, or participating in complex social interactions, and even learning language very difficult. Even among those children who develop language, ToM disturbance exists and may lead to a host of pragmatic communicative problems as well, such as difficulties with understanding figures of speech (e.g., irony) or in gauging the timing constraints of discourse, or difficulty in perceiving the informational needs of others and the conventions of topic maintenance. Thus, according to the ToM model, many of the social deficits of individuals with autism may be understood in terms of this type of social-cognitive disturbance (Baron-Cohen, 1995). Although recent research suggests that ToM task deficits may not be as specific to autism as once thought (Yirmiya, Erel, Shaked, & Solomonica-Levi, 1998), numerous experimental studies support the hypothesis that children with autism have difficulty on theory of mind measures relative to MA, language and IQ matched controls (Baron-Cohen, 1995).

ToM difficulty may be related to an earlier developing difficulty in joint attention development. Several lines of theory have suggested that to easily coordinate attention with others in joint attention, infants must come to the incipient understanding that others possess covert mental intentions that may be directed or shared. Hence, joint attention reflects the early development of social cognition (Tomasello, 1995; Wellman, 1993). Similarly, although differing in the description of the mechanisms involved, several researchers have suggested that deficits in both joint attention and theory of mind observed in children with autism reflect common social-cognitive paths of disturbance (e.g., Baron-Cohen, 1995; Mundy et al., 1993). However, surprisingly little empirical data has been provided on this issue. One study, though, followed a sample of 13 typically developing infants from 20 to 44 months of age as part of a study on the early identification of autism (Charman et al., 2000). At 20 months, an alternating gaze measure was employed which involved children spontaneously initiating eye contact with a tester or parent when presented with an interesting toy spectacle. Alternating gaze measures are often used as indexes of IJA (e.g., Mundy et al., 1986; Tomasello, 1995). After controlling for differences in IQ and language development, the 20-month IJA alternating gaze measure was a significant predictor of 44-month ToM performance.

Thus, both theory and data suggest that joint attention and theory of mind skills may share common processes. Therefore, if brain-behavior research were to indicate that ToM performance was associated with DMFC/AC activity, this would lend credence to recent observations of a similar association of the DMFC/AC with joint attention development. Indeed, support for this common neurodevelopmental foundation is evident in recent research on ToM task performance.

ToM and basic brain research

Fletcher et al. (1995) used positron emission tomography (PET) to examine the cortical metabolic activity associated with performance either on ToM problem solving stories or 'physical' non-social problem solving stories. Performance of six typical adult men on the ToM stories was associated with increased blood flow in an area of the left medial-frontal gyrus corresponding to Brodmann's area 8. This was not the case, however, for the physical stories. Goel, Grafman, Sadato, and Hallet (1995)
reported a study that also used PET to examine the neural correlates of socio-cognitive task performance in typical adults. They observed that only tasks involving inferences about other people’s minds activated a neural network in the left dorsal medial-frontal gyrus, including part of the left medial-frontal gyrus. These authors concluded that, when inferential reasoning depends on constructing a mental model about the beliefs and intentions of others, the participation of the DMFC is required. Of course, even with the control conditions used in these studies, the possibility remains that the observed associations of the DMFC with ToM task performance were affected in some fashion by non-social-cognitive processes. This issue of specificity is far from resolved. Nevertheless, at least one study suggests that, while general inferential reasoning processes also seem to involve frontal activation, this activation appeared to be centered on more dorsolateral areas of the frontal cortex (Brodmann’s area 46) rather than the more dorsal-medial areas 8/9 associated with social cognition (Goel, Gold, Kapur, & Houle, 1997).

Another important issue is that, since imaging studies of ToM often use stories or verbal stimuli, language-related processes may affect the functional localization of ToM skills. Several studies have addressed this possibility. Gallagher et al. (2000) used functional magnetic resonance imaging (fMRI) to examine brain metabolic activity in response to both verbal ToM stories and non-verbal ToM tasks that involved the processing of visually presented cartoons. They observed considerable overlap in the bilateral brain activation associated with both tasks, specifically in the paracingulate area of the DMFC. The paracingulate area refers to a sub-cortical frontal structure that forms the ventral border between the dorsal medial-frontal cortex and the anterior cingulate cortex of the limbic system. Brunet, Sarfati, Hardy-Bayle, and Decety (2000) used PET to examine processing of comic strips depicting stories either involving the attribution of intention to characters or understanding physical casual sequences with characters. The comparison of these conditions suggests that the former involved regional cerebral blood flow increases (rCBF) in the right dorsal medial-frontal cortex (BA 9) and bilateral anteriorcingulate, as well as the areas of the right inferior-frontal cortex, right cerebellum and right and left temporal cortices. Several researchers have also utilized another non-verbal ToM paradigm that capitalizes on the tendency of people to anthropomorphize and to perceive animate and intentional behavior in cleverly organized movement sequences of geometric forms (Castelli, Happe´, Frith, & Frith, 2000; Klin, 2000; Schultz, Romanski, & Tsatsanis, 2000). Klin (2000) has coined the term Social Attribution Task or SAT for this type of paradigm. Castelli et al. developed one version of a SAT task and observed that task performance of six healthy adults was associated with PET indices of activation in the medial-frontal cortex (BA 9) as well as the superior and ventral temporal regions and the occipital cortex. Similarly, Schultz et al. (2000) have reported that processing on the Klin (2000) version of a SAT task recruited bilateral activation of the DMFC (BA 9) in their typical sample.

