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ORIGINAL PAPER

The Implications of Social Neuroscience for Social Disability

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Abstract Social disability represents a unifying feature in the diverse group of individuals with autism spectrum disorder (ASD). Social neuroscience is the study of brain mechanisms supporting interpersonal interaction. In this paper, we review brain imaging studies of the social brain and highlight practical applications of these scientific insights. Understanding of social brain mechanisms holds promise as a tool for defining meaningful subgroups of children with ASD to facilitate genetic analyses and to inform treatment selection. Because social brain systems emerge in infancy, social neuroscience may help to detect atypical development before symptoms manifest. This conceptualization of ASD is a hopeful one, as social brain systems remain malleable well into development and are thus amenable to targeted intervention.

Keywords Autism spectrum disorder · Social neuroscience · Translational neuroscience

A Social Disorder and a Social Brain

Autism is a disorder of brain development that emerges in the first 3 years of life. The current edition of the classification system used for psychiatric diagnoses in the United States, the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (American Psychiatric Association 2000), lists autism in the category of Pervasive Developmental Disorders. In this class, Autistic Disorder, Asperger's Disorder, and Pervasive Developmental Disorder—not otherwise specified, together, are conceptually grouped as autism spectrum disorder (ASD). ASD is characterized by difficulties in (a) social interaction and (b) communication, along with (c) repetitive or restricted interests and behaviors. Diagnostic evaluation is based on clinical observation and parent-report of problems in these areas; children with significant difficulties spanning the social domain and either or both of the other domains may qualify for a diagnosis of ASD. There are 12 individual diagnostic criteria, and a child may meet diagnostic threshold while exhibiting as few as 2 or 3 of these symptoms. Thus, there is wide variability in the specific symptoms that any child may display. This *phenotypic heterogeneity* mirrors variability in the genetic causes of ASD (Geschwind and Levitt 2007; Gupta and State 2007). Research has identified many genetic anomalies associated with individual cases of ASD, but each accounts for only a small portion of cases (Weiss et al. 2008). The large number of potential genetic mechanisms suggests that no single explanation will apply to the majority of cases (Abrahams and Geschwind 2008). There is currently no biological test for ASD.

Despite the wide variation in presentation of children with ASD, important commonalities have been observed since Leo Kanner (1943) first described the disorder and emphasized its particular impact on social functioning. In the years of research that have followed, despite wide variation in factors such as intellectual ability, executive function, and attentional characteristics, social impairment stands as a universal feature of the disorder. Though diagnostic criteria have evolved during the past 70 years and continue to evolve, social dysfunction remains a required symptom to qualify for a diagnosis of ASD. Differences in social functioning are present for simple (e.g., eye contact) and complex behaviors (e.g., navigating

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group conversations), bearing remarkable similarity in manifestation between very high- and low-functioning individuals. Likewise, difficulties with social perception occur across both visual (Pelphrey et al. 2002) and auditory (Dawson et al. 1998) sensory modalities. While repetitive behaviors or language deficits are seen in other disorders (e.g., obsessive–compulsive disorder and specific language impairment, respectively), basic social deficits of this nature are unique to ASD. Furthermore, in the course of autistic development, onset of the social deficits appears to precede difficulties in other domains (Osterling et al. 2002; Osterling and Dawson 1994; Zwaigenbaum et al. 2005) and may emerge by 6 months of age (Maestro et al. 2002).

These behaviorally observed and quantified differences in social behavior provide a target for understanding the brain bases of ASD. During the last few decades, research has elucidated specific brain circuits that support perception of other living beings, in humans and in other species. This *social perception* refers to "the initial stages in the processing of information that culminate in the accurate analysis of the dispositions and intentions of other individuals" (Allison et al. 2000). Both in terms of the evolution of a species and brain development within a person's lifetime, basic social perception represents a necessary precursor to more sophisticated social behaviors, such as thinking about the motives and emotions of others. Leslie Brothers (1990) first put forward the notion of a *social brain,* a network of brain regions dedicated to processing social information and enabling us to recognize other individuals and to evaluate their mental states (e.g., intentions, dispositions, desires, and beliefs). The social brain is hypothesized to consist of the superior temporal sulcus (STS), the amygdala, the orbital frontal cortex (OFC), and the fusiform gyrus (FG), among other structures. Though all work in coordination to support social processing, each appears to serve a distinct role. In humans, the STS region, particularly the posterior STS in the right hemisphere, analyzes biological motion cues, including eye, hand, and other body movements, to interpret and predict the actions and intentions of others (e.g., Bonda et al. 1996; Pelphrey et al. 2005). The FG, located in the ventral occipitotemporal cortex, has been implicated in face detection (identifying a face as a face) and face recognition (identifying one's friend versus a stranger; e.g., Kanwisher et al. 1997; Puce et al. 1996). The OFC supports social reinforcement and reward processes more broadly (e.g., Rolls 2000). Finally, the amygdala helps us recognize the emotional states of others through analysis of facial expressions (e.g., Morris et al. 1996) and also experience and regulate emotion (e.g., Davis and Whalen 2001; Kluver and Bucy 1939; LeDoux 1992).

