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Sex differences in the neural basis of false-belief and pragmatic language comprehension

Chiyoko Kobayashi Frank [a,b,*], Simon Baron-Cohen [c], Barbara L. Ganzel [a]

[a] Bronfenbrenner Center for Translational Research, Cornell University, Ithaca, NY, USA
[b] School of Psychology, Fielding Graduate University, Santa Barbara, CA, USA
[c] Autism Research Centre, Cambridge University, Department of Psychiatry, Cambridge, UK

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ABSTRACT

Increasing research evidence suggests that women are more advanced than men in pragmatic language comprehension and Theory of Mind (ToM), which is a cognitive component of empathy. We measured the hemodynamic responses of men and women while they performed a second-order false-belief (FB) task and a coherent story (CS) task. During the FB condition relative to the baseline (unlinked sentences [US]), we found convergent activity in ToM network regions, such as the temporoparietal junction (TPJ) bilaterally and precuneus, in both sexes. We also found a greater activity in the left medial prefrontal cortex (mPFC) and a greater deactivation in the ventromedial prefrontal cortex (vmPFC)/orbitofrontal cortex (OFC) bilaterally in women compared to men. However, we did not find difference in the brain activity between the sexes during the FB condition relative to the CS condition. The results suggest a significant overlap between neural bases of pragmatic language comprehension and ToM in both men and women. Taken together, these results support the extreme male brain (EMB) hypothesis by demonstrating sex difference in the neural basis of ToM and pragmatic language, both of which are found to be impaired in individuals with Autism Spectrum Disorder (ASD). In addition, the results also suggest that women use both cognitive empathy (dorsal mPFC) and affective empathy (vmPFC) networks more than men for false-belief reasoning.

Introduction

Theory of Mind (ToM) refers to the ability to attribute mental states (such as beliefs, intentions, thoughts, and emotions) to self or others, and to use such knowledge to make sense of and predict the behavior of agents (Dennett, 1980). ToM has been suggested to be fundamental for human social interaction (Baron-Cohen, 1994; Frith and Frith, 2003). ToM has often been used interchangeably with "mindreading" (Carruthers, 2009), "mentalizing" (Frith and Frith, 2003) and "cognitive empathy" (Baron-Cohen, 2011). Among the variety of ToM tasks, the false-belief (FB) test (Wimmer and Perner, 1983; Perner and Wimmer, 1985) is perhaps the most widely used. The FB task assesses understanding of others' beliefs when these differ from one's own (Baron-Cohen et al., 1985, 1999). In the most common form of the FB test, dubbed the "Sally-Anne" task (Baron-Cohen et al., 1985), an object (e.g., a marble) is moved while the protagonist (Sally) is absent so that Sally mistakenly believes the marble is still in its last location, while the other character (Anne) knows it is now somewhere else. It has been found that while a typically-developing 4-year-old child passes these FB tests (Wimmer and Perner, 1983), most children with Autism Spectrum Disorder (ASD) are delayed in passing these tests (Baron-Cohen et al., 1985; see also Baron-Cohen et al., 2000).

It has been demonstrated that children with ASD are not only impaired in false-belief understanding but also in precursor capacities of ToM such as joint attention and pretend play (Frith and Frith, 2003). These impairments might be closely related to the key characteristic of ASD involving primary deficits in pragmatic aspects of language (Landa, 2000; Tager-Flusberg, 2000; Frith, 2003; Tager-Flusberg and Joseph, 2005). It has been demonstrated that the way in which older children/adolescents with ASD approach FB tasks is different from typically developing children in that they rely on syntax and semantics more than pragmatics (Tager-Flusberg, 2007). Pragmatic aspects of language involve bringing in general world knowledge, integrating the individual utterances with the context, and making inferences based on one's prior knowledge of the situation (Ferstl et al., 2008). When someone says, "can you pass the salt?", a child with ASD understands the utterance not as a request but as a question of his or her ability to pass a salt bottle (Frith, 2003). A host of studies has shown that children with ASD have difficulties in detecting vocal cues to irony and sarcasm (Wang et al., 2001, 2006, 2007) that rely on the second-order pragmatic language comprehension (Wilson, 2000). For instance, Chevallier and colleagues have recently shown that children with high functioning

* Corresponding author at: School of Psychology, Fielding Graduate University, Santa Barbara, CA, USA.
E-mail address: ckobayashi@fielding.edu (C.K. Frank).