An important control condition was also included in a study by Sabbagh and Taylor (2000). Recording event-related potentials (ERP) using a dense EEG electrode array (128 sites), they presented university students with a paradigm that compared false-belief theory of mind task performance with an analogous non-social task. Just as a false-belief task involves thinking about the belief held within someone’s mind, this analogous non-social task involved thinking about the pictures held within a camera (see Leslie & Thaiss, 1992). Sabbagh and Taylor observed significantly larger ERPs from the left dorsolateral and dorso-medial cortex in the ToM false-belief task (e.g., ERP from electrode sites approximately above BA 9/10/46) compared to the false-image task in their sample.

Studies with clinical groups

In addition to studies of typically developing groups, clinical studies also point to the involvement of the dorsal medial-frontal cortex in ToM performance. In a PET study of autism spectrum disorders, Happé et al. (1996) reported that five adults with Asperger disorder did not display activity in the medial-frontal gyrus in the context of reading and solving ToM stories but did display activity in an immediately adjacent area. This pattern of DMFC activity distinguished Asperger disorder from controls. Similarly, Castelli, Frith, Happe´, and Frith (2002) have reported that individuals with autism or Asperger disorder report fewer and less accurate mental state attributions (also see Klin, 2000). Moreover, the autism/Asperger group showed less activation in the dorsal medial-frontal cortex as well as temporal cortex in response to the SAT task compared to controls (Castelli et al., 2002).

Related but somewhat different observations have been reported in an fMRI study by Baron-Cohen et al. (1999) who presented six individuals with Asperger disorder and 12 typical controls with a task that involved inferring emotional states, versus information about gender, from pictures of eyes. The results of this study indicated that activity in part of the ‘social brain’ network, involving orbito-frontal cortex, the amygdala, and the superior temporal gyrus, were involved in ToM processing. Moreover, significant differences were found between the Asperger and typical controls in task-related brain activity in the amygdala and other parts of this network. In this study activation of the left and right dorsal medial-frontal cortex was also observed to be a specific component of ToM task performance. However,
unlike the data from Happé et al. (1996) and Castelli et al. (2002), the clinical group did not differ from controls in task-related activation of this cortical area. Perhaps task differences account for this variability across studies (i.e., processing ToM stories vs. drawing inferences from pictures of eyes). It was apparent, however, that the typical controls in Baron-Cohen et al. (1999) displayed evidence of bilateral medial-frontal activation on ToM tasks. By contrast, the people with Asperger disorder displayed evidence of unilateral left medial-frontal activation but no evidence at all of right medial-frontal activation in association with the ToM tasks (Baron Cohen et al., 1999). Thus, there may have been a medial-frontal group difference in this study that was not detected by the analyses provided.

Russell et al. (2000) have also employed the ‘eyes’ task (Baron Cohen et al., 1999) in an fMRI study that examined the neural metabolic activation patterns associated with ToM in individuals affected by schizophrenia. The schizophrenic participants made more errors on the measures of attributions of mental state than did the controls. Moreover, the controls displayed relatively more activity in the medial-frontal lobe (Brodmann’s area 9 and 45) in association with ToM task performance relative to the individuals with schizophrenia. As in several of the basic studies, though, data in this study indicated that in addition to the dorsal frontal medial cortex, more ventral ‘social brain’ components of the left inferior frontal gyrus (Brodmann’s areas 44/45/47) and the left middle and superior temporal gyri (Brodmann’s areas 21/22) contributed to clinical groups’ differences on ToM-related performance.

