Developmental deficits in social perception in autism: the role of the amygdala and fusiform face area

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Abstract

Autism is a severe developmental disorder marked by a triad of deficits, including impairments in reciprocal social interaction, delays in early language and communication, and the presence of restrictive, repetitive and stereotyped behaviors. In this review, it is argued that the search for the neurobiological bases of the autism spectrum disorders should focus on the social deficits, as they alone are specific to autism and they are likely to be most informative with respect to modeling the pathophysiology of the disorder. Many recent studies have documented the difficulties persons with an autism spectrum disorder have accurately perceiving facial identity and facial expressions. This behavioral literature on face perception abnormalities in autism is reviewed and integrated with the functional magnetic resonance imaging (fMRI) literature in this area, and a heuristic model of the pathophysiology of autism is presented. This model posits an early developmental failure in autism involving the amygdala, with a cascading influence on the development of cortical areas that mediate social perception in the visual domain, specifically the fusiform “face area” of the ventral temporal lobe. Moreover, there are now some provocative data to suggest that visual perceptual areas of the ventral temporal pathway are also involved in important ways in representations of the semantic attributes of people, social knowledge and social cognition. Social perception and social cognition are postulated as normally linked during development such that growth in social perceptual skills during childhood provides important scaffolding for social skill development. It is argued that the development of face perception and social cognitive skills are supported by the amygdala–fusiform system, and that deficits in this network are instrumental in causing autism.

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1. Introduction

Autism is part of a spectrum of disorders characterized by a triad of symptoms, including deficits in all aspects of social reciprocity; pragmatic communication deficits and language delays; and an assortment of behavioral problems, such as restricted interests, sensory sensitivities and repetitive behaviors (American Psychiatric Association, DSM IV, 1994). Its early onset and familial pattern strongly suggest a biological basis, and, in fact, there are now substantial data implicating brain based as well as genetic mechanisms (Volkmar et al., 2004). From the perspective of current heuristic models of the functional neuroanatomy of typical children and adults, there is no apparent core mechanism that could explain the assortment of symptoms found in autism; the triad of deficits suggests that a diverse set of neural systems are affected. At the same time, however, the pattern of brain abnormality is discrete, because autism spares many perceptual and cognitive systems. For example, severe autism is not incompatible with normal or even

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superior intelligence, as measured by conventional IQ tests. This fact would seem to rule out any neurobiological explanation of autism that focuses on deficits of complex information processing as a necessary ingredient.

Thus, a key question for understanding the neurobiology of autism is whether the range of symptoms is caused by “hits” against multiple independent neural systems, or whether there is an initial insult in one or two that give rise to many more symptoms (Schultz et al., 2000a). Although the full syndrome as expressed in later childhood and adolescence clearly appears to involve insults to multiple systems, it is not clear if these multiple systemic brain disturbances are under independent control processes, or whether the initial insult might have been more circumscribed. It is possible that the initial insult is localized, and that through transactional processes during development, deficits in one system negatively impact the development of other neural systems, and a more pervasive set of impairments evolves. This type of “big bang” model places emphasis on how one set of defining impairments adversely affects the cumulative experiences of the developing child. This type of model suggests that it is through experiences, either alone or in combination with other vulnerabilities, that affects of the initial insult become more widespread. This review will adopt this framework in order to explore the pathophysiological and developmental bases of the pervasive and early appearing social deficits that are the sine qua non of autism.

This review will specifically focus on face perception deficits in autism, describing current literature on abnormalities in the fusiform face area (FFA) and the amygdala. It will be argued that an abnormality early in development in the amygdala can give rise to later social perceptual deficits in face identity and facial expression perception. Moreover, emerging data suggest that the same visual cortices involved in face perception are also involved in representing semantic knowledge about people. Thus, aberrations in face perception, stemming perhaps from developmental failures of the amygdala signaling system, not only affect social perception, but are compounded to create deficits in the social knowledge system as well. This would have a profound influence on the social skill areas that are deficient in autism.

2. Diagnosis, phenomenology, and the primacy of social deficits

Autism was first identified and described in 1943 by Leo Kanner, a child psychiatrist at Johns Hopkins University (Kanner, 1943). Although the cases included in his original report suffered multiple problems, Kanner’s description emphasized the social and emotional features of the disorder. He speculated that persons with autism “… have come into the world with an innate inability to form the usual, biologically provided affective contact with other people” (p. 250). This emphasis is consistent with most present day conceptualizations, i.e., the social deficits are viewed as the primary and unique characteristic of autism vis-à-vis other neuropsychiatric disorders (Diagnostic and Statistical Manual, fourth ed., DSM IV, 1994). Current conceptualization of the social deficits as embodied by the nomenclature of the DSM IV entails an emphasis on absent or deficient behaviors important for social reciprocity. The critical diagnostic criteria include poor eye contact; a failure to develop peer relationships appropriate to their developmental level; abnormal emotional intonations in voice and speech; marked impairment in the use of multiple nonverbal behaviors such as eye-to-eye gaze, facial expression, body postures, and gestures to regulate social interaction; and failure to spontaneously seek to share enjoyment, interests, or achievements with other people (e.g., by a lack of showing, bringing, or pointing out objects of interest).

One argument for focusing on the social dysfunction when searching for root causes is that relative to the other aspects of the behavioral phenotype, the social deficits are specific to autism. This is in contrast to the other two domains of the diagnostic triad in that those are frequently shared with other disorders. For example, language delay and communication deficits are the defining features of primary language disorders. The repetitive behaviors, sensory sensitivities and restricted interests are also clearly non-specific features, as they are shared by many mental retardation syndromes (Bodfish et al., 2000).

The social dysfunction in autism might also be “superordinate”, in the sense that it may be capable of moderating or otherwise explaining the emergence during development of other aspects of the phenotype. Early emerging language among children with autism appears to lack intentionality—the desire to share the contents of their own minds and connect with the minds of others (Charman, 2003; Mundy et al., 1990). According to one influential model, normal infant language development (in particular, word learning) is driven in part by the infant’s capacity to understand the mental states of other people (Bloom, 2004). In autism, where there are profound deficits in joint attention and intersubjectivity evident by the latter part of the first year of life, this model would predict language delays. Indeed, longitudinal studies of joint attention and language development in autism show that these deficits are intimately related, such that earlier emerging deficits in social development preclude timely and otherwise normal language development (Carpenter et al., 1998, Mundy and Gomes, 1998; Mundy et al., 1990, 1994). Siller and Sigman (2002) showed that the degree of maternal synchronization of attention with their infant was predictive of language gains up to 16 years later. Moreover, treatment aimed at improving non-verbal communication skills can enhance formal language ability as well (Kasari et al., 2001). Mundy and co-workers (1995, 2001), Klin et al. (2003), as well as Dawson and co-workers (1989, 1998) have advocated for a social developmental model of autism. Whereas in typically
developing infants and toddlers, socially directed behaviors serve as the primary regulator of other forms of cognitive development, in autism, the paucity of social motivation and interaction is argued to be the primary causal precursor to subsequent failures of language and general cognitive development.

