NeuroImage 77 (2013) 222–236

Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

White matter structures associated with empathizing and systemizing in young adults☆

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ARTICLE INFO

Article history:
Accepted 2 April 2013
Available online 8 April 2013

Keywords:
Empathizing
Systemizing
D score
White matter
Voxel based morphometry
Structure
Diffusion tensor imaging
External attention system
Default mode network
Mirror neuron system

ABSTRACT

Empathizing is defined as the drive to identify the mental states of others in order to predict their behavior and respond with an appropriate emotion. Systemizing is defined as the drive to analyze a system in terms of the rules that govern it to predict its behavior. We undertook voxel-by-voxel investigations of regional white matter volume (rWMV) and fractional anisotropy (FA) of diffusion tensor imaging to discover the WM structural correlates of empathizing, systemizing, and their difference (D score: systemizing − empathizing). Whole brain analyses of covariance revealed that across both sexes, the D score was negatively correlated with rWMV in the WM area in the bilateral temporal lobe, near the right inferior frontal gyrus, near the ventral medial prefrontal cortex, and near the posterior cingulate cortex and positively correlated with FA in an area involving the superior longitudinal fasciculus. Post-hoc analyses revealed that these associations were generally formed by both the correlation between WM structures and empathizing as well as the opposite correlation between WM structures and systemizing. A significant effect of interaction between sex and the D score on rWMV, which was mainly observed because of a positive correlation between rWMV and empathizing in females and a negative correlation between rWMV and systemizing in females, was found in an area close to the right inferior parietal lobule and temporoparietal junction. Our results suggest that WM structures involving the default mode network and the mirror neuron system support empathizing, and that a WM structure relating to the external attention system supports systemizing. Further, our results revealed an overlap between positive/negative WM structural correlates of empathizing and negative/positive WM structural correlates of systemizing despite little correlation between empathizing and systemizing, which supports the previously held idea that there is a trade-off between empathizing and systemizing in the brain.

Introduction

Empathizing is defined as the drive to identify the mental status of other individuals in order to predict their behavior and respond with an appropriate emotion (Baron-Cohen et al., 2005). Systemizing is defined as the drive to analyze a system in terms of the rules that govern the system in order to predict its behavior (Baron-Cohen et al., 2005). Empathizing and systemizing are important subjects of scientific study partly because stronger systemizing and weaker empathizing are believed to explain or underlie a wide range of characteristics associated with males and subjects with Autism Spectrum Conditions (ASCs), such as Asperger's Syndrome, compared with females and subjects without ASCs (Baron-Cohen and Wheelwright, 2004; Baron-Cohen et al., 2003). The D score, which is the discrepancy between systemizing and empathizing (systemizing − empathizing), is a psychological variable. It is this, rather than empathizing or systemizing alone, that is suggested to describe ASCs and to differentiate typical males from typical females (Baron-Cohen, 2004). The sum of the empathizing and systemizing scores does not differ between males and females. On the basis of this evidence, it is suggested that empathizing and systemizing are competing "neurally in the brain" and that the D score provides information on the trade-off between the two (Goldenfeld et al., 2005). However, there is little correlation between empathizing and systemizing (e.g., Wakabayashi et al., 2007; Wheelwright et al., 2006), and this notion is a matter of debate (Andrew et al., 2008).

In our previous study (Takeuchi et al., submitted for publication), we proposed a hypothesis that empathizing may be associated with the function of the regions that consist of the default mode network (DMN), while systemizing may be associated with the function of

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http://dx.doi.org/10.1016/j.neuroimage.2013.04.004

the regions that consist of the external attention system (EAS) which consists of the lateral prefrontal cortices (LPFCs), the dorsal part of the anterior cingulate cortex (ACC), inferior parietal lobes (IPLs) and so on (Buckner et al., 2008; Corbetta and Shulman, 2002). The DMN is active at rest and usually suspended during externally-directed, attention-demanding tasks, while the network consisting from LPFCs and IPLs is the opposite (Buckner et al., 2008). Regions such as the medial prefrontal cortices (mPFCs), precuneus, posterior cingulate cortex areas and some lateral temporal cortex areas and the superior temporal sulcus (STS) belong to the DMN (Buckner et al., 2008).

The basis of our hypothesis above (more extensive discussions can be seen in Takeuchi et al., submitted for publication) is that empathizing/systemizing is supposed to underlie the wide range of inferiorities/superiorities associated with ASCs, and that these are in turn associated with the functions of DMN/EAS, respectively. In summary, on one hand, empathizing is supposed to underlie the inferiorities associated with ASCs with respect to a wide range of social, emotional, and empathetic skills or abilities, including theory of mind (TOM) (for a review, see Baron-Cohen (2004)). On the other hand, regions in DMN are also involved in cognitions related to such inferiorities. These conditions include internally focused tasks (such as self-related recognition, which includes knowing one's own emotions) and social cognition, which includes TOM and the recognition of another's perspective (Amodio and Frith, 2006; Buckner et al., 2008). On the other hand, systemizing is supposed to underlie, partly explain, or be associated with the supposed superior spatial ability, modus tollens reasoning ('if p, then q'), and attention to detail associated with ASCs (Baron-Cohen, 2004; Baron-Cohen et al., 2005, 2009). LPFCs and IPLs are associated with spatial tasks (Richter et al., 2000), attention (Awh and Jonides, 2001), and reasoning (Kroger et al., 2002).