The foregoing data provide additional evidence of the role of the DMFC/AC in ToM performance, and at least two studies (Happé et al., 1996; Castelli et al., 2002) raise the possibility that atypical DMFC/AC activation on social-cognitive tasks is characteristic of some individuals with autism. Consistent with this possibility, Ernst, Zametkin, Matochik, Pasterculaca, and Cohen (1997) have observed a disturbance of dopaminergic activity in the dorsal medial-frontal cortex of children with autism. Morphometric studies have also revealed atypical gray matter density in components of the DMFC/AC system (i.e., anterior-cingulate, paracingulate sulcus, left superior frontal gyrus), as well as the amygdala, temporal lobe, left inferior parietal lobe and cerebellum (Abell et al., 1999; Hardan et al., 2002).

Two individual difference studies have also directly implicated the DMFC/AC system activity in the social symptom presentation of autism. Ohnishi et al. (2000) examined PET regional cerebral blood flow (rCBF) and symptom presentation in children with autism and IQ matched controls. Symptom presentation was measured using factor-based scale scores for ‘Impairments in Communication and Social Interaction’ and ‘Obsessive Desire for Sameness’ from the Childhood Autism Rating Scale (Schopler, Reichlet, DeVellis, & Daly, 1980). Children with autism displayed decreased baseline rCBF relative to controls in the superior temporal gyrus (BA 22), left inferior frontal gyrus (BA 45) and left medial prefrontal cortex (BA 9/10). Moreover, less activity in the DMFC (BA 9/10) was correlated with more disturbance on the Impairments in Communication and Social Interaction factor-based CARS scores. rCBF in the right hippocampus and the amygdala was correlated with the Obsessive Desire for Sameness factor scaled score.

In another study, Haznedar et al. (2000) used PET and MRI co-registration to examine the hypothesis that the amygdala and hippocampus would display metabolic rate and morphometric differences in 17 high-functioning individuals with autism relative to typical controls. Few differences in these areas, however, were revealed. Individuals with the diagnosis of Asperger disorder displayed larger left amygdala volumes than did individuals with the diagnosis of autism. Larger left amygdala volume was also associated with lower nonverbal communications scores on the Autism Diagnostic Interview (ADI). In addition to these observations, though, a consistent pattern of significant findings was revealed for areas of the anterior cingulate (Brodmann’s area 24 and 24’). Volumetric data indicated that the autism group displayed smaller brain volume in the right anterior cingulate region, especially Brodmann’s area 24’ relative to the control sample. The autism sample also displayed hypometabolism in the right anterior cingulate cortex relative to controls. The Asperger subsample displayed left anterior cingulate hypometabolism relative to controls. This hypometabolism was not observed in more ventral portion of the anterior cingulate (Brodmann’s area 25). Finally, metabolism in left Brodmann’s area 24 was correlated with the social interaction, verbal communication and nonverbal communication scores of the ADI in the autism sample. Thus, consistent with the notion that the DMFC/AC system may be integral to the development of joint attention and social cognition, these studies provide some evidence that activity in this system may be related to social symptom presentation in autism. They also provide a useful reminder of the utility of studies of individual differences to complement and inform group comparison in research on the nature of autism.

In summary, theory has long suggested that infant joint attention and later social-cognitive measures may reflect common processes (e.g., Wellman, 1993). Recent research also suggests that activity in the DMFC/AC system is a common correlate of joint attention and theory of mind task performance. At present, however, the functional resolution of the data is inexact, especially with respect to joint attention behavior. Thus, the degree to which this apparent commonality across tasks and measures actually involves the same functional units within the DMFC/AC system is not clear. Nevertheless, the
current data support the plausibility of the hypothesis that common DMFC/AC neuropsychological functions play a role in IJA, ToM, and related social impairments in individuals with autism. Much of the following discussion is based on this premise, albeit with the recognition that a more detailed appraisal of this hypothesis remains as an essential goal for future research.

In considering the following discussion it is also important to recognize that dorsal frontal contributions to social behavior in samples with typical development, or autism, do not occur in isolation. Rather, current data would suggest that DMFC/AC processes contribute to both joint attention and theory of mind skill in conjunction with processes associated with more ventral ‘social brain’ and cerebellar systems (Baron-Cohen et al., 1999; Brunet et al., 2000; Castelli et al., 2000, 2002; Henderson et al., 2002; Russell et al., 2000). Thus, it may be helpful to adopt a complex systems approach (e.g., Bressler, 1995) in attempts to fully understand the dynamic neural interplay involved in these behavior domains. Prior to such an inclusive and dynamic level of analysis, however, an understanding of the component processes involved in the system will be necessary. To this point, though, little has been stated about what the DMFC/AC component may bring to such a system. This issue is addressed in the following brief overview of theory and research on the functions of the DMFC/AC.