Although less well studied, and much more speculative, there may also be a direct influence of the social deficits on the emergence of repetitive behaviors. Whereas the signs of social dysfunction are evident within the first 6–12 months of life (Adriani et al., 1993; Maestro et al., 2002; Osterling and Dawson, 1994), restricted and repetitive behaviors are typically not present at these younger ages, but rather emerge and intensify between about 2 and 4 years of age (Cox et al., 1999; Lord, 1995; Moore and Goodson, 2003). In non-human primates, stereotypes and self-injurious behaviors can be reliably caused by long-term social deprivation (McKinney, 1974; Suomi and Harlow, 1971), and these types of repetitive behaviors are believed to have an important function in reducing the stress that results from the social deprivation (Mason, 1991). This raises the interesting possibility that to the extent that the social deprivation experienced by the developing child with autism is stressful, the later emerging repetitive behaviors may then be in part a consequence of those social deficits. In other words, the repetitive behaviors might represent in part a compensatory reaction or coping mechanism that may later become an independent behavioral repertoire that is sustained by multiple factors. The idea that these behaviors are sustained by multiple factors is important, as most phenomenological studies show little or no correlation between the magnitude or severity of repetitive behaviors and the other two symptom domains (e.g., Tanguay et al., 1998).

Autism is recognized as a heterogeneous disorder and as part of a continuum of disability shared with Asperger syndrome and Pervasive Developmental Disorder Not Otherwise Specified (PDD NOS). Collectively these syndromes are referred to as the autism spectrum disorders (ASDs), with the belief that the underlying neurobiological bases are shared and that characterization of individual cases is best conceptualized along one or more continuous dimensions of severity. Asperger syndrome involves autistic-like disturbance in social reciprocity, but it does not share the developmental disability of communication and language. PDD NOS, on the other hand, is a subsyndromal manifestation of autism.

Even within autism proper, there is a good deal of variability in presentation between cases. In fact, the discrepancies in clinical presentation between individual cases of even classic autism can be striking. There is also a marked range of associated problems in autism. While the majority of persons are mentally retarded, and many are mute, there are still many cases with average or even superior intelligence (Volkmar et al., 2004). This heterogeneity is further cause for judicious choices regarding phenotypic entrance points for studying neurobiological mechanisms. Because the social deficits provide the common linkage between the ASD subtypes, studying the social disability may very well be a more powerful way to elucidate the underlying neural substrates that are fundamental to this class of disorders.

In summary, the specificity of the social deficits for autism, and their possible modulatory effects over language and repetitive behaviors, stand out as a significant clue and starting point, both for understanding the ontogeny of autism, and in our research laboratories for guiding our choices of specific neural systems to study as we attempt to explain the pathobiology of the disorder. The prediction here is that studying the social system deficits will ultimately provide greater opportunity for understanding the key components of autism at the level of brain development and function than studying any other component of the disorder.

3. Face perception

Although not part of current diagnostic criteria, much evidence suggests that persons with an ASD have marked deficits in face perception (Deruelle et al., 2004; Grelotti et al., 2002; Joseph and Tanaka, 2002; Klin et al., 1999). Recognition of individual faces is an integral part of interpersonal interactions and successful functioning within a social group. It is important to be able to quickly differentiate friends, potential mates, strangers, enemies, etcetera during any encounter. Typical children and adults have developed perceptual processes capable of distinguishing between faces with extraordinary skill. Although faces may appear to be quite different from one another, features of the face and their placement are actually remarkably uniform compared to those of other common objects, and thus our skill in discriminating faces is largely unparalleled. When seeing a familiar face, an immediate flash of recognition occurs that is automatic and apparently without conscious effort. Given that all faces are perceptually similar in terms of their features (eyes, nose, mouth) and configuration (the eyes are above the nose which is above the mouth), this seemingly simple act of everyday face recognition turns out to be an unprecedented feat of visual perception; we seldom have to make such fine discriminations among other classes of objects (Diamond and Carey, 1986).

Indeed, our ability to recognize faces quickly and accurately has led many researchers to argue that virtually all adults are experts in the recognition of faces (Carey, 1992; Diamond and Carey, 1986; Tanaka and Gauthier, 1997). This type of perceptual expertise involves a sensitivity to the configuration of the major features, such that slight distortions of their spatial relationship are quickly recognized by experts but not by novices (Gauthier and Tarr, 2002). The classic example of this type of “holistic” perceptual effect involves rotating pictures of faces 180°; inverted faces are much more difficult to accurately
recognize than upright faces (e.g., Freire et al., 2000; Leder and Bruce, 2000; Yin, 1969). Inversion appears to interfere with face perception by distorting the local relational information between face parts (e.g., the relative position of the eyes, the nose and the mouth), which in turn affects the normal “holistic” processing of the face, i.e., binding the features together as a whole gestalt. In contrast, inverting other common objects for which the observer has no special perceptual expertise, e.g., houses, has much less effect on one’s recognition performance because we are less sensitive to the configuration of the features that compose this class of objects. These differences in the “inversion effect” demonstrate that common object (novice) perception is more driven by feature level processes than holistic perceptual processes. Studies of the process by which one becomes a perceptual expert show that fundamental changes occur in the perceptual processes, including a shift from piecemeal processing to holistic processing (Gauthier and Tarr, 1997; Gauthier et al., 1998). Moreover, experts with non-face objects, e.g., birds or cars, also show a large inversion effect for the objects of their expertise (Diamond and Carey, 1986). Thus, the holistic processing style that characterizes normal face recognition is shared by experts of other non-face object categories.

Whereas most people qualify as face experts, individuals with an ASD are selectively impaired in their ability to recognize faces (Boucher and Lewis, 1992; Braverman et al., 1989; Davies et al., 1994; de Gelder et al., 1991; Hauck et al., 1999; Hobson, 1986a, 1986b; Hobson et al., 1988a, 1988b; Joseph and Tanaka, 2002; Langdell, 1978; Tantum et al., 1989; Weeks and Hobson, 1987). Face perception can be subdivided into two general types—recognition of person identity via the structural features of the face, and recognition of internal affective state of another individual, independent of their identity, via the shape of individual features and changes in their relative distance from one another during the expression. On the surface, deficits in facial expression perception might appear to have the most relevance for the social deficits in autism. This may indeed prove to be true, but at this point in time, deficits in person identity from the face are better understood, especially with regard to the functional neuroanatomy of autism. Moreover, it may be the degree to which a face is “emotionally salient”, even during the perception of non-emotional aspects, such as simple face identity, that is most important in explaining the social deficits in the ASDs (Schultz et al., 2000a, 2000b; Grelotti et al., 2002, 2005).