Current Understanding of Social Perception in ASD

Because the functions of the social brain correspond closely to social difficulties in ASD, this network has become a focus of study. Multiple brain imaging technologies have been employed, but here we focus on the two most commonly used methods, functional magnetic resonance imaging (fMRI) and event-related potentials (ERP). FMRI and ERP are complementary imaging methods; though both are appropriate for the study of brain function in ASD from infancy through adulthood, each measures a distinct facet of brain activity and contributes unique strengths to scientific inquiry. FMRI entails the use of powerful magnets to measure the levels of oxygen within the brain that vary with changes in neural activity. That is, as the neurons in specific brain regions "work harder" when performing a specific task, they require more oxygen. By having people listen to or view social percepts in an MRI scanner, fMRI specifies the brain regions that evidence a relative increase in blood flow. In this way, fMRI provides excellent spatial information, pinpointing with millimeter accuracy the brain regions most critical for different social processes. ERP, in contrast, directly measures the firing of groups of neurons in the cortex. As a person views or listens to specific types of information, neuronal activity creates small electrical currents that can be recorded from non-invasive sensors placed on the scalp. ERP provides excellent information about the timing of processing, clarifying brain activity at the millisecond pace at which it unfolds. The excellent *spatial resolution* of fMRI and *temporal resolution* of ERP offer complementary information, and both have been critical in understanding the nature of social perception in ASD. From fMRI, we learn what brain regions are involved and whether different regions are activated in people with ASD and typically developing people. From ERP, we learn the specific stages of processing that might be affected (the same brain regions can perform distinct functions at different points in a perceptual process) as well as differences in the timing of social perceptual processes. Both imaging methods have revealed much about the functions of the social brain in both typical and atypical development. To date, the most thoroughly investigated nodes of the social brain in ASD are the STS, underlying perception and interpretation of biological motion, and the FG, supporting face perception.

Heightened sensitivity to biological motion serves an essential role in the development of humans and other social species, orienting vulnerable young to critical sources of sustenance, support, and learning. The ability to detect biological motion emerges in the first days of life and develops independently of visual experience. Babies as young as two days of age recognize and preferentially attend to biological motion (Simion et al. 2008), and people

can infer complex attributes about identity, activity, and emotional state from even dramatically simplified displays of human form (Dittrich et al. 1996; Troje 2002). Identification of biological motion occurs rapidly; by 200 ms, the brain distinguishes biological motion from other forms of movement (Hirai et al. 2003; Hirai and Hiraki 2005; Hirai et al. 2009; Jokisch et al. 2005; Reid et al. 2008; Reid et al. 2006). This remarkable sensitivity to biological motion serves as an inborn "life detector" that provides a foundation for subsequent development of more complex social behaviors (Johnson 2006). Behavioral studies have shown that, from very early in life, children with ASD display reduced sensitivity to biological motion (Klin et al. 2009). Neuroimaging studies show that individuals with ASD show reduced activity in portions of the STS during biological motion perception while individuals at genetic risk for ASD who do not develop symptoms of the disorder show increased compensatory activity in these regions (e.g., Kaiser et al. 2010).