**Functions of the DMFC/AC**

What processes and functions of the DMFC/AC complex may make it important to social development? How do these functions develop? Are there systems and functions of the DMFC/AC that are specific to social behavior? If so, are these systems dedicated to social behavior from birth, or does the DMFC/AC acquire social functions through an interactive organism–environment developmental process? Is impairment in the DMFC/AC social functions integral to the pathogenesis of autism? If so, does a developmental impairment of the DMFC/AC system make a primary contribution to autism, or are functions in the DMFC/AC complex disrupted in autism secondary to neurodevelopmental deficits in upstream cerebellar mechanisms or ventral-brain social information perception and processing?

While definitive answers to these questions are not close at hand, a wealth of information is beginning to be available on the functions of the DMFC and AC which may guide inquiry in this arena. Moreover, several hypotheses concerning the specific social-cognitive, as well as non-social-cognitive, functions of the DMFC have been generated, and these display interesting points of intersection with current theory on autism.

The DMFC/AC complex makes numerous contributions to the planning, self-initiation and self-monitoring of goal-directed behaviors. Goal-directed behaviors refer to a range of activities, from control of overt behavior like saccades in visual orienting, to the more covert mental activity involved in generating or operating on mental representations (cognition). Self-monitoring, in part, refers to DMFC/AC evaluation of whether or not goal-directed behavior leads, or does not lead, to reward (e.g., Amador, Schlag-Rey, & Schlag, 2000; Buch, Luu, & Posner, 2000; Feratlı & von Cramon, 2001). Related to this is its role in the appraisal of the valence of stimuli and the generation or modulation of emotional responses to stimuli (e.g., Fox, 1991; Lane, Fink, Chua, & Dolan, 1997; Ochsner, Bunge, Gross, & Gabrieli, 2002; Teasdale et al., 1999). Self-monitoring also involves the DMFC/AC’s role in the maintenance of representations of multiple goals in working memory and the capacity to flexibly switch between goal representations (e.g., Birrell & Brown, 2000; DiGirolamo et al., 2001; Koechlin, Basso, Pietrini, Panzer, & Grafman, 1999).

**Bridges to theories of autism**

The foregoing is a far from exhaustive list of DMFC/AC functions. Nevertheless, even this constrained view of this system may provide a unifying bridge between varied perspectives on autism. For example, up to this point we have focused on the two dimensions of autism that involve social and communicative disturbance. There is a third major symptom dimension, though, that involves a repetitive or a restricted range of behaviors. Interestingly, research on this dimension has suggested that repetitive behaviors in autism may be indicative of a disturbance in self-monitoring and the supervisory attentional system (Turner, 1997). The supervisory attentional system (SAS) has been described by Norman and Shallice (1986) as part of an executive system that guides the flexible implementation of goal-directed behaviors. Studies have also suggested that eye movement disturbance in autism may be indicative of impairment in the frontal eye fields (Goldberg et al., 2002), and that atypical preparation on motor planning tasks in autism is consistent with a disturbance of functions in the supplementary motor cortex and anterior cingulate (Rinehart, Bradshaw, Brereton, & Tonge, 2001). Other studies have suggested that motor movement anomalies may be an early marker of development disturbance in the first few years of life of children with autism (e.g., Osterling et al., 2002). Thus, cortical areas contiguous with the DMFC/AC system may be associated with repetitive behaviors, motor disturbance and social impairments in autism. Of course, research indicates that it is not just motor functions that support the contribution of the DMFC to social behavior.
Nevertheless, the confluence of these data suggests that it may be useful to consider the multiple roles of DMFC/AC system in attempts to understand the non-social as well as social symptoms of autism.

Data on DMFC/AC functions also provides a bridge to theories of autism that emphasize impairment in general cognitive rather than social-cognitive domains. Minshew, Johnson, and Luna (2001) have argued that autism involves a selective disorder of complex information processing. This disorder of complex information processing is reportedly manifest, at least in higher-functioning individuals, as a fundamental impairment in concept formation where this involves the capacity to 'spontaneously initiate a strategy for eliminating alternatives and ... the strategy needs to be monitored and changed in accordance with experience of success or failure while processing the solution' (Minshew et al., in press, p. 5). Broken down into its components, Minshew et al. (in press) suggest that autism may reflect a disturbance in: a) the spontaneous initiation of cognition goals and strategies, and/or b) the resolution of conflict between alternative cognitive strategies, and/or c) the monitoring and changing of strategies according to goal outcomes. Current research suggests that the DMFC/AC system may make important contributions to all three activities (e.g., Buch et al., 2000).