In the largest study to date of face recognition skills in ASD, Klin et al. (1999) measured this ability in 102 young children with autism, PDD NOS and non-PDD disorders (MR and language disorders) matched on age and IQ (non-verbal and verbal IQ, different matched samples) (Klin et al., 1999). There were pronounced deficits of face recognition skill in the ASD group relative to the comparison groups. Importantly, there were no group differences on two visual perceptual control tasks, indicating that perceptual deficits were specific to faces and not representative of a more pervasive deficit in object perception. This selective impairment has been found across many studies (Boucher and Lewis, 1992; Davies et al., 1994; Hauck et al., 1999; Hobson et al., 1988a, 1988b; Tantum et al., 1989). One interpretation of this pattern of findings is that persons with an ASD fail to develop expertise for faces because of inadequate attention to faces across development, owing in some way to a failure to perceive faces as emotionally salient. I have hypothesized with my colleagues that faces are less emotionally stimulating to persons with an ASD, and that they therefore do not attract and sustain the attention of the observer with an ASD to the same extent as a typically developing person (Grelotti et al., 2002, 2005; Klin et al., 2002, 2003; Schultz et al., 2000a, 2000b). What drives this lack of salience is not completely clear, though we argue for a role of the amygdala. However, this explanation is incomplete, as there needs to be some initial set of conditions in typical infants that causes faces to attract attention; in some way faces must be rewarding. We hypothesize that the deficient emotional salience of faces/reward value leads to a failure to acquire normal face perception skill. While typically developing children become “addicted to faces” in the sense that faces more readily pop out of complex environments during normal perception, children with autism appear to lack this addiction.

Newborn infants as young as 36 h show a preference for face-like patterns as compared to other types of visual patterns (Goren et al., 1975; Simion et al., 1998). Although this preference might very well be due to more general constraints in the newborn visual system (Kleiner and Banks, 1987; Cassia et al., 2004), it does not alter the fact that infants seem geared to accumulate experience with faces. What is still not clear is whether this biological preparedness is driven at a perceptual level alone, or whether the social rewards that come from interacting with other people are the more influential factor in motivating preferential orienting to faces. Careful observation of behaviors during infancy of children later diagnosed with an ASD, e.g., in retrospective studies of home movies, finds that these infants show much less attention toward the face of others. In fact, the lack of interest in the faces of others is evident in the first 6 months of life, and is one of the best predictors of later diagnosis (Maestro et al., 2002). Using home videos, Osterling and Dawson (1994) conducted a retrospective study of the first birthday parties of 11 children who later were given a diagnosis of autism, and compared the behaviors of these children to that of 11 typically developing children. The children with autism showed significantly less interest in the faces of other persons and were less likely to show objects to other people, to point to objects, or to orient to a person calling their name. Thus, there is a clear and early lack of interest in faces among those who go on to develop the full syndrome of autism, and this
would seem to place the child at great risk for failing to become a perceptual expert in this domain.

Not only are persons with an ASD less quick and accurate on experimental tasks of face perception, but they also appear to rely too heavily on feature level analyses, and do not adequately make use of configural strategies (Hobson et al., 1988a, 1988b; Klin et al., 2002; Langdell, 1978; Tantum et al., 1989). Persons with an ASD, for example, show much less of an inversion effect for faces, i.e., their performance is not much degraded for the recognition of upside down faces versus upright faces (Langdell, 1978; Teunisse and de Gelder, 2003). Joseph and Tanaka (2002) directly studied configural and feature level perception using the parts-whole method of Tanaka and Farah (1993). Whereas typically developing children used holistic face processing strategies, children with an ASD of comparable age and ability did not. Other studies have emphasized that individuals free of social disability orient to the eyes for information regarding the mental states of others, while people with an ASD have significant difficulty extracting the “language” of complex emotional states from the eyes (Baron-Cohen et al., 1999, 2000).

Consistent with these findings, Klin and co-workers (2002) recently used infrared eye-tracking technology to measure visual scan paths and percent viewing time on predefined regions of interest (ROI) among 15 males with autism and 15 control males (matched on age and IQ) as they watched short film clips from Who’s Afraid of Virginia Wolf. Each film clip was chosen for its rather intense interpersonal interactions, with screen shots dominated by close-ups of faces. Persons with an ASD focused much more than typical viewers on one feature of the face—the mouth—and less on the rest of the face, particularly the eye region. In fact, the distribution of percent viewing time on the eye region for each group did not overlap at all, showing that this one behavioral variable could classify participants with 100% sensitivity and specificity. While replication studies would not be expected to necessarily show such good separation of diagnostic groups, it would be predicted that this finding is very robust. Moreover, this type of perceptual bias for a single feature is commensurate with a deficit in holistic processing of faces.

Even though persons with ASD do not show visual perceptual deficits on complex object perception tasks not involving faces, it remains an open empirical question as to whether there nevertheless exists more general perceptual abnormalities in the visual system of persons with an ASD that could be a necessary precursor to the failure to develop perceptual expertise for faces. This issue is interesting as it may help clarify the neural systems involved, i.e., a perceptual and probably cortical explanation for the face perception deficits in autism versus a limbic and affective explanation (though these need not be mutually exclusive). The preference shown by persons with an ASD for feature level perception extends beyond their interactions with faces, as they often attend more to minor features of the environment that are overlooked by others. Concomitant with a lack of interest in social objects, persons with an ASD are often preoccupied with inanimate objects or parts of objects (e.g., edges of object, wheels on a toy, fuzzy specks on the floor) (DSM IV, 1994). This preference for local details has been confirmed in a number of experiments; individuals with an ASD do better than typically developing controls on tasks in which success depends upon processing of local features, and they do worse on tasks that require global processing (Mottron and Belleville, 1993; Mottron et al., 1999; O’Riordan and Plaisted, 2001; Plaisted et al., 1999, 2003).

This feature level bias may indicate a preference for “high spatial frequency” information. Any visible object can be described in terms of its different spatial frequency components. The high spatial frequencies (HSFs), i.e., the sharp changes in brightness (the edges), are especially important for individual feature identification. Low spatial frequencies (LSFs), on the other hand, capture information about the spatial configuration of the features. At a neural systems level, there is evidence that the magnocellular visual system is more sensitive to LSF information, and that the parvocellular system is biased to HSF information (Livingston and Hubel, 1988; Merigan and Maunsell, 1993; Vidyasagar, 1999). While this dichotomy is appealing, and automatically suggests a hypothesis to be explored in persons with an ASD, it may be overly simplistic, as the functions of each pathway are overlapping.

