Review

Biological Psychiatry

Autism and the Social Brain: The First-Year Puzzle

Mayada Elsabbagh and Mark H. Johnson

ABSTRACT

The atypical features of social perception and cognition observed in individuals with a diagnosis of autism have been explained in two different ways. First, domain-specific accounts are based on the assumption that these end-state symptoms result from specific impairments within component structures of the social brain network. Second, domain-general accounts hypothesize that rather than being localized, atypical brain structure and function are widespread, or hypothesize that the apparent social brain differences are the consequence of adaptations to earlier occurring widespread changes in brain function. Critical evidence for resolving this basic issue comes from prospective longitudinal studies of infants at risk for later diagnosis. We highlight selected studies from the newly emerging literature on infants at familial risk for autism to shed light on this issue. Despite multiple reports of possible alterations in brain function in the first year of life, overt behavioral symptoms do not emerge until the second year. Our review reveals only mixed support, within this very early period, for localized deficits in social brain network systems and instead favors the view that atypical development involving perceptual, attentional, motor, and social systems precede the emerging autism phenotype.

Keywords: Autism, Brain development, Eye tracking, Imaging, Infant, Risk

http://dx.doi.org/10.1016/j.biopsych.2016.02.019

Autism, a developmental disorder characterized by suboptimal social and communication behavior, is commonly attributed to the atypical development of brain networks subserving social perception and cognition. However, the fundamental question of why the so-called social brain network is differentially affected remains unanswered. For this reason, over the last decade, several groups have begun the prospective study of infants who are at increased risk for developing autism (1–3). Later-born siblings of children with autism are more likely to receive a diagnosis of autism themselves compared with infants with no family history of autism. Specifically, ~20% of these infants receive an autism diagnosis by 3 years of age, and a further 20% may have other developmental difficulties or show subclinical aspects of the phenotype (4). Emerging results from studies of infant siblings have begun to provide information about the developmental precursors and risk processes that lead to the emergence of the autism phenotype in toddlerhood. There is consensus that during the second year of life many infants in whom autism is later diagnosed begin to be differentiated based on their behavior from infants at risk who do not receive a diagnosis and infants in low-risk control groups (1–3).

Despite this progress in characterizing the emerging phenotype, what has been described as the first-year puzzle (1) remains unresolved: within the earliest period of postnatal life, overt behavioral signs of later autism are subtle and variable and do not obviously map on the profile of atypicality seen later (5,6). Much of the research on infants at familial risk has centered on the attempt to identify precursors of the later diagnosis. To date, many published studies have specifically focused their investigations on social orienting and perception in infancy, on the assumption that such tasks will provide the best predictive markers of later diagnosis. As such, many studies have adopted the general assumption that domain-specific deficits in infancy become increasingly compounded during postnatal development to result in the social impairments observed in diagnosed autism. Infant social brain network precursors are assumed to also be the origins of the later emerging social, cognitive, and attention features observed in this population (7).

In this review, we question the "social-first" assumption prevalent in the literature on the grounds that the evidence in support of this view is more mixed than has sometimes been portrayed, and evidence from infants in the first year is more consistent with subtle widespread atypicality across multiple brain systems. Our review of the literature on infants is largely consistent with evidence from research on adults identifying neurocognitive differences in perceptual and cognitive systems in addition to the differences observed in social brain networks.

SOCIAL-FIRST ASSUMPTION

Although autism is diagnosed on the basis of social and communication impairment, the phenotype encompasses much broader differences in perception and cognition. Several

 ISSN: 0006-3223

accounts, supported by research on children and adults with autism, have shifted the focus away from social impairment. For example, the enhanced perceptual functioning account posits that autism is characterized by locally oriented visual and auditory perception and enhanced low-level discrimination (8). More recently, a predictive coding account has been applied to autism (9). Predictive coding suggests that higher brain areas attempt to "explain" input from sensory brain areas and then project these predictions down to lower areas, where the predicted sensory information is subtracted from the input. This account may explain how brain differences in autism lead to a bias favoring local over global processing. More specifically, hypersensitivity in visual or auditory processing may underlie symptoms such as altered social engagement and speech delay. These alternative accounts have also indicated that islands of enhancement, in addition to deficits, may better characterize some aspects of the phenotype.