Another potential point of connection exists between the literature on DMFC/AC functions and the recently developed cognitive/perceptual model of autism that revolves around the weak central coherence (WCC) hypothesis (Frith & Happé, 1994). Briefly, WCC in autism reflects a bias toward processing stimulus details. Alternatively, holistic stimulus processing that involves integration of multiple dimensions of information (central coherence) is more difficult for people with autism. Hence, they often have difficulty with the types of gestalt and contextually bound information processing that is necessary to adaptive social information processing, such as in face processing or the processing of pragmatic aspects of communication. One indication of weak central coherence is the difficulty verbal children with autism have on homograph tasks that demand processing of the entire context of a sentence to interpret the correct meaning of words in phrases such as, 'a tear in her eye' vs. 'a tear in her dress' (Happé, 1997). Interestingly, holistic text interpretation processes have recently been observed to be associated with left dorsal medial-frontal activation in an MRI study (Ferstl & von Cramon, 2001). Indeed, Ferstl and von Cramon suggest that the 'frontomedian area [of the cortex] has a function for the self-initiation of a cognitive process in the context of tasks that require the active utilization of the individual's background knowledge' (p. 338). This function described by Ferstl and von Cramon (2001) would appear to have much in common with the nature of central coherence. Allman, Hakeem, Erwin, Nimchinsky, and Hof (2001) have also suggested that the spindle cell structures of the anterior cingulate may serve to connect widespread areas of the brain in order to achieve the integration of information in difficult problem solving situations. These cells may contribute to the type of integrated processing necessary to central coherence. Furthermore, Ring et al. (1999) have observed that activation in DMFC (BA 9), among several other brain areas, was associated with performance on a nonverbal measure of central coherence and that less task-associated activation in BA 9 was characteristic of people with Asperger disorder versus controls. Hence, it may be that the DMFC/AC system also contributes to weak central coherence disturbance in autism.

**The DMFC/AC and social attention in autism**

The executive functions of the DMFC/AC may also contribute directly to social behavior disturbance in autism. Impairments in DMFC/AC self-monitoring, as well as maintaining multiple goals and representations (Birrell & Brown, 2000; DiGirolamo et al., 2001; Koechlin et al., 1999), may conceivably be essential to the meta-representational processes necessary to theory of mind development and its impairment in autism (cf. Leslie, 1987). Impairment in this DMFC/AC facility may also contribute to autism impairment in the Initiating Joint Attention capacity to shift attention between social and non-social goals and representations (Mundy et al., 1986, 2000).

It may also be the case though that, with development, as general executive processes of the DMFC/AC are applied to the management of social interactions, sub-facilities develop that might be designated as specific 'social-executive functions' (SEF). Some of these SEFs may arise in conjunction with the self-monitoring and self-initiating facilities of the DMFC/AC system.

The hypothesis that the DMFC/AC plays an integral role in self-monitoring stems from several findings (Craik et al., 1999; Frith & Frith, 1999, 2001; Johnson et al., 2002). Prominent here is research that has led to the observation that, when people make erroneous saccadic responses in an attention deployment task, there is a negative deflection in the stimulus and response locked ERP called the error-related negativity or ERN (Luu, Flaisch, & Tucker, 2000; Buch et al., 2000). Source location suggests the ERN emanates from an area of the DMFC proximal to the anterior cingulate cortex (Luu et al., 2000). Observations of the ERN suggest that there are specific cell groups within the DMFC/AC that are not only active in initiating a behavioral act, such as orienting to a stimulus, but also distinct cell groups involved in the processing of the positive or negative outcome of the response behavior (i.e.,
accuracy and reward or reinforcement information) (e.g., Buch et al., 2000; Holroyd & Coles, 2002; Stuphorn, Taylor, & Schall, 2000). Thus, cell groups within the DMFC/AC come to serve as part of a supervisory attentional system (SAS) (Norman & Shallice, 1986) that functions to guide behavior, especially attention deployment, depending on the motivational context of the task (Amador et al., 2000; Buch et al., 2000; Luu et al., 2000).