Behavioral studies have consistently shown that face recognition among typically developing controls is facilitated more by the LSFs than the HSFs (Costen et al., 1996; Morrison and Schyns, 2001; Parker et al., 1996). Moreover, during infancy, the preference for faces appears to be mediated by the LSF components of the face (Farroni et al., 2000). Among typically developing young adults, the optimal spatial frequency range for face perception ranges from 8 to 32 cycles per face (CPF) (Morrison and Schyns, 2001). In contrast, Curby and Gauthier (2002), Curby et al. (2003) have shown that a young adult male with Asperger syndrome relied on much higher spatial frequencies (>45 CPF) to make identity judgments. This is consistent with the recent findings of Deruelle et al. (2004). In a study of 11 children with autism or AS, compared to two groups of normally developing children, they found between group differences in performance to be mediated by spatial frequency information. While children with an ASD did better with HSF as compare to LSF faces, the controls had the opposite pattern of performance, with more errors on the HSF faces versus the LSF faces. Thus, there is consistent evidence suggesting that persons with an ASD are biased toward details or HSF information as compared to configurual or LSF information. The preference for faces, especially the LSF information, that is normally first demonstrated in infancy suggests that the deficits found in autism probably have their roots in a failure of an early developmental process.
Recent electrophysiological results add further to this line of reasoning. There is a negative amplitude visual evoked potential averaging 170 ms after retinal exposure to any complex object. This “N170”, however, is consistently larger to faces compared to other objects (Bentin et al., 1996; Rossion et al., 2000). This larger N170 amplitude for faces has been shown in one recent study to be driven by the LSF components and not the HSF components (Goffaux et al., 2003). Moreover, the amplitude of the N170 is largest for objects that one is especially good at differentiating. Thus, the N170 is larger in response to pictures of dogs than birds for dog experts, but it is bigger for birds than dogs in bird experts (Tanaka and Curran, 2001). The N170 also shows a face-like pattern of modulation as a result of expertise training on non-face objects (Rossion et al., 2002). The N170 is larger to faces compared to other objects (Bentin et al., 1996; Rossion et al., 2000). This larger N170 amplitude for faces has been shown in one recent study to be driven by the LSF components and not the HSF components (Goffaux et al., 2003). Moreover, the amplitude of the N170 is largest for objects that one is especially good at differentiating. Thus, the N170 is larger in response to pictures of dogs than birds for dog experts, but it is bigger for birds than dogs in bird experts (Tanaka and Curran, 2001). The N170 also shows a face-like pattern of modulation as a result of expertise training on non-face objects (Rossion et al., 2002). Thus, at both the behavioral and electrophysiological levels, LSF appears to be more important for face perception. Finally, we have shown in a preliminary study that compared to typical adolescents, persons with an ASD show a smaller N170 amplitude to faces relative to non-face objects (Klaiman et al., 2004). This particular study did not differentiate LSF and HSF information, but this is the obvious next step.

4. The fusiform face area (FFA)

Dozens of functional neuroimaging studies among typically developing controls over the last decade have verified the presence of a patch of cortex within the lateral aspect of the middle part of the fusiform gyrus (FG) that is more strongly activated during face perception (implicit or explicit face identification) than any other class of visual stimulus (e.g., Haxby et al., 1994, 1999; Kanwisher et al., 1997, 2000; Puce et al., 1995). This area has come to be known as the FFA (Kanwisher et al., 1997). In a recent literature review, Kanwisher (2000) notes that FFA activity is at least twice as strong to faces as to a wide range of non-face stimuli, such as assorted objects, animals without heads, and the backs of human heads. The importance of this tissue for face recognition has been confirmed by lesion studies which show that damage to this tissue results in an inability to recognize faces (prosopagnosia) (Damasio et al., 1990; De Renzi, 1986; Farah et al., 1995; Whiteley and Warrington, 1977). Anatomically, the middle portion of the FG is split along its rostral-caudal extent by a shallow, mid-fusiform sulcus. In functional magnetic resonance imaging (fMRI) studies, the center of activation in face perception tasks is typically offset toward the lateral aspect of the FG, in the right hemisphere (Haxby et al., 1999) (see Fig. 1 for an example of fMRI activation of the FFA). Whereas individual subjects may or may not also show left FG activation during face perception, group composites always show right side activations to be stronger and larger.

The specificity of the FFA is for perceptual identification of the face; it is distinct from those other brain areas that are involved in the perceptual recognition of facial expressions, such as the superior temporal sulcus (e.g., Allison et al., 2000; Haxby et al., 2000; Winston et al., 2004). However, the FFA is engaged even during tasks of facial expression discrimination (e.g., Pessoa et al., 2002a, 2002b; Winston et al., 2004), though, it is important to note that lesions to the fusiform do not cause deficits in emotional expression decoding (Damasio et al., 1990; Farah et al., 1995; Tranel et al., 1988; Wada and Yamamoto, 2001). FFA engagement seems to be automatic when presented with any face, neutral or expressive, and to involve both person detection processes as well as person identification processes (Grill-Spector et al., 2004; Winston et al., 2004).
Gauthier and co-workers have challenged the notion that the FFA is really a dedicated face module (e.g., Gauthier et al., 1999, 2000). Rather, they see the “FFA” as a misnomer, and they conceptualize this region of the FG as an area engaged by any type of expert visual perception. They have shown, for example, that car experts engage their FFA (as defined by a separate face localizer task during fMRI) more for cars than for other objects, such as birds; bird experts, on the other hand, show the opposite pattern, with FFA engagement greater for birds than cars (Gauthier et al., 2000). No stimulus engages the area more than faces, perhaps because our experience and expertise with faces is greater than any other class of object for which we might also be expert (but see Grelotti et al., 2005, discussed below, for some new evidence concerning this and autism). In an earlier study, Gauthier et al. showed that training a group of college students to be “greeble” experts (greebles are a class of computer generated, 3D objects with consistent variations in a set of spatially distributed features) resulted in significant increases in the amount of FFA activity, from baseline to post-training (Gauthier et al., 1999). This study is also interesting because it shows plasticity of this brain region, even in young adulthood, an encouraging sign that the FFA is really a dedicated face module (e.g., Gauthier et al., 1999). Rather, they see the “FFA” as a misnomer, and they conceptualize this region of the FG as an area engaged by any type of expert visual perception. They have shown, for example, that car experts engage their FFA (as defined by a separate face localizer task during fMRI) more for cars than for other objects, such as birds; bird experts, on the other hand, show the opposite pattern, with FFA engagement greater for birds than cars (Gauthier et al., 2000). No stimulus engages the area more than faces, perhaps because our experience and expertise with faces is greater than any other class of object for which we might also be expert (but see Grelotti et al., 2005, discussed below, for some new evidence concerning this and autism). In an earlier study, Gauthier et al. showed that training a group of college students to be “greeble” experts (greebles are a class of computer generated, 3D objects with consistent variations in a set of spatially distributed features) resulted in significant increases in the amount of FFA activity, from baseline to post-training (Gauthier et al., 1999). This study is also interesting because it shows plasticity of this brain region, even in young adulthood, an encouraging sign that for those engaged in the treatment of persons with an ASD. One final piece of data from these expertise studies is of great relevance to the social deficits found in the ASDs. Persons who develop an expertise for cars or birds devote a considerable amount of time to their hobby, and they show an emotional attachment and devotion that is quite striking. Bird experts love birds; dog experts love dogs. Anecdotal evidence from those trained to be greeble experts suggests that some participants attached personalized mnemonics like “this one is the wise one”, to facilitate the acquisition of the perceptual skill (Gauthier, personal communication). Such accounts suggest that emotional involvement may be a very important and common source of motivation for the acquisition of expertise, though other types of semantic mnemonics limited to physical descriptions probably are helpful in facilitating training too. Nevertheless, our working hypothesis is that affective involvement is normally a key factor in the successful acquisition of perceptual expertise for faces or any category of complex objects.