Face perception is also an important function of the social brain that has been well studied in ASD (Schultz 2005). In typical development, preferential attention to faces and the ability to recognize individual faces emerge in the first days of life (Bushnell et al. 1989; Goren et al. 1975; Johnson et al. 1991). Brain specialization for face perception is evident by 3 months of age (de Haan et al. 2003; Leppanen and Nelson 2009) and throughout the lifespan (Haxby et al. 1994; Kanwisher et al. 1997; Puce et al. 1995; Bentin et al. 1996). In ASD, decreased attention to human faces has been documented by 6 to 12 months (Maestro et al. 2002; Osterling and Dawson 1994), and behavioral difficulties and attentional differences in face perception and recognition are evident in children and adults (Hobson 1986; Hobson et al. 1988; Joseph and Tanaka 2003; Klin et al. 1999; Langdell 1978; Schultz 2005; Klin et al. 2002; Spezio et al. 2006). Children with autism show reduced activity in the FG during free viewing of faces (Hubl et al. 2003; Pierce et al. 2001; Schultz 2005; Schultz et al. 2000) that may reflect underlying differences in visual attention (Dalton et al. 2007; Dalton et al. 2005). People with ASD also show slowed processing of faces (McPartland et al. 2004; McPartland et al. 2011b; O'Connor et al. 2005, 2007; Webb et al. 2006), a finding that has also been observed in parents of children with ASD (Dawson et al. 2005) and infants at-risk for ASD by virtue of having an older sibling with the disorder (McCleery et al. 2009).

Research has yet to clarify to what extent these atypicalities in the social brain reflect causes of autism versus experience-dependent reflections of developing with autism. For example, social deficits might result from inborn difficulties with perceiving faces; in contrast, difficulties with face perception might simply reflect a consequence of failing to attend to faces during important periods of development. Most likely, some combination of these factors is at play. Autistic dysfunction originates in social brain systems but exerts secondary impact on the same systems through developmental effects, such as lost learning; an initial problem with social function worsens over time. This premise underlies the social motivation hypothesis, an account theorizing that reduced social drive in ASD leads to inattention to people and consequent failure of developmental specialization in experience-driven brain systems, such as the face perception system (Dawson et al. 2005).

Practical Implications and Future Directions

Harnessing Heterogeneity

Scientific findings from social neuroscience evidence heterogeneity similar to that described by preceding behavioral and clinical studies. These differences among samples of children with ASD possess great potential for defining meaningful subgroups of ASD, or *parsing the heterogeneity* of ASD. Because of the limited specificity of the behavioral methods used to diagnose ASD and the current diagnostic rubric, which permits similar diagnoses despite distinct symptom profiles (McPartland et al. 2011a), it is likely that the group of children currently referred to as having ASD may actually represent different syndromes with distinct causes. Studies of the social brain promise to reveal meaningful subgroups of children with ASD. Measurements of brain activity in specific regions and the timing of this activity provide reliable sources of detailed information to more accurately profile children with ASD. For example, even well replicated findings, such as atypical brain activation during face perception, are not evident in all samples of individuals with ASD (Hadjikhani et al. 2004; Jemel et al. 2006; Kemner et al. 2006; Kleinhans et al. 2008; Lahaie et al. 2006; Pierce et al. 2004; Senju et al. 2005; Webb et al. 2009). One of the goals of social neuroscience research is to harness this informative variance to effectively define subgroups. We see the integration of imaging methods as critical for this endeavor. Using face perception as an example, the combination of fMRI and ERP could specify the subgroup of individuals showing anomalies in the fusiform gyrus and further determine the stage of processing at which such atypicalities occur. Because different processing stages reflect varied cognitive processes, this level of understanding could inform treatment. For example, differences observed in the early processing stages might reflect problems with low-level visual perception, while later differences would indicate problems with higher-order processes, such as emotion decoding.

These same principles can be applied to the broader network of social brain regions and combined with measures of behavioral functioning to offer a comprehensive profile of brain-behavior performance for a given individual.

One straightforward objective of this subgroup approach is to improve the ability to tailor treatments to the individual. For example, a common target for social skills intervention in ASD is face perception (e.g., recognition of identity or emotion). Based on social neuroscience findings of atypical FFA activity in ASD, computer programs have been designed to target the specific processing mechanisms typically applied to faces (e.g., processing them in a holistic rather than piecemeal way; Wolf et al. 2008). However, detection of normative activity in some children with ASD suggests that such interventions might not be appropriate for all children. With the insight provided by multimodal assays of the social brain, treatment providers would be equipped with specific knowledge to address the unique profiles of strengths and vulnerabilities evident in their patients. Over time, as practitioners and scientists work together to learn which profiles respond best to particular interventions (i.e., specific content or mode of intervention), these descriptive profiles could enable providers to predict likely response to treatment; a critical goal in establishing a hierarchy of intervention objectives and in long-term planning for children on the autism spectrum. We are working towards this objective in our research group at present. By identifying individuals demonstrating atypical brain responses in an emotion regulation task, we can refer them to cognitive-behavioral therapy specifically addressing this skill. Furthermore, by recording ERP and fMRI before and after treatment, we are able to directly tie brain change to behavior change (Sukhodolsky et al. 2011). In some cases, such prognostications might be made very early in life; in children who develop learning disabilities, neonatal ERP responses predict functioning up to 8 years later (deRegnier et al. 2000; Molfese 2000). In addition to specifying areas of vulnerability as treatment targets, brain research might also highlight areas of proficiency upon which to capitalize. Recent work from our group demonstrates that unaffected siblings of children with ASD share some anomalies in social brain function but demonstrate apparent compensatory activity in other regions of the social brain (Kaiser et al. 2010). This finding suggests that interventions designed to bolster functioning of this brain region or its behavioral correlates might effectively improve social function of individuals with ASD.