Social-orienting disturbance in autism

The last phrase in the above passage was italicized because it suggests a potentially important connection between basic research on the DMFC/AC and new theory and research on the social impairments of autism. Several research groups have begun to suggest that autism may be characterized by a fundamental disturbance in the motivational and executive processes that serve to prioritize and organize orienting to salient social stimuli (Dawson, Metzoff, Osterling, Rinaldi, & Brown, 1998; Mundy, 1995; Klin, Jones, Schultz, & Volkmar, 2003). This disturbance is manifest in auditory social-orienting paradigms (Dawson et al., 1998) and visual eye tracking paradigms (Klin et al., 2003) as well as directly in social behavior disturbance such as joint attention impairments (Mundy & Neal, 2001). Furthermore, this domain of disturbance is thought to arise early enough, and in a sufficiently robust fashion, to lead to a significant impoverishment of social information input in infancy and early childhood in autism (Mundy & Crowson, 1997). The resulting impoverishment of social information during the first years of life may be so significant as to contribute to disruptions of typical brain development through impairment of experience-expectant neurodevelopmental processes (Greenough, Black, & Wallace, 1987; Mundy & Neal, 2001). In particular, the early onset of a fundamental social-orienting disturbance in autism is hypothesized to contribute to the subsequent disorganization and impairment of brain and behavior systems that support the development of subsequent social-emotional and social-cognitive skills (Dawson et al., 2002; Klin et al., 2003; Mundy & Crowson, 1997; Mundy & Neal, 2001).

Social-orienting disturbance in autism may occur because of reduced sensitivity to the reward value of social stimuli (Klin et al., 2003; Mundy, 1995) and this reduced sensitivity may stem from atypical functions of the ‘social brain’ system, especially those involving the orbito-frontal cortex and amygdala (Dawson, Osterling, Rinaldi, & Carver, 2001; Dawson et al., 2002; Mundy, 1995; Schultz et al., 2000; also see Tremblay & Schultz, 1999). The literature reviewed in this chapter, however, suggests several reasons why it may be useful to expand this focus to include consideration of the contributions from the DMFC/AC complex. First, infant measures of IJA provide one operationalization of the tendency to spontaneously orient to socially salient stimuli such as an interactive social-partner (Mundy & Neal, 2001), and there is now empirical evidence to directly link this tendency with DMFC/AC activity (Henderson et al., 2002; Mundy et al., 2000). Second, the DMFC/AC system may also be integral to the integration of reward appraisal in learning and goal-directed behavior, especially as this involves the control of visual orienting (Amador et al., 2000; Luu et al., 2000; Stuphorn et al., 2000). Third, in addition to the possible effects of ventral brain areas on more dorsal brain systems (Schultz et al., 2000), it is also important to recognize that the DMFC/AC may come to regulate the emotional responses to stimuli that are mediated by the amygdala or orbital frontal cortex (Ochsner et al., 2002). Indeed, it may be that the DMFC/AC system’s role in emotional regulation and integrating reward with goal-directed orienting leads to its critical contribution to the early regulation of social orienting and social attention (Posner & Rothbart, 2000). This hypothesized role of the DMFC/AC in social orienting may be one of the first manifestations of a specific social-executive function.

In considering this possibility it is noteworthy that dopaminergic projections to the anterior cingulate may play a role in the mediation of reward-related activity (Allman et al., 2001; Holroyd & Coles, 2002). Moreover, Allman et al. note that spindle cell formations in the anterior cingulate may be a novel specialization of neural circuitry found only in great apes and humans. The cells appear to emerge postnatally, at about 4 months of age, and their development may be affected by environmental factors. Thus, spindle cell systems of the anterior cingulate may have the potential to be involved in the types of experience-expectant, as well as experience-dependent, coactive neurodevelopmental processes described in recent neurodevelopmental theory of autism and social orienting (Mundy & Neal, 2001).

Of course, one challenge to the notion that the frontal eye fields and/or DMFC may play a role in the early onset of social-orienting disturbance in autism is that frontal oscillomotor control of attention deployment may be relatively late to develop in infancy (Johnson, Posner, & Rothbart, 1991). However, recent research suggests that by 3 to 4 months, ‘the cortical eye fields are actively involved in the prospective control of saccades and visual attention’ (Canfield & Kirkham, 2001). It is also important to note that, although a social-orienting disturbance may be a robust phenomenon in children with autism (Dawson et al., 1998; Klin, 1991), a more general impairment in orienting to non-social stimuli is apparent as well (Dawson et al., 1998; Townsend et al., 2001). Indeed, autism may be characterized by a general, rather than socially specific orienting disturbance that arises from impairment in a complex axis of cerebellar, parietal and frontal functions involved in the development and control of attention.
(Carper & Courschesne, 2000; Townsend et al., 2001). Thus, an important goal of research on autism is to better understand the interplay between the DMFC/AC complex, orbitofrontal and amygdala functions, and cerebellar input in the development of social and non-social attention regulation in people affected by this disorder. One way to do this may be to integrate new, sophisticated methods for studying eye tracking and orienting in individuals with autism (Klin et al., 2003) with research methods used to study functions of the DMFC/AC system (Amador et al., 2000) and other brain areas, as well as those used to study joint attention and early social-orienting disturbance in autism (Dawson et al., 1998; Mundy et al., 2000).