5. Hypoactivation of the FFA in ASDs

In the first published neuroimaging study of face recognition in ASD, we used fMRI to study face and subordinate-level object perception in 14 high functioning individuals with autism or Asperger syndrome, compared to two age and IQ matched typical adult control groups of 14 each (Schultz et al., 2000b). Persons with an ASD showed significantly less activation of the middle aspect of the right FG compared to controls (see Fig. 2 for example fMRI maps for individual cases taken from the sample of Schultz et al., submitted for publication). The difference was observed for both persons with autism and persons with Asperger syndrome. It should be noted, that both groups of persons with an ASD were very socially impaired as measured by the Autism Diagnosis Observation Schedule (ADOS; Lord et al., 1999). Moreover, activation of non-face object areas during object discrimination was normal, as was behavioral performance on the object discrimination task, suggesting that the behavioral and neural abnormalities in autism are specific to faces.

Hypoactivation of the FFA has now been replicated by 9 other labs (Aylward et al., 2004; Curby et al., 2003; Critchley et al., 2000; Davidson and Dalton, 2003; Hall et al., 2003; Hubl et al., 2003; Pierce et al., 2001; Piggot et al., 2004; Wang et al., 2004). Critchley and co-workers demonstrated the effect in a group of nine adult males with a clinical diagnosis of either autism (n = 2) or Asperger syndrome (7), using an active face perception task requiring the participants to categorize faces as expressive or not. Pierce and co-workers also used an active perceptual task involving gender discrimination of neutral faces in a sample of six adults with autism. Hubl et al. showed FFA hypoactivation in seven adult males with autism using both a gender discrimination and a neutral versus expressive discrimination task. Aylward et al. examined FFA activation to familiar and unfamiliar faces in a group of 11 persons with an ASD as compared to 10 healthy controls; the FFA was only hypoactive to the unfamiliar faces. Hall and co-workers used positron emission tomography (PET) in a group of eight high functioning males with autism as compared to
eight healthy male controls during an emotion recognition task and showed hypoactivation of the FFA, as well as other deficits. Wang and co-workers used two tasks in a group of 12 males with an ASD. In one task, participants had to pick the facial expression from two alternatives that matched the facial expression of the target face. In the other task, participants had to pair a verbal label with a facial expression. Hypoactivation of the FFA was found only in the purely perceptual task, perhaps because of the overall increase in the face perceptual load in that condition versus the verbal labeling condition. Piggot and co-workers were the first to use a sample of all children, 14 boys with an ASD. This was a companion to the Wang et al. study in that both used the same task methodology, and interestingly, both found hypoactivation only under task conditions devoid of verbal stimulation. It is impossible to know without simultaneous eye tracking data how the verbal labels may have affected attention and FFA activation, but it is significant that both studies were sensitive to the hypoactivation of the FFA effect in ASDs only under the pure face condition. Attention effects were explicitly examined by Davidson and co-workers, who showed hypoactivation of the FFA across two samples of males with an ASD. However, posterior regions of the FG showed strong attentional effects, in that activation was increased significantly when participants focused on the eye region as opposed to other aspects of the display.

Grelotti et al. (2005) studied an 11-year-old boy with autism who was expert at distinguishing a novel class of objects known as “Digimon” (digital monsters), cartoon characters of Japanese origin. This Digimon “expert” was compared to another boy with autism and a healthy control during several tasks involving Digimon discrimination as well as face and common object discrimination. Both boys with autism showed hypoactivation of their FFA to faces, but the Digimon expert showed enhanced activation to the Digimon images, supporting an expertise model of FFA functions. In their detailed case study of face perception of a young adult with AS, Curby and co-workers used fMRI to map out FFA responses to HSF and LSF filtered faces. They showed that this case had the expected hypoactivation of the FFA to broad spatial frequency faces. However, consistent with the argument being developed here, he showed greater than normal FFA activation to HSF faces, and hypoactivation to LSF faces.

Finally, using active face discrimination tasks in two new samples of persons with an ASD (total ASD n = 44), we have replicated the FFA hypoactivation effect using neutral face pictures in one study, and expressive faces in the second (Schultz et al., submitted for publication). Importantly, we showed in both samples a strong significant correlation to degree of face expertise, such that those with better scores on a standardized test of face perception outside of the magnet showed more FFA activation during fMRI, regardless of group membership (i.e., ASD or controls). Moreover, degree of social impairment as measured by the ADOS social domain also correlated with degree of FFA hypoactivation, such that the more socially impaired participants had the least FFA activation to faces. Because degree of social disability also was associated with ASD subtype, with persons with autism proper being more socially impaired than those with Asperger or PDD NOS, we found that persons with autism also had significantly less FFA activation than the combined Asperger and PDD NOS, which in turn had significantly less than the normal controls.

Counting our two new samples, the two case studies, and the two samples included within Davidson et al. (2004), there are now 15 reports of FFA hypoactivation with a total sample size of 157 persons with an ASD, and a combined control sample of 167. There are also now two reported failures to find hypoactivation of the FFA in ASD. Pierce et al. (2004) used familiar and unfamiliar faces in an fMRI study of eight adult males with autism and 10 healthy control males. Like Aylward et al. (2004) and Grelotti et al. (2005), Pierce et al. found significantly greater activation to familiar as compared to unfamiliar faces in the autism sample. While controls showed more FFA activation to unfamiliar faces than did the men with autism, this difference failed to reach statistical significance. It is not clear why this study failed to confirm the group difference in FFA engagement to unfamiliar faces, but it is noteworthy that the means were in the direction reported by other studies, and thus the results of this study might simply be due to insufficient statistical power. However, it is also noteworthy that the fMRI task employed in this study did not demand person identification processes, but rather entailed a button press to each occurrence of a female face. As Grill-Spector et al. (2004) have nicely demonstrated, the FFA is involved in both person detection (such as the gender task of Pierce et al.) and person identification (i.e., differentiating unique individuals), and this latter process may significantly bolster FFA activation above and beyond levels achieved with simple person or gender detection. Moreover, it may be the FFA’s contributions to person identification processes that drives the comparatively low levels of activation in the ASDs reported in the majority of studies to date. Related to this is the finding that “mere exposure” alone is insufficient for training people to become perceptual experts in a new domain, e.g., birds, but rather one needs repeated active individuation to become an expert and to have that expertise generalize beyond the training set (Tanaka et al., in press).

Another interesting contribution of the study by Pierce and co-workers is the demonstration that personally meaningful faces (friends and family) modulate FFA engagement; this is consistent with the argument that will be more fully developed in the next section.