Overall, these perspectives suggest that viewing autism in terms of a focal impairment in the social brain is overly simplistic. A more complex pattern of interactions between social and perceptual systems may underlie the pattern of symptoms or individual differences observed in this condition. These alternative accounts have received much less attention from the more recent research area examining early development in autism, which has more often continued to pursue the hypothesis of a social-first deficit. Studying the early emergence of autism signs and symptoms can help explain the mechanisms underlying their development before symptoms are amplified and complicated over the course of atypical development.

There are several good reasons why researchers studying infants at risk for autism have tended to focus on early markers of the social brain. First, social brain deficits are assumed to underlie key diagnostic features of the diagnosed syndrome, and as such emerging atypical social behaviors (usually observed in the second year) clearly precede the diagnostic phenotype (1–3). Second, because of the limited attention span of infants in their first year, researchers are forced to make pragmatic decisions about prioritizing particular domains for tests. Third, a mature literature on the typical development of the social brain readily allows for the adoption of paradigms and theoretical ideas to be applied to at-risk populations.

The social brain is a network of regions implicated in the processing of social information, including cortical areas such as orbitofrontal cortex, superior temporal sulcus, temporoparietal junction, and the fusiform face area as well as subcortical structures, such as amygdala and pulvinar (10). Although many aspects of this adult brain specialization remain to be understood, much progress has been made in understanding the developmental course of social perception and orienting. Because moving the eyes is the most important means of selecting visual input in infants and adults, eye tracking is being increasingly used. Although eye movement measures have been used since the 1970s, the advent of eye-tracking technology has substantially expanded the utility of these measures across multiple basic and clinical research fields. Measuring cognitive phenomena through eye tracking requires a careful experimental design, and its use to measure "social brain" functions can be viewed as a subset of studies using looking behavior to assess cognition.

Early in postnatal life, the brain has basic orienting mechanisms that support rapid attention to salient stimuli, particularly those of social relevance (11). One such system is based on a subcortical route and biases the human newborn to attend toward faces (12). Various studies have allowed further specification of the key characteristics of faces preferentially attracting attention (13). These preferences are robust in the face of manipulation of low-level perceptual and motion features of the scenes. Although this putative system is based on simple low-spatial frequency patterns characteristic of faces, it is sufficient to bias the input to developing cortical visual areas (14). In response, some of these cortical areas increase their specialization for processing faces and related social stimuli, resulting in increasingly selective patterns of cortical activation with increasing age.

Beginning life with these rudimentary biases, infant social behavior does not simply mature over development giving rise to complex and well-developed social and communication abilities in toddlers. Instead, social orienting reflects experience-dependent changes across perceptual, cognitive, and social brain systems. The developmental course of fixations changes rapidly over development (15–17): newborn infants tend to fixate mainly around the edge of the face; later, similar to adults, infants begin to fixate on the internal features of the face, such as eyes and mouth. Subsequently, they show a strong preference for the internal features of the face when they are watching their mother's face when it displays communicative expressions, such as maintained eye contact, smiling, speaking in infant-directed speech, and nodding. Given this relatively mature literature on typical development, it is not surprising that hypotheses on the origins of autism based on the social-first assumption have been so actively pursued.

ASSESSING THE SOCIAL-FIRST HYPOTHESES

Several groups have theorized that early deficits in social information processing early in life may interfere with the emergence of developmental milestones that are critical for social learning, such as shared attention (7,12,18,19). According to this view, these cascading influences could preclude the typical development of sociocommunicative skills, eventually leading to deficits in language acquisition, theory of mind, and understanding of others. In individuals with a diagnosis of autism, it may be possible to dissociate differences in social orienting from differences in social reward systems (7). However, at the present time, it is impossible to investigate this putative dissociation in infants $<$12 months old, and so we do not differentiate these hypotheses in the current analysis.

Because deficits in social engagement are characteristic symptoms of autism, the most direct and parsimonious hypothesis regarding the origins of these symptoms is impairment or absence of rudimentary social orienting biases. Retrospective studies looking back at the first 2 years of life (20) show less orienting toward social stimuli and a reduced response to name calling in the first years of life in infants in whom autism is later diagnosed compared with infants in whom developmental delay is later diagnosed. Consistent with