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ASD are impaired in recognizing pragmatically different levels of vocal cues not specific to ToM (Chevallier et al., 2011). These results suggest that the neural underpinnings of ToM and pragmatic language at least partly overlap.

Increasing research evidence suggests that women and girls are typically superior to typically-developing men and boys in empathy. Men and boys, in turn, are typically superior in empathy to people with ASD. For example, it has been found that girls outperform boys on tasks of emotion processing (Brown et al., 1996) and the Reading-the-Mind-in-the Eyes test (Baron-Cohen et al., 1997, 2000), and that girls demonstrate more sensitivity to sad looks and show sympathetic and comforting attitudes to others (Hoffman, 1977). These findings led to hypotheses about differences in the organization of the mind and brain between men/boys and women/girls. The empathizing–systemizing (E–S) theory of human psychological sex differences (Baron-Cohen, 2003) hypothesizes that the "male brain" or "Type S (systemizing) brain" has, on average, a weaker drive to empathize, alongside a stronger drive to systemize (Baron-Cohen, 2003, 2006; Chakrabarti and Baron-Cohen, 2006). In contrast, the "female brain" or "Type E (empathizing) brain" is defined as the opposite profile. These are psychometric definitions and by no means suggest that only men and boys have Type S brains, only that more men/boys than women/girls show this profile. This acknowledges that some women/girls have a Type S brain and some men/boys have a Type E brain (Goldenfeld et al., 2005). Although it has been found that more men/boys score higher on systemizing than on empathizing tasks (Auyeung et al., 2009), it has also been demonstrated that scores of systemizing and empathizing in women/girls are not correlated (Valla et al., 2010), suggesting sex differences in processing these tasks.

An extension of the E–S concept is the "extreme male brain (EMB)" hypothesis (Baron-Cohen, 2003), which hypothesizes that ASD may be an extreme form of the Type S brain (Baron-Cohen, 2006). In psychometric terms this comprises below-average empathy alongside intact or even above-average systemizing. A number of studies report results consistent with these profiles (e.g., Baron-Cohen et al., 1997; Lawson et al., 2004). Most recently, Auyeung et al. (2012) administered the Empathy Quotient (EQ) and Systemizing Quotient (SQ) (Baron-Cohen et al., 2003; Baron-Cohen and Wheelwright, 2004) to a large cohort of mothers of adolescents and another group of mothers of adolescents with ASD. As predicted, girls received significantly higher scores on the EQ than boys, who received significantly higher scores than adolescents with ASD. Adolescents with ASD were scored higher on the SQ than boys, who were scored higher than girls.

It has been suggested that empathy and ToM are distinct but overlapping concepts (Singer, 2006; Schulte-Rüther et al., 2008). Baron-Cohen (2011) defined empathy as "… our ability to identify what someone else is thinking or feeling and to respond to their thoughts and feelings with an appropriate emotion" (p. 16) which highlights that empathy encompasses two separate components: the cognitive component (ToM) and the affective component. This two-factor model of empathy is consistent with other definitions of empathy and ToM (Schulte-Rüther et al., 2008; Shamay-Tsoory et al., 2009). Regarding the tasks that tap these components respectively, the aforementioned emotion processing (Brown et al., 1996) and the Reading-the-Mind-in-the Eyes test (Baron-Cohen et al., 1997, 2000) tap the emotional empathy while white lie deception tasks (Villanueva et al., 2000), social narratives (Bosacki, 2000) and FB task examine the cognitive empathy. Compared to the affective empathy, studies that tested sex difference in the cognitive empathy (ToM) yielded mixed results. Specific to false-belief understanding, while Charman et al. (2002) found only a moderate advantage of girls over boys in the FB task, other researchers have found significant differences between the sexes. Walker (2005) found that 3- to 5-year-old girls perform better on standard FB tasks than boys of the same age. Likewise, Calero et al. (2013) tested 6- to 8-year-old children with a suite of ToM tasks developed by Wellman and Liu (2004) and found a significant gender difference in the FB task performance. As Calero et al. (2013) note, these results may suggest a progressive increase in the gender gap in ToM processing.