The DMFC/AC, social cognition and intersubjectivity

The DMFC/AC may be involved not only in self-monitoring but in the related process of developing self-representations that may also play an important role in autism (Craik et al., 1999; Frith & Frith, 1999, 2001; Johnson et al., 2002). Frith and Frith (1999, 2001) have argued that, as the DMFC/AC comes to participate in the development of representations of the self, it also integrates information from ventral social brain systems (e.g., superior temporal sulcus – STS) that provide information about the goal-directed behaviors and emotions of others (e.g., Ochsner et al., 2002). This integrative activity may be facilitated by the abundance of connections between the DMFC/AC, the STS, and the orbitofrontal cortex in primates (Morecraft, Guela, & Mesulam, 1993). Again, it may be useful to think of this facility for the integration of proprioceptive self-action information with exteroceptive information on the actions and behaviors of others as another emergent SEF (social-executive function) of the DMFC/AC. Ultimately, this SEF serves to compare and integrate the actions of self and the action of others, perhaps utilizing the DMFC/AC facility for the maintenance of representation of multiple goals in working memory. This integration gives rise to the capacity to infer the intentions of others by matching them with representations of self-initiated actions or intentions (Leslie, 1987). Once this integration begins to occur in the DMFC/AC, a fully functional, adaptive human social-cognitive system emerges with experience (Frith & Frith, 1999, 2001).

In relation to this hypothesis it has earlier been suggested that episodes of joint attention, especially those initiated by the child, provide a context for infants to integrate proprioceptive information on the actions and intentions of self with exteroceptive information from observations of the actions and intentions of others, in reference to some third object or event (Mundy et al., 1993). For example, during the act of showing, infants have the opportunity to monitor their own experience of an object (e.g., enjoyment), while also observing the response of a social partner (e.g., their direction of gaze and affect) to both the object and the infant’s behavior. Thus, self-initiated bids for joint attention provide a rich opportunity for infants to compare information about a social partner’s awareness and responses to the displayed object with their own (Bates, 1976). In this way, self-initiated bids for joint attention may provide infants with an opportunity to learn about the internal psychological process of the self and of others (Mundy et al., 1993).

Theoretically, engagement in this process within joint attention episodes facilitates social-cognitive development, as well as social-emotional attunement in typical development (Mundy et al., 1992; Mundy et al., 1993). A failure in the development of this fundamental and complex interactive skill, through as yet poorly understood, has been suggested as an essential component of the genesis of social-cognitive disturbance in autism (Hobson, 1993; Mundy et al., 1993). Some have described this, and related phenomena, as a fundamental disturbance in the capacity for children with autism to engage in shared experience or intersubjectivity (Hobson, 1993; Mundy & Hogan, 1994). This observation, in conjunction with the seminal theoretical analysis of Frith and Frith (1999, 2001), leads to the hypothesis that the activity of the DMFC/AC complex may well be integral to this function. Stated more forthrightly, an interesting, albeit speculative extrapolation of the foregoing literatures is that the DMFC/AC complex may contribute to a neurofunctional platform from which the essential human capacity for intersubjectivity springs. Here again, though, more ventral social brain processes may also be involved in intersubjectivity (Trevathan & Aitken, 2001), and input from these ventral systems may facilitate the capacity of the DMFC/AC to mediate episodes of intersubjectivity that involve affective sharing, as well as more social-cognitive episodes. Indeed, the anterior-cingulate may be viewed as an amplifier and filter that interconnects emotional and cognitive aspects of the mind (Devinsky & Luciano, 1993; Ochsner et al., 2002). This interconnecting facility may contribute to the role of DMFC/AC in the type of affective sharing or intersubjectivity that is integral to the development of initiating joint attention behavior and its impairment in autism (Mundy, 1995).