The second report failing to show hypoactivation of the FFA in ASD was by Hadjikhani et al. (2004). They studied 11 adult males with an ASD (6 autism, 4 Asperger, and 1 PDD NOS) compared to 10 adult males; notably the control sample was significantly younger (mean age of 26 years versus 36 years for the participants with an ASD). This
failure to find hypoactivation of the FFA might be attributable to the particulars of this study, including the use of a passive viewing of faces as the “task” during fMRI recording (all other studies to date have used an active task, to monitor attention and insure that all participants were actively processing the faces), a sample that was much older than those of the other studies, a slice thickness that varied between participants, and probably most important, a sample of patients who were on average less socially impaired compared to other studies. Given that we have reported a significant relationship between degree of FFA activation and degree of social impairment, this seems to be the most likely factor contributing to the reported activations (Schultz, 2004; Schultz et al., submitted for publication). However, Hadjikhani et al., also used pictures of faces that subtended 20° of visual angle; this is much larger than any prior study (note, not all studies report image size), and is about four times larger than face pictures that we have employed in our studies. Images greater than about 3–5° of visual angle cannot be viewed in their entirety (foveated) without eye movements. Moreover, smaller images effectively emphasize LSFs, as details will be blurred. Recalling that Curby et al. (2003) found greater FFA activation to HSF faces in their case study, the relative emphasis on HSFs might also have been an important influence to the results of Hadjikhani and co-workers. This possibility is especially intriguing.

In light of the majority of findings indicating that the fusiform gyrus has some specific role in autism spectrum disorders, studies are now beginning to appear examining its morphology by way of high resolution structural MRI. Waiter et al. (2004) recently studied 16 males with an ASD between the ages of 12 and 20 and compared their brain structure to a group of 16 healthy controls using an automated procedure known as voxel brain morphology (VBM). They found about a dozen brain areas that were specifically enlarged in the ASD group, consistent with the findings of overall brain enlargement that has been reported multiple times (see Courchesne et al., this issue, for a review). Their second strongest finding involved a specific enlargement of the right fusiform gyrus, with the location of the peak size difference consistent with peak coordinates found in fMRI studies of the FFA. Moreover, we have now measured the structure of the FG in a sample of 110 males with an ASD compared to 103 male controls, with a large age range (from age 5 to 55 years) with a mean of about 17 years for the two groups combined. We find bilateral enlargement of the fusiform, as well as overall brain enlargement (Schultz et al., submitted for publication). In the entire group, the fusiform enlargement is not significant after accounting for the whole brain enlargement; however, when the two groups are divided at the median age of 15 years old, we find significant enlargement in the older group of ASD versus the controls, even when controlling for overall brain size, and a positive correlation with age only in the ASD group. This suggests some aberrant growth process extending into early adulthood. Thus, the functional abnormalities of the FFA may have demonstrable structural underpinnings and also longer-term causal influences on the structure of the brain itself.

6. The amygdala, autism and social perception

The amygdala often is given a central role in theories of social perception and cognition (e.g., Adolphs et al., 1998; Bachevalier, 1994; Baron-Cohen et al., 2000; Brothers, 1990; Schultz et al., 2000a). Whereas the fusiform gyrus is important for the perception of facial identity, the amygdala has been shown to play a critical role in the early stage processing of facial expression (Breiter et al., 1996; Calder et al., 2001; Morris et al., 1998a, 1998b, 1999; Zald, 2003). While it is not believed to be involved in advanced computations for facial expressions (this is more the purview of cortical areas, such as the superior temporal sulcus [STS], e.g., see Allison et al., 2000; Haxby et al., 2000; Tranel et al., 1988; Winston et al., 2004), the amygdala is a fast responding structure that quickly reacts to emotionally potent stimuli, signaling other brain areas as to the salience of an event (LeDoux, 1996; Schultz et al., 2000a). The amygdala plays a critical role in emotional arousal, assigning significance to environmental stimuli and mediating the formation of visual-reward associations, i.e., “emotional learning” (Anderson and Phelps, 2001; Anderson and Sobel, 2003; Gaffan et al., 1988; LeDoux, 1996). It is reliably engaged during judgments of personality characteristics from pictures of the face or part of the face (Adolphs et al., 1998; Baron-Cohen et al., 1999; Winston et al., 2002). Activation of the amygdala appears to be automatic and stimulus driven (but see Pessoa et al., 2002b), as it can be engaged by images of facial expressions out of conscious awareness (Pasley et al., 2004; Williams et al., 2004).

LeDoux (1996) and others (e.g., Pasley et al., 2004) have argued that the amygdala, because of its especially fast magnocellular transmission lines, is capable of providing critical information (e.g., anything with high emotional salience, such as threats or fearful faces) to cortical areas. Following this logic, it would be sensible that the amygdala could provide social communicative information to relevant cortical systems for further processing. One hallmark of social interactions is the rapid pace of social communication, much of which can be quite nuanced and dependent on integrating information quickly across short time frames. The amygdala has dense reciprocal connections with the ventral visual processing stream (Amaral and Price, 1984), and by this pathway would be able to influence and amplify processing of complex object perception areas, including the FFA. In fact, even though the FFA is not directly involved in the analyses of facial expressions, e.g., lesions to the FG do not lead to problems discriminating facial expressions (Tranel et al., 1988; Wada and Yamamoto, 2001), the FFA is
more strongly activated by facial expressions than by neutral faces (e.g., Pessoa et al., 2002a; Vuilleumier, 2002).

In Fig. 1, we show one example of this amplification effect (Schultz, previously unpublished). In this example, participants were shown side-by-side faces and asked to determine if they were the same or different person. The face pairs were blocked, such that some groups of items were all neutral faces, and others were all expressive faces, such that the impact of facial expression on the degree of FFA activation could be examined, even though the task remained constant. As shown in the figure, the FFA was more engaged by the expressive faces than the neutral faces. For sometime it has been hypothesized that this type of enhanced FFA activation is due to amplifying inputs from the amygdala (e.g., Morris et al., 1998a, 1998b). Vuilleumier et al. (2004) recently showed more direct evidence in support of this hypothesis. They studied with fMRI 26 patients with varying degrees of lesion to the amygdala, hippocampal or both in comparison to 13 healthy controls using tasks involving fearful or neutral faces. While controls and those with hippocampal damage alone showed amplification of the FFA to fearful faces as compared to the neutral faces, those with the amygdala lesions did not. Moreover, there was strong correlation between degree of amygdala lesion and the degree of under activation in the FFA to the emotionally salient faces. This finding is consistent with an earlier report by Anderson and Phelps (2001) showing that amygdala lesions impaired the perception of emotionally salient events. Collectively, these data strongly suggest a direct modulatory role on the FFA by the amygdala, and suggest that the hypoactivation of the FFA in autism might be explained in part by amygdala-based processes. Moreover, Winston et al. (2003) have shown that the modulation of the FFA by emotional faces is mediated by the LSF components of the face.

The amygdala has attracted great interest among autism researchers and those interested in the social brain. Initial interest stemmed from consistent findings of stunted neuronal arborization within this structure as seen in a series of postmortem cases (Bauman and Kemper, 1994; Kemper and Bauman, 1998). Across cases, neurons of the amygdala appeared too small and too densely packed because of the limited development of the dendritic tree. In addition, there are now three published fMRI studies on the amygdala in autism; each has shown the amygdala to be hypoactive during a face perceptual task (Baron-Cohen et al., 1999; Critchley et al., 2000; Pierce et al., 2001). These findings are of great interest and are thought to be strongly related to the to known deficits in emotion perception among persons with an ASD (Celani et al., 1999; Fein et al., 1992; Hobson, 1986a, 1986b; Hobson and Lee, 1989; Hobson et al., 1988a, 1988b; MacDonald et al., 1989; Ozonoff et al., 1990).