The close relationship between ToM and communicative language is relevant to the present study since it has been consistently demonstrated that girls outperform boys in a number of language processing tasks (Dionne et al., 2003; Bornstein et al., 2004). It has been shown that girls Q6 learn vocabulary faster (Roulstone et al., 2002), demonstrate more spontaneous conversations (Bauer et al., 2002; Lutchmaya et al., 1995), Q7 and show earlier onset of language use (Murray et al., 1990). Furthermore, it has been found that these advantages continue into adulthood (Parsons et al., 2005). With respect to the sexual dimorphism in the neural basis of language, it has been found that women, relative to men, activate more bilateral brain regions including the inferior frontal gyrus (Clements et al., 2006; Burmann et al., 2008) and posterior superior middle/temporal gyrus (Kansaku et al., 2000; Rossell et al., 2002) in a less modality-specific manner (Burmann et al., 2008) during various language processing tasks.

To date, a number of neuroimaging studies have explored the neural correlates of ToM in adults. These studies have consistently found ToM-specific activity in the temporoparietal junction (TPJ) (Saxe and Kanwisher, 2003; Saxe and Wexler, 2005; Kobayashi et al., 2007), and the medial prefrontal cortex (mPFC) (Fletcher et al., 1995; Goel et al., 1995; Brunet et al., 2000; Gallagher et al., 2000, 2002; Vogeley et al., 2001; Kobayashi et al., 2006). Within the sub-regions of the mPFC, the anterior rostral (ar)-mPFC is specifically implicated in mentalizing or ToM (Amodio and Frith, 2006), the posterior-rostral (pr)-mPFC is more important for monitoring personally-guided or one's own intentions (Grezes et al., 2004; Walton et al., 2004), and the orbital (o)-mPFC is more specialized for anticipating outcomes or rewards of other-guided actions (Walton et al., 2004; Knutson et al., 2005). Other regions that are often correlated with ToM tasks include the temporal pole (Gallagher et al., 2000; Vogeley et al., 2001), the precuneus (Saxe and Kanwisher, 2003; Kobayashi et al., 2006), the orbitofrontal cortex (OFC), and the amygdala (Baron-Cohen, 1994; Baron-Cohen et al., 1999). Together, these regions constitute a network often referred to as the "social brain" (Brothers, 1990).

It has been hypothesized that neural correlates of affective empathy are overlapping but different from those underlying cognitive empathy (ToM): the former relies on phylogenetically older structures such as the amygdala, limbic system and anterior insula, while the latter relies on newer structures such as the prefrontal cortex (Singer, 2006; Singer et al., 2009). In addition to the aforementioned structures, increasing evidence suggests that the OFC is more associated with affective empathy than with ToM. It has been demonstrated that empathy tasks are more often associated with activity in the ventral mPFC (vmPFC),while ToM tasks are more often associated with ar-ToM network, including the mPFC (Sebastian et al., 2012). It has also been found that patients with OFC damage are impaired in affective empathy but not in ToM (Shamay-Tsoory et al., 2010). These results are consistent with the hypothesis that the cognitive empathy system (ToM) has both overlapping and distinct neural correlates from affective empathy system.

Regarding the relationship between ToM and pragmatic aspects of language, a number of brain imaging studies have consistently found a significant overlap between the neural underpinnings of discourse or story comprehension and ToM understanding (Ferstl and von Cramon, 2002; Ferstl et al., 2008; Mason et al., 2008; Mar, 2011). Ferstl and von Cramon (2002) found a significant overlap between neural correlates of coherent story comprehension and text-based ToM in the dorsal mPFC. In addition, it has been demonstrated that understanding verbal irony recruits the ToM network, including the bilateral TPJ and mPFC (Bašnáková et al., 2011; Spotorno et al., 2012). In particular, Bašnáková and colleagues have shown that deriving speakers' communicative intention relies on several brain regions implicated in ToM and affective empathy, including the mPFC and right TPJ (Bašnáková et al., 2013).

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