



Neural networks underlying language and social cognition during self-other processing in Autism spectrum disorders



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ABSTRACT

The social communication impairments defining autism spectrum disorders (ASD) may be built upon core deficits in perspective-taking, language processing, and self-other representation. Self-referential processing entails the ability to incorporate self-awareness, self-judgment, and self-memory in information processing. Very few studies have examined the neural bases of integrating self-other representation and semantic processing in individuals with ASD. The main objective of this functional MRI study is to examine the role of language and social brain networks in self-other processing in young adults with ASD. Nineteen high-functioning male adults with ASD and 19 age-sex-and-IQ-matched typically developing (TD) control participants made “yes” or “no” judgments of whether an adjective, presented visually, described them (*self*) or their favorite teacher (*other*). Both ASD and TD participants showed significantly increased activity in the medial prefrontal cortex (MPFC) during self and other processing relative to letter search. Analyses of group differences revealed significantly reduced activity in left inferior frontal gyrus (LIFG), and left inferior parietal lobule (LIPL) in ASD participants, relative to TD controls. ASD participants also showed significantly weaker functional connectivity of the anterior cingulate cortex (ACC) with several brain areas while processing self-related words. The LIFG and IPL are important regions functionally at the intersection of language and social roles; reduced recruitment of these regions in ASD participants may suggest poor level of semantic and social processing. In addition, poor connectivity of the ACC may suggest the difficulty in meeting the linguistic and social demands of this task in ASD. Overall, this study provides new evidence of the altered recruitment of the neural networks underlying language and social cognition in ASD.

1. Introduction

Autism Spectrum Disorder (ASD) is characterized by two categories of behaviors defined by the DSM-V: 1) impairments in social communication; and 2) restricted, repetitive patterns of behaviors, interests or activities (American Psychiatric Association, 2013). The social communication deficits in ASD may manifest in problems in social cognition and in reciprocal social interactions. One of the basic aspects of problems related to social cognition and reciprocal social interaction in autism may be an atypical representation of self and other. Flexibly switching between self and other perspectives may be required for imitation, perspective-taking, theory-of-mind (ToM), and empathy (de Guzman et al., 2016; Frith and De Vignemont, 2005). Even in the

earliest descriptions of autism (Kanner, 1943), the self-absorbed and aloof nature of individuals with autism was mentioned. Later studies suggest impairments in self-other processing in autism in terms of naïve egocentrism (in which the self is the only point of reference) (Frith and De Vignemont, 2005), poor autobiographical memory marked by errors of omission (Bruck et al., 2007), in eliciting statements about self in social contexts (Lee and Hobson, 1998), and imitation (Rogers, 1999; Rogers and Williams, 2006; Shih et al., 2010). More recent studies (Santesteban et al., 2012; de Guzman et al., 2016) reported an increase in empathic corticospinal responses, self-reported empathy, ability to control imitation, and ability to take another's visual perspective in individuals who were trained to control representations of self and other. In addition, there seems to be a deficit in ASD in interoceptive

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awareness, a system that combines sensory feedback to create a cortical image or awareness of the body (Craig, 2003). Specific brain areas, including the cingulate cortex, thalamus, and insula, might function interactively to create a lower-order processing of self in terms of bodily functions and their sensory integration, culminating in a basic self-identity. Altered recruitment of these regions in individuals with ASD may underlie their failure to adopt the bodily-anchored psychological and communicative stance of another person (Hobson and Meyer, 2005). Thus, a deficit in self-other representation may play a central role in the sociocognitive and behavioral profile of autism.

While self-other representation plays a significant part in social cognition and social interaction, its role in language, specifically semantic processing, and communication cannot be undermined. For example, pronoun reversal (switching between “I” and “you”; Tager-Flusberg, 1994; see Brehme, 2014 for a review), echolalia (meaningless repetition of another person's spoken words; Fay, 1969; Sterponi and Shankey, 2014; Sterponi and Kirby, 2016), and a reduced or reversed production-comprehension lag (speaker using less sophisticated language than he or she can comprehend; see Gernsbacher et al., 2016 for a review) have been reported in individuals with ASD. Studies also report that individuals with ASD are more likely to have a difficulty with understanding and expressing emotional words (Mosely et al., 2015; Tager-Flusberg, 1992; Hobson and Lee, 1989). Furthermore, difficulty in understanding non-literal language (e.g., idioms, hyperbole, and pun) (Gold et al., 2010; Kerbel and Grunwell, 1998; Kana and Wadsworth, 2012) and difficulty with comprehension of context specific language are also reported in ASD (Harris et al., 2006). Finally, self-consciousness or self-awareness has also been suggested to produce a bias in neural processes, particularly in language related tasks involving the self. For example, Macrae et al. (2004) reported that typically developing (TD) individuals performing a self-other judgment task remembered significantly more self-related words, which they attributed to increased prefrontal cortex activation during self-related judgments. Further, in an incidental memory task with three categories of questions (phonological, semantic, and self-referential), Toichi et al. (2002) reported significantly better memory performance for the self-referential words in TD participants; whereas, participants with autism did not. This may question whether a “privileged status” for self-related words exists in autism.