The preference for faces shown by typical newborns (Goren et al., 1975; Simion et al., 1998; Slater and Quinn, 2001) and young infants is believed to be mediated by a subcortical visual system (Morton and Johnson, 1991) that passes information from the retina to the superior colliculus, to the pulvinar nucleus of the thalamus, and then into the amygdala (see Pasley et al., 2004 for recent evidence and a review). At birth, the visual cortex is functionally immature (Kraemer and Sjostrom, 1998), and thus probably incapable of supporting the strong preference for face-like patterns. Thus, one hypothesis worthy of additional study is that congenital abnormality of this subcortical visual system, perhaps just involving the amygdala, is responsible for the diminished attention to faces seen as early as the first months of life in autistic children (Maestro et al., 2002). Abnormalities in this subcortical visual system could be the first failure in a cascade of social developmental problems for persons with autism. Congenital abnormality of the amygdala in ASDs could lead to a failure to orient to salient social stimuli such as faces, and would preclude the development of the type of face expertise mediated by the FFA. Thus, in this model, abnormalities in this subcortical visual system may be the first stage of a neurodevelopmental process that later includes deficits in FFA mediated face perception. Interestingly, in another recent study, Vuilleumier et al. (2003b) recently showed that the subcortical visual pathway is preferentially biased toward LSF information as opposed to HSF. This finding converges with the data presented already on the HSF bias found in persons with an ASD to further implicate the amygdala in the pathogenesis of autism.

Our Digimon expert already described (Grelotti et al., 2005) provides support for this developmental model of amygdala–fusiform interactions in autism. In addition to his perceptual skill in differentiating Digimon, which was significantly greater than his skill for faces and other complex objects, this boy was unique because of his strong preoccupation with Digimon; he was emotionally “cathedected” to this class of objects. Even though he showed classic hypoactivation of the FFA to faces compared to other complex objects, he showed significant FFA activation to Digimon (even when their heads were masked) compared to faces and other objects. Perhaps most importantly, he also showed amygdala engagement to Digimon but not to faces or other complex objects. While this boy showed significantly greater FFA activation to familiar faces (family members) than unfamiliar faces, this enhanced FFA activation paled in comparison to the magnitude of activation to the Digimon pictures. These results are important for they show that the FFA can be engaged by a class of stimuli for which the person (1) finds emotionally meaningful and (2) for which he or she has developed a high level of perceptual understanding. The key to this process may be amygdala involvement.

Fig. 3 presents a heuristic model of how face perceptual skills might normally develop from birth onward, and in this regard it presents a stage theory to hypothesize when deficits seen in autism might arise. Babies appear to have an inborn bias for face-like objects, i.e., a bias for high spatial
frequency information in the top half of the visual field (Cassia et al., 2004). Faces happen to conform to this visual bias, and thus they get preferential attention at the outset. However, some set of circumstances must quickly become involved to maintain and develop this preference for faces over other types of objects. I know of no experimental literature on this issue, but surmise that a combination of instrumental and associative learning processes provide the context and rewards to reinforce this bias and to promote perceptual learning. This is clearly an important area for future research. This model posits that the amygdala in conjunction with closely connected dopaminergic reward centers of the ventral brain (the so called “extended amygdala”) are involved in reinforcing the preference to look at faces. However, it is problematic that no fMRI studies in later childhood, adolescence or adulthood have ever implicated such reward centers during face perception. Thus, this conjecture can only be sensible if we also postulate a time limited role for these reward processes, such that they expire prior to the child reaching later childhood and adolescence (the age when fMRI studies have been done). The important issue that I wish to draw attention to for this first stage of the model is that the initial processes are under the influence of the amygdala and related structures and that these influences lead to the further enhancement of face salience. This in turn leads to greater time spent processing faces. It is through experience that the amygdala has its greatest impact on the development of the cortical sites that perform the actual computational analyses involved in the face perception, e.g., the FFA and the STS. Greater experience, especially when part of an active perceptual process involving individuation of faces, would then lead to greater perceptual skill (Tanaka et al., in press).

In the next stage of the model, skill in perceiving faces to obtain information on person identity and emotional state is hypothesized to be of critical importance for the development of social skills. These face perception skills provide the “scaffolding” necessary during social interactions to understand the barrage of non-verbal communications that occur in rapid succession and that are transmitted largely through the face. In fact, there are important parallels to those with congenital blindness; while these individuals are typically not classically autistic, they do show a significant increase in autistic behaviors and striking social impairments (Hobson and Bishop, 2003), suggesting that the experience and inputs from vision are indeed critical for social skill development. Children with an ASD are hypothesized to fail to develop age appropriate skills in part because of difficulties interpreting what they see during social interactions. As described in the next section, the FFA becomes an integral part of a social cognitive network gradually across childhood. Amygdala lesions after childhood have less of an impact on social functions, because the cortical regions are then fully developed. Likewise, select cortical damage to areas such as the FFA are believed to have less of an impact on social functions, because the cortical regions are then fully developed. Likewise, select cortical damage to areas such as the FFA are believed to have less of an impact after early childhood because the social functions are regulated by a distributed system of social nodes that is buffered against insult to a limited region of the cortex (Schultz et al., 2003).

7. The FG’s role in social cognition

The data presented thus far argues for the role of the amygdala and FFA in the social perceptual deficits, specifically the face perception deficits found in the ASDs.
However, the fMRI data on amygdala and FFA under activation in autism during face perceptual tasks are not at all convincing by themselves with respect to the argument that deficits in the FFA and amygdala are actually part of the brain mechanisms that cause autistic social difficulties. In fact, the most parsimonious interpretation of the FFA data would turn the argument on its head and suggest that autism causes hypoactivation of the FFA to faces. In other words, those born into the world with the brain precursors of mature autism (e.g., amygdala dysfunction) fail to show an intrinsic interest in faces and across time fail to accumulate sufficient experience with faces so as to develop perceptual expertise for faces. Then, in later childhood and adolescence, when they are recruited into a study, placed inside an fMRI scanner and made to look at faces over and over again, their brain registers the fact that they have both a lack of interest in faces and a lack of highly developed perceptual skill for faces. In this regard, it can cogently be argued that the hypoactivation of the FFA is a result of having autism. But is there any evidence that FFA abnormalities are part of the mechanism that causes autistic dysfunction? I believe there is. Although the data are still rather sparse, there are some provocative studies to support a “social knowledge” hypothesis of the FFA functions, and in this regard a more direct causal link to autistic deficits in social behavior.

First, there is a growing appreciation of the important connection between perception and knowledge among typically developing individuals such that perceptual knowledge appears to be strongly grounded in modality specific perceptual systems (see Barsalou et al., 2003, for a comprehensive treatment of this important topic). Having the neural tissue involved in perception also be involved in semantic representations and knowledge about that perceptual category would be a very efficient use of brain resources. In fact, it would make little sense to have a separate complex of neurons to re-invent what the perceptual systems already code about a class of stimuli for the sake of associating additional semantic knowledge.

