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Association between resting-state functional connectivity and empathizing/systemizing

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ABSTRACT

Empathizing is the drive to identify the mental status of other individuals and respond to it with an appropriate emotion; systemizing is the drive to analyze a system. Previously, we have shown that structures associated with the default mode network (DMN) and external attention system (EAS) are associated with empathizing and systemizing, respectively. Here we investigated the association between resting-state functional connectivity (RSFC) and empathizing/systemizing in 248 healthy young adults. We considered the medial prefrontal cortex (mPFC) and bilateral dorsolateral prefrontal cortices (DLPFCs), which are key nodes of DMN and EAS, as seed regions, and investigated correlations across subjects between individual empathizing/systemizing and RSFC between each seed region and other brain regions. We found that higher empathizing was associated with larger RSFC between the mPFC and areas in (a) the dorsal anterior cingulate cortex (dACC), (b) precuneus, and (c) left superior temporal sulcus (STS). Furthermore, there was an interaction effect between sex and systemizing on RSFC between the left DLPFC and dACC: males showed positive correlations between this RSFC and systemizing, whereas females showed the opposite tendency. Thus, empathizing was associated with increased positive functional coupling with the key node and other nodes of DMN, as well as the area associated with feeling another's pain. Systemizing was associated with increased positive functional coupling between the key nodes of EAS in males. These findings provide further support for the concept of an association between DMN/EAS and empathizing/systemizing.

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). Thus, this term involves both emotional empathy and more cognitive forms of empathy (such as perspective taking). 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). These concepts are a key area in psychology, partly because autism spectrum conditions are characterized by lesser empathizing and higher systemizing (Baron-Cohen et al., 2003; Baron-Cohen and Wheelwright, 2004). Certain cognitive characteristics of autism spectrum conditions such as deficits in theory of mind are believed to be explained by lesser empathizing (Krill et al., 2008), whereas other characteristics of these conditions such as enhanced abilities in math, physics, and engineering and enhanced spatial abilities are believed to be explained by higher systemizing (Baron-Cohen, 2003; Baron-Cohen et al., 2005).

In our previous study (Takeuchi et al., submitted for publication-b; Takeuchi et al., 2013e), we proposed the hypothesis that empathizing is associated with the function of regions of the default mode network (DMN), while systemizing is associated with the function of regions of the external attention system (EAS), which consists of the lateral prefrontal cortices (LPFCs) and inferior parietal lobes (IPLs) (Buckner et al., 2008a; Corbetta and Shulman, 2002). DMN is active at rest and is usually suspended during externally directed attention-demanding tasks, whereas the opposite is true for the network associated with

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LPFCs and IPLs (Buckner et al., 2008a). The medial prefrontal cortex (mPFC), precuneus, posterior cingulate cortices (PCC), and some lateral temporal cortex areas belong to DMN (Buckner et al., 2008a).

The basis of our hypothesis is that empathizing/systemizing is supposed to underlie the wide variety of inferior/superior characteristics associated with autism spectrum conditions, and these are in turn associated with the functions of DMN/EAS. In summary, deficiencies in empathizing are supposed to underlie the inferior characteristics associated with autism spectrum conditions, including a wide variety of social, emotional, and empathetic skills or abilities such as theory of mind (TOM) (for a review, see Baron-Cohen, 2003). Regions in DMN are involved in cognition related to these characteristics, including 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., 2008a). Systemizing is supposed to underlie, partly explain, or somehow be associated with the superior characteristics of autism spectrum conditions in terms of improved spatial abilities, modus tollens reasoning (if p, then q), and attention-to-detail (Baron-Cohen, 2003; 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).

Findings from previous neuroimaging studies have generally supported the contention that regions in DMN are associated with empathizing, whereas those in EAS are associated with systemizing. These studies showed that empathizing was associated with (a) regional gray matter volume of the left perisylvian areas in children (Sassa et al., 2012), regional gray matter volume of the mPFC and precuneus areas together with other areas in young adults (Takeuchi et al., 2014) and regional gray matter volume of the mPFC together with other areas in adults (Cheng et al., 2009) and (b) regional white matter volume in the white matter area near the ventral mPFC and near the posterior cingulate cortex together with other areas in young adults (Takeuchi et al., 2013e). On the other hand, systemizing was associated with (a) regional gray matter volume of the posterior parietal cortex in children (Sassa et al., 2012) and regional gray matter volume of the right LPFC area in young adults (Takeuchi et al., 2014), (b) white matter integrity in the left superior longitudinal fasciculus (Takeuchi et al., 2013e), which connects nodes of EAS (Petrides and Pandya, 2002) and (c) LPFC functional activity in young adults (Billington et al., 2008). Moreover, previously we found the positive correlation between systemizing and regional white matter volume in males and the negative correlation between systemizing and regional white matter volume in females in white matter regions close to the right LPFC and right dorsal anterior cingulate cortex (dACC), suggesting the sex dimorphic relationship (Takeuchi et al., 2013e).