Previous neuroimaging findings are generally congruent with the idea that regions in DMN are associated with empathizing, while those in EAS are associated with systemizing. These previous studies have shown that empathizing is associated with regional gray matter volume (rGMV) of (a-1) the left perisylvian areas and STS in children (Sassa et al., 2012), (a-2) mPFC and precuneus areas together with other areas in young adults (Takeuchi et al., submitted for publication), and (a-3) mPFC together with other areas (Cheng et al., 2009). On the other hand, systemizing was associated with (b-1) rGMV of the posterior parietal cortex in children (Sassa et al., 2012), (b-2) rGMV of the DLPFC area and the dorsal part of ACC together with other areas in young adults (Takeuchi et al., submitted for publication), and the dorsal part of ACC to the middle cingulate cortex in young adults (Lai et al., 2012), as well as (c) LPFC functional activity in young adults (Billington et al., 2008).

Further, although we focused on the nodes of DMN as anatomical correlates of empathizing, there are some theories that focus on the mirror neuron system as a correlate of empathy/empathizing or autistic traits (Cheng et al., 2009; Hadjikhani et al., 2006). The mirror neuron system is defined as the areas that are active during both action execution and observation in humans and involve parts of the frontal and parietal areas including regions such as the inferior frontal gyrus and areas in the posterior parietal lobule (Cattaneo and Rizzolatti, 2009). These theories state that the mirror neuron system makes it possible for one to understand the intentions of another's actions and plays an important role in empathy and empathic dysfunction in ASCs (Iacoboni and Dapretto, 2006; Rizzolatti and Craighero, 2005). Consistently, rGMV correlates of empathizing in some (though not all of) studies of empathizing seem to include the inferior frontal gyrus and/or some posterior parietal areas (Cheng et al., 2009; Sassa et al., 2012; Takeuchi et al., submitted for publication).

None of these previous neuroimaging studies of empathizing/systemizing has investigated the white matter (WM) structural correlates of empathizing/systemizing. Recently, Chou et al. (2011) used diffusion tensor imaging (DTI) to investigate WM structural integrity [fractional anisotropy (FA)] correlates of empathizing and systemizing. This study revealed that empathizing was associated with the structural integrity of various regions such as the left superior temporal gyrus, and that systemizing was associated with the structural integrity of WM regions such as the left prefrontal lobe. Considering the involvement of these areas with DMN and EAS (Buckner et al., 2008), these findings may be at least partly congruent with our hypothesis. However, several significant areas other than these regions have shown sporadic associations. Further, in their study all of the significant results showed the effects of interaction between empathizing and sex or between systemizing and sex. These findings may thus rather suggest the importance of sexual dimorphism in the determination of correlates of empathizing/systemizing, as the authors suggested.

However, previous anatomical studies of empathizing/systemizing have not successfully revealed any regional WM volume (rWMV) correlates of empathizing/systemizing or FA/rWMV correlates of the D score, and determining these relationships thus became the purpose of our present investigation. One study of adult males with a relatively wide age range ($N = 88$, age range 18–45) investigated rWMV correlates of the D score but failed to detect any significant findings (Lai et al., 2012). Recent studies (Takeuchi et al., 2012a,b) have suggested that structural studies of cognition (especially those of WM volumetry) tend to require greater statistical power, and whether the lack of significant findings is due to a lack of statistical power remains unclear. Further, as noted above, sexual dimorphism is important in determining the structural correlates of empathizing/systemizing (Chou et al., 2011), and the sexual dimorphism of rWMV correlates of empathizing/systemizing/D score remains to be investigated. WM structural analyses enable direct determination of whether brain structural connectivity associated with DMN, mirror neuron system and EAS supports empathizing/systemizing. This is important considering the key roles of empathizing/systemizing in ASCs, as noted above. FA and rWMV were moderately to weakly related, but they were highly sensitive to the different characteristics of white matter (Fjell et al., 2008). The associations between the two seem particularly weak in deep white matter areas (Hugenschmidt et al., 2008). Distributions of the associations between FA and group/individual differences and distributions of the associations between rWMV and group/individual differences differ sometimes (Hugenschmidt et al., 2008; Jäncke et al., 2009). Thus, by utilizing both methods, we are able to investigate different neural substrates. rWMV is known to successfully correlate with cognitive functions (e.g., in the cases of our studies, see Takeuchi et al. (2011e, 2012c)). In particular, our previous studies concurrently investigating rWMV and FA correlates of cognitive functions showed more significant results for rWMV analyses in regions congruent with our hypothesis (Takeuchi et al., 2011e, 2012b). Despite there being little correlation between empathizing and systemizing, our previous study found an overlap in several areas in negative rGMV correlates of empathizing and positive rGMV correlates of systemizing (Takeuchi et al., submitted for publication), suggesting a basis for calculating the D score from a neuroimaging perspective.

Here we used voxel-based morphometry (VBM) (Ashburner and Friston, 2000; Good et al., 2001) to assess regional WM volume (rWMV) associated with empathizing/systemizing/D score. We also used voxel-based fractional anisotropy (FA) for diffusion tensor imaging (DTI) (Le Bihan, 2003) to assess WM structural integrity associated with empathizing/systemizing/D score. As discussed in our previous study (Takeuchi et al., 2010a), FA is interpreted as an indicator of WM pathway strength or integrity. Increased WM structural integrity as assessed by DTI is like rWMV, believed to underlie increased cognitive functions that involve WM regions (for details on the mechanism, refer to Takeuchi et al. (2010a)). We recruited 567 subjects (329 males and 238 females) with a limited age range to increase the statistical power of our study.

We hypothesized that (i) WM structures adjacent to GM structures of the mirror neuron system and those of the DMN and (ii) major WM