Simulation theory and self-organization

Frith and Frith’s (1999, 2001) model also has obvious parallels with simulation theory as applied to social cognition (e.g., Stich & Nichols, 1992). Simulation theory suggests that individuals use their awareness (i.e., representations) of their own mental processes to simulate and analyze the intentions of others (Gallese & Goldman, 1998). That is, with development people learn to use self-knowledge, derived from self-monitoring, to extrapolate and make
inferences about the covert psychological processes that contribute to the behaviors of other people. In a recent presentation of simulation theory, Gallese and Goldman (1998) have discussed the possible role of mirror neurons in the social-cognitive simulation facility of the DMFC/AC. Mirror neurons are a specific class of motor neurons that are involved both when a particular action is performed by an individual and when an individual observes the same action performed by another person. According to Gallese and Goldman (1998), the motor and premotor cortex, adjacent to, or overlapping with, the DMFC is rich in mirror neurons (Rizzolatti & Arbib, 1998). Too little is yet known about the nature and distribution of mirror neurons to provide an extended discussion here. Nevertheless, since imitation constitutes a domain of impairment in autism (Rogers & Pennington, 1991), it may be useful to explore the link between motor neurons, imitation and the social functions of the DMFC/AC in future research on typical and atypical development (Gallese & Goldman, 1998).

Finally, it is important to recall the distinction between social input and social output systems raised in the beginning of this paper. Much of the research on autism involves the study of the fidelity of input systems. However, various perspectives on development suggest that critical aspects of early neurodevelopment and learning are dependent upon self-monitoring of self-generated interactions with the environment (Piaget, 1952; Greenough et al., 1987; Mundy & Neal, 2001). For example, Piaget (1952) developed the notion that early cognitive development derived in large part from the actions infants took on objects in their world. Indeed, a major component of cognitive development was described in terms of the re-description of overt action (sensorimotor schemes) to covert mental representations of action in the first two years of life. For the most part, Piaget's formulations focused on the development of knowledge about objects, and unfortunately did not speak as clearly to social-cognitive development. Nevertheless, it may also well be that the infant's capacity to initiate actions in social interaction (e.g., initiating a joint attention bid), and to note social reactions to self-initiated actions, constitutes a major early building block of social-emotional and social-cognitive development (Braten, 1998). Following this line of thinking, impairment in the early tendency to initiate and organize social behaviors, such as social orienting and joint attention bids, may be especially pernicious to the development of the child with autism because it disrupts his/her capacity for social action, which ultimately contributes to the foundation of social self-knowledge requisite to social-cognitive development. Hence, early difficulty in organizing and initiating social action may play a significant and unique role in the interactive organism–environment etiology of autism (Mundy & Neal, 2001). Indeed, one common goal of intervention with people with autism is to counter this difficulty and increase their tendency to self-initiate adaptive goal-directed actions in social, as well as non-social situations. The literature reviewed in this paper would suggest that a disturbance in the functions of the DMFC/AC play a fundamental role in this broad domain of impairment. Specifically, DMFC/AC impairment may make a fundamental contribution to a continuous path of disturbance in autism that begins with the early onset of difficulty in the self-initiation of action (e.g., in social orienting or IJA) in infancy, and eventually is manifest in difficulty in the self-initiation of aspects of social cognition (Frith & Frith, 1999; 2001). Thus, deficits in the self-initiation of early social behavior and later social cognition may be a critical feature of autism associated with impairments to a neural system involving the DMFC/AC.

**Conclusion**

The study of autism presents an enormously complex puzzle and, unfortunately, several of the pieces critical to the solution of the puzzle seem to be missing at this time. One of these pieces may involve the role of the DMFC/AC complex in social, emotional and cognitive development. The DMFC/AC may be involved in the basic disturbance in social orienting in autism (Dawson et al., 1998) that has been observed using a variety of methods, from infant joint attention measures (Mundy et al., 1986) to new eye tracking methods (Klin et al., 2003). The DMFAC/AC may also play a role in the capacity to relate self to others (Frith & Frith, 2001) and disturbance in this domain may contribute to the atypical development of intersubjectivity, joint attention and social cognition that may impair the lives of people with autism (Mundy et al., 1993). Indeed, impairment of the DMFC/AC complex reportedly produces a symptom profile including apathy, inattention, dysregulation of autonomic functions, variability in pain sensitivity, akinesis and emotional instability (Buch et al., 2000) that has other obvious commonalities with characteristics of people affected by autism. However, it may be the case that severe DMFC/AC impairment-related behavioral deficits emerge only when they are combined with disturbances in other related functional neural networks (Devinsky & Luciano, 1993). Thus, further research into the neurodevelopmental role of the DMFC/AC complex in the pathogenesis of autism may best be conducted in integration with research on the other neural systems, such as ventral social brain systems, that may be involved in autism.

**Acknowledgments**

The preparation of this paper was supported, in part, by NIH Grant HD38052, *Joint Attention and*
Developmental Outcome, and by State of Florida funding for the University of Miami Center for Autism and Related Disabilities (UM-CARD).

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Manuscript accepted 12 March 2003