Second, it is important to revisit the human lesion literature, as there are important clues there as to the strong relationship between perceptual and conceptual knowledge. Lesions to ventral temporal-occipital lobes cause a continuum of impairment in face (prosopagnosia) and object recognition (object agnosia), from low level perceptual difficulties, such as the inability to recover even primitive features of the face, to the other extreme where perceptual processes are largely intact, but the patient cannot assign meaning to the percept (Bauer and Demery, 2003; Behrmann and Kimchi, 2003). It is the latter which is most relevant here. These distinctions were first recognized by Lissauer (1890), when he differentiated “apperceptive agnosia”, involving more basic perceptual difficulties, from “associative agnosia”, which typically involves rather intact low level vision, but difficulty ascribing (“associating”) meaning to object or faces. In extreme cases there may be a more or less complete loss of conceptual knowledge about an entire class of objects (Chao et al., 1999). Careful study of associative agnostic cases can reveal a pattern of performance quite reminiscent of autism—a slavish feature-by-feature reliance on local detail at the expense of global configuration (Levine, 1978; Humphreys and Riddoch, 1987; Levine and Calvanio, 1978; Farah, 1990). Stage models posit that visual perception occurs prior to a later gnostic stage in which visual perceptual elements are linked to stored representations (Bauer and Demery, 2003). Thus, associative visual agnostics have trouble linking object perception with prior experience, with naming the seen object, and with demonstrating its functional properties, all of which suggests a more general loss of semantic knowledge about the seen object.

The ventral temporal pathway is comprised of a series of short U fibers that connect adjacent regions of striate, peristriate, and inferior temporal cortex (Tusa and Ungerleider, 1985). These connections may be damaged to differing extents and locations in apperceptive versus associative agnosia, and by implication, in the ASDs as well. The hypothesis, however, is that autism has close parallels to associative agnosia, and in particular may represent a naturally occurring form of “developmental associative prosopagnosia”, involving some basic perceptual anomalies, such as a greater reliance on HSF information at the expense of holistic processing, as well a more fundamental impairment in deriving and retaining social semantic knowledge from face-to-face experiences. In autism this entails a deficit in associating rich personal identity information with the seen face, and deficiencies in a deeper appreciation of the affective states of another person as displayed through facial expressions. Within the developmental model of the social perceptual and social cognitive deficits in autism that has been the centerpiece of this paper, there would be strong links between deficits first arising in the amygdala and then later impacting the temporal lobe cortices (see Fig. 3). Deficiencies in social motivation are posited to emerge quite early in life and derail the normal set of experiences necessary to develop both basic perceptual and conceptual representations of people. It may also be true that the congenital anomalies of amygdala functioning posited here, interact with other congenital anomalies, such as those that might directly affect fiber pathways of the occipitotemporal projection system, and that through a combination of neural vulnerabilities, the social perceptual and social cognitive deficits that define autism emerge.

Third, James and Gauthier (2003) recently provided a very nice example of semantic representations in modality specific perceptual cortices. They trained a group of normal college aged students to visually discriminate a group of greebles. However, some of the greebles were also given three pieces of semantic information each by way of verbal labels. One group of greebles was tagged with auditory semantic information, e.g., one greeble was said to make
noises, such as singing, squealing and howling, while another would squeak, laugh and croak. This semantic information was trained to a criterion of performance for each participant prior to neuroimaging. However, during the fMRI experiment, the task was a simple visual perceptual judgment—“are these two greebles the same or different?” Those greebles tagged with auditory semantic information engaged the primary auditory sensory cortex significantly more than those tagged with other types of semantic knowledge. There was a parallel group of greebles tagged with movement-related descriptors (e.g., runs, crawls and chews), and these greebles automatically activated motion sensitive cortices (area MT). Thus, James and Gauthier concluded that modality specific sensory cortices were involved in storage of conceptual information about visual objects, and that the simple act of seeing an object could provoke involuntary, i.e., without conscious effort, activation of that conceptual information within those sensory cortices.

The parallel argument for the FFA would be that seeing a face automatically and involuntarily activates FFA-based semantic knowledge about people and in some sense primes the observer for a social interaction. For those participants with an ASD who have a relatively impoverished social knowledge base, there would be significantly less FFA activation. This is quite possibly one contributor to the observed FFA hypoactivation in autism.

Evidence from an auditory fMRI study supports this line of conjecture. Kriegstein and Giraud (2004) reported significant right fusiform activation at the typical peak of the FFA during a task requiring person identification by voice recognition alone, absent any visual input. This FFA engagement may represent activation of circuits coding more general semantic knowledge necessary for person identification through the voice. In further support of this argument, we recently showed that the FFA can be activated by simple, animations of interacting 2D geometric shapes (e.g., a square, triangle and circle) when typical adult participants are asked to make a social judgment as opposed to a physical as opposed to a social attribution. Moreover, activation of FFA was the only area in the brain that correlated with individual differences in performance on the social attribution task. Thus, these data argue for a role of the FFA–amygdala system in social cognition more generally, and retrieval of specific social knowledge about what constitutes a friendly social interaction or not. Collectively these data suggest that the amygdala–FFA system and its failure to strongly activate during face perception tasks points to a genuine causal mechanism involved in autism, though this remains a hypothesis awaiting additional supportive data.

8. Summary

This paper has reviewed the current fMRI and neuropsychological data for deficits in face perception and deficiencies in underlying brain systems that mediate face perception and the detection of emotionally salient percepts. It has been argued that the amygdala is a key structure in alerting other brain systems to the emotional salience of perceptual events, and that it may have a particularly important role in the early development of autism, and in shaping of the evolving autistic brain. To date, the best evidence from the field of neuroimaging for brain-based differences in the ASDs involves hypoactivation of the FFA, with more than a dozen reports on this effect. This paper has presented three possible factors that moderate the degree of FFA engagement, and that together can explain the autism findings. The first factor is the degree of attention applied to the stimulus while performing a perceptual task inside the fMRI magnet. This was discussed with reference to amplifying effects of amygdala inputs to the FFA, but in fact there is additionally broad support for attentional effects on the FFA and other perceptual cortices that was not reviewed (e.g., Anderson and Phelps, 2001; Maunsell and Cook, 2002; O’Craven et al., 1999; Wojciulik et al., 1998; Vuilleumier et al., 2001). Second, chronic levels of abnormal attention to faces appear to lead to reduced perceptual skill and hypoactivation of the FFA in autism. Finally, and more speculatively, the FFA appears to encode social knowledge, such that tasks not involving faces, but requiring social judgments strongly activate the FFA (Schultz et al., 2003). This appears to be one example of a broader principle of brain organization whereby those cortices involved in perception are also engaged in long term storage of information related to those perceptual properties (James and Gauthier, 2003) and more generally points to the deep relationship between perceptual and conceptual processes (Barsalou et al., 2003). Thus, activity within the FFA represents both perceptual and social conceptual processes and in this way may represent a core mechanism for the pathobiology of autism. It will be important to provide further tests of this model, to better understand how the fusiform–amygdala system contributes to the pathogenesis and maintenance of autistic behaviors and difficulties.
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