A second objective of dissecting heterogeneity is to improve the power of other scientific tools. Most studies of individuals with ASD are designed to compare groups of individuals. This commonly entails contrasting individuals on the autism spectrum with typically developing peers; however, studies have also attempted to compare children on the spectrum grouped by differential diagnosis (e.g., Asperger's Disorder versus Autistic Disorder) or by other characteristics (e.g., cognitively able versus intellectually disabled). The power of a scientific study to detect differences is only as strong as the accuracy of the factor used to define groups. With the more complex, descriptive approaches detailed above, subtler and more accurate distinctions will become possible. This is especially critical for investigations into the genetic bases of ASD. Distinct findings from neuroimaging, or *biomarkers,* can guide genetic research. *Endophenotypes*, or characteristics that indicate a genetic liability for disease, reflect the most basic components of a complex clinical presentation and are less developmentally malleable than overt behavior (Gottesman and Shields 1973). By describing specific characteristics in these objective ways, neuroimaging research will facilitate identification of genetic contributions to ASD.

Detecting Atypical Development in the Absence of Atypical Behavior

At present, clinical detection of autistic symptoms and ultimate diagnosis of the disorder is entirely reliant on observation of behavior. Across development, but especially during infancy, behavior is widely variable and often unreliable. Moreover, many of the social features of autism do not emerge in typical development until after 12 months of age, and one cannot be certain whether they will manifest during the limited periods of observation involved in clinical evaluations or in pediatrician's offices. In published research to-date, even highly sophisticated behavioral methods, such as eye tracking, do not reveal differences in children with ASD until 12 months (Ozonoff et al. 2010). The imaging methods we have described offer promise for earlier detection of the derailment of social development. Measuring brain activity associated with social perception can detect differences that are not evident in behavior until much later. ERP studies of typical social development reveal that 3-month old infants make social-perceptual distinctions unobservable with behavioral methods until 6 months later (Gliga and Dehaene-Lambertz 2005). A recent study demonstrated that ERP measures of brain response to eye gaze in infants as young as 6 months who showed normal patterns of visual fixation predicted subsequent development of autism, suggesting the great promise of brain imaging for early recognition of ASD (Elsabbagh et al. 2012). With earlier detection, treatments could move from treating extant symptoms to preventing their emergence by altering the course of abnormal brain development, steering it toward normality.

Hope for Improved Outcomes

We see the neuroimaging research described above, as well as social brain theories of autism, more broadly, as harbingers of hope for the future of ASD treatment. Many of the functions of the social brain reflect significant *plasticity*, meaning that, despite clear roles in development, their functioning can be affected by experience over time. For example, the same brain regions involved in face perception are co-opted for other cognitive functions when people learn intensively about them. When aficionados of birds or cars immerse themselves in the area of interest, to efficiently process the depth of information required for rapid identification, they begin to employ face-processing regions developmentally experienced in making these types of rapid distinctions (Tanaka and Curran 2001). Because these experts were not "reared" on these objects, it makes clear that nodes of the social brain can be re-activated even when the typical window of developmental exposure has lapsed. In contrast to theories that the brains of people with autism have difficulty processing complex information or communicating across large expanses of cortex (Minshew and Williams 2007), we see this characteristic of the social brain as a positive prognosticator for the development of treatment; the brains of people with ASD are not *broken*, but rather they are not wired to process social information optimally in a world in which these calculations are taken for granted. The plasticity of the social brain suggests that, rather than representing an insurmountable obstacle, remediation of these difficulties may be possible with appropriate and timely intervention.

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Conflict of interest The authors report no conflicts of interest.

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