Neuroimaging studies of self-other processing in TD populations have found a network of brain regions primarily involved in self-other representation while completing language tasks. This network includes the following regions: the medial prefrontal cortex (MPFC), the precuneus, anterior cingulate cortex (ACC), left inferior frontal gyrus (LIFG), and left inferior parietal lobule (LIPL) (Chiu et al., 2008; D'Argembeau et al., 2007; Kelley et al., 2002; Chaminade and Decety, 2002; Decety et al., 2002a, 2002b; Ruby and Decety, 2001). Activation in cortical midline structures like the MPFC and the precuneus have been suggested to link self-related thought to planning (Northoff et al., 2006). While primarily associated with semantic tasks, the LIFG and the LIPL also serve in representing social knowledge and abstract social concepts (Wood et al., 2003; Zahn et al., 2007), in attributing personality traits (Heberlein and Saxe, 2005), with inner speech activity during self-awareness tasks (Morin and Michaud, 2007), affect recognition (Radua et al., 2010) and imitation (Chaminade and Decety, 2002). In ASD, several of these brain regions have been found to be under-activated, relative to TD individuals, during similar tasks (Lombardo et al., 2010; Kennedy and Courchesne, 2008). In addition, Lombardo et al. (2010) reported reduced functional connectivity between the ventromedial prefrontal cortex (vmPFC) and areas associated with lower level embodied representations (somatosensory cortex, ACC) suggesting that a higher level representation of self relies on the input of lower order sensorimotor systems (Barsalou, 1999; Aziz-Zadeh and Damasio, 2008; Lombardo et al., 2010).

Further, the default mode network (DMN) also has been characterized (collectively) by functions of a self-referential nature. It is

possible that the suppression of DMN activity during cognitively demanding tasks may not happen optimally in ASD individuals (Kennedy et al., 2006). Some regions of the DMN, part of a larger CMS network, have also been found to be important in self-referencing during verbal tasks, including the ventromedial prefrontal cortex (vmPFC), ACC, dorsomedial prefrontal cortex (dMPFC), precuneus, and the supplementary motor area (SMA; Northoff et al., 2006). While most of the studies mentioned above investigated self-other representation using non-linguistic stimuli, some studies have tested whether self-related words have a privileged status in cognitive and neural processing (Kelley et al., 2002; Lombardo et al., 2010). This task perfectly integrates social and linguistic demands in the context of self-other processing. Considering the social and communicative difficulties in ASD, along with cognitive and neural integration problems, this task provides an ideal milieu to test this hypothesis.

In the current study, we used a variation of a popular semantic processing task mentioned above (Kelley et al., 2002; D'Argembeau et al., 2007; Lombardo et al., 2010; Toichi et al., 2002) in which participants were asked if adjectives presented in the scanner described themselves, their favorite teacher, or if it contained the letter “e.” Participants then completed a memory recall task outside of the scanner to determine if one category of words (self) were remembered more than the others. The rationale for this fMRI study of self-other processing comes from these premises: 1) semantic processing has been found to be associated with less activation in core language areas in ASD individuals, although these differences are often heterogeneous and not well-characterized (e.g., LIFG, MPFC, LMTG, LIPL) (Harris et al., 2006; Lombardo et al., 2010; Herringshaw et al., 2016). The findings of this study will provide insights into the brain bases of both linguistic and social aspects of self-other processing in ASD; 2) atypical self-other representation may underlie abnormalities in social cognition or language comprehension, or both. This study may help tease apart the cognitive and neural differences underlying this; 3) Considering behavioral evidence of alterations in self-other processing in individuals with ASD, this study will further test it in the context of neurobiological level; and 4) The current study also takes a network perspective at the whole brain level in understanding the neural bases of self-other processing, which is different from region-based approach in previous studies (e.g., Chiu et al., 2010). This approach may provide a more comprehensive view of self-other representation in ASD. The main hypotheses of this study are: (1) the ASD group will show significantly less activation in the MPFC, LIFG, LIPL, and ACC when compared to TD controls, as these areas are involved in both semantic and self-other processing; (2) we predict weaker functional connectivity in ASD, relative to TD participants, between regions primarily involved in social and language processing; (3) participants with ASD will not show a privileged status for self-processing, as they will not differ in remembering self-related words from other-related words; and (4) the ASD population will have hypoactivation in motor and limbic regions, suggesting an inability to create a lower-order sense of self. Previous studies of semantic and self-other processing have reported mixed findings in terms of hypo-or-hyper-activity in individuals with autism. The findings of this study will provide more evidence on cognitive and neural aspects of self-other processing in autism.

2. Methods

2.1. Participants

Nineteen high functioning male adolescents and adults with autism (mean age = 21.7 years, range = 15–35 years) and 19 age-sex-and-Performance-IQ-matched TD control participants (mean age = 21.9 years, range = 16–34 years) were included in this study. Due to excessive motion during scanning, four participants in each group were excluded from further analyses, making the final sample size to 15 in each group. After exclusion of these participants, the groups no longer

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