As described in our previous study (Takeuchi et al., 2012b), recently, resting-state functional connectivity (RSFC) has been widely used in functional magnetic resonance imaging (fMRI) studies. This approach detects inter-regional correlations among spontaneous low-frequency fluctuations in the fMRI signal during rest (Biswal et al., 1995). Certain sets of regions show positively synchronized brain activity during rest (positive correlations between the brain activities of these regions) and form functional networks (Damoiseaux et al., 2006). DMN and EAS are two such major networks (Buckner et al., 2008b). In particular, autism spectrum conditions are rather consistently shown to be associated with decreased RSFC in DMN (Broyd et al., 2009), whereas some evidence suggests an association of these conditions with increased RSFC involving TPN (Noonan et al., 2009). Therefore, empathizing/systemizing may also well associate with these changes in RSFC involving DMN and TPN.

Although a number of neuroimaging studies have investigated the functional activities and brain structures related to empathizing/systemizing (Billington et al., 2008; Chakrabarti et al., 2006; Sassa et al., 2012; Takeuchi et al., submitted for publication-b; Takeuchi et al., 2013e), no study has examined the association between RSFC and empathizing/systemizing. We hypothesized that RSFC associated with the key nodes of DMN/EAS is associated with empathizing/systemizing. In addition, considering the sexually dimorphic relationship between systemizing and EAS-related white matter structures that may well associate with RSFC (Au Duong et al., 2005), we hypothesized the existence of a sexually dimorphic relationship between systemizing and RSFC.

Using functional magnetic resonance imaging (fMRI) we investigated correlations between empathizing/systemizing and (a) RSFC between the key node of DMN, mPFC, and regions elsewhere in the brain as well as (b) RSFC between the bilateral dorsolateral prefrontal cortices (DLPFCs) and regions elsewhere in the brain.

RSFC of DMN and EAS is of interest to the investigation of the neural basis of empathizing/systemizing because from the perspective of functional integrity of the networks, RSFC analysis provides direct evidence of the assumed association between the two major intrinsic cognitive networks and empathizing/systemizing. RSFC analysis also makes it possible to investigate associations between cognitions and interactions between specific brain regions. RSFC analysis is also important because autism spectrum conditions are assumed to have altered resting-state cognitions (Broyd et al., 2009), and RSFC analysis provides insight into the different resting-state cognitions underlying empathizing/systemizing.

Methods

Subjects

The present study, which is part of an ongoing project to investigate the associations between brain imaging, cognitive function, and aging (Sassa et al., in press; Takeuchi et al., 2010a, 2010b, 2011a, 2011d, 2011f, 2012d, 2013c; Taki et al., 2010, 2011), included 248 healthy, right-handed individuals (126 men and 122 women). Our previous study also involved these same 248 subjects, and data from these subjects as well as from another 55 subjects were used to investigate associations between empathizing/systemizing and gray and white matter structures (Takeuchi et al., submitted for publication-b; Takeuchi et al., 2013e). Some of the subjects enrolled in this study also became subjects of our intervention studies (Takeuchi et al., 2011a, 2013a) (psychological and imaging data recorded before the intervention were used in this study). Psychological tests and MRI scans not described in this study were performed together with those described in this study. The mean age of the subjects was 21.1 years [standard deviation (SD), 1.8]. All subjects were university students or postgraduates with normal vision and no history of neurological or psychiatric illness. Handedness was evaluated using the Edinburgh Handedness Inventory (Oldfield, 1971). Written informed consent was obtained from each subject for their participation in this project. All study procedures were approved by the Ethics Committee of Tohoku University. Data from two subjects, who misunderstood the rules of the tasks, were not analyzed.

SQ/EQ questionnaire

Japanese version (Wakabayashi et al., 2007) of the systemizing quotients (SQ)/empathizing quotients (*EQ*) questionnaire (Baron-Cohen et al., 2003; Baron-Cohen and Wheelwright, 2004) was administered to the subjects. The EQ score was used as an index of empathizing and the SQ score was used as an index of systemizing. This questionnaire consists of 40 items for each quotient and 20 unscored filler items. The scales consist of self-descriptive statements scored on a four-point scale ranging from Strongly Disagree to Strongly Agree. Half the items are worded to produce an “Agree” response and half a “Disagree” response. Items are randomized to avoid a response bias. Each strong systemizing/empathizing response is awarded two points and each slight systemizing/empathizing response is awarded one and the rest of the responses are awarded zero (i.e., each item is scored 2,1,0,0) giving a range of total scores between 0 and 80 for each quotient.

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