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Individual differences in local gray matter density are associated with differences in affective and cognitive empathy

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Abstract

The understanding of empathy from a neuroscientific perspective has recently developed quickly, with numerous functional MRI studies associating different brain regions with different components of empathy. A recent meta-analysis across 40 fMRI studies revealed that affective empathy is most often associated with increased activity in the insula, whereas cognitive empathy is most often associated with activity in the midcingulate cortex and adjacent dorsomedial prefrontal cortex (MCC/dmPFC). To date, however, it remains unclear whether individual differences in brain morphometry in these regions underlie different dispositions in affective and cognitive empathy. In order to test this hypothesis, voxel-based morphometry (VBM) was used to examine the extent to which gray matter density predicts scores from an established empathy measure (Questionnaire of Cognitive and Affective Empathy; QCAE). One hundred and seventy-six participants completed the QCAE and underwent MRI in order to acquire a high-resolution, three-dimensional T1-weighted structural scans. A factor analysis of the questionnaire scores revealed two distinct factors of empathy, affective and cognitive, which confirmed the validity of the QCAE. VBM results revealed gray matter density differences associated with the distinct components of empathy. Higher scores on affective empathy were associated with greater gray matter density in the insula cortex and higher scores of cognitive empathy were associated with greater gray matter density in the MCC/dmPFC. Taken together, these results provide validation for empathy being a multi-component construct, suggesting that affective and cognitive empathy are differentially represented in brain morphometry as well as providing convergent evidence for empathy being represented by different neural and structural correlates.

Keywords: affective empathy, cognitive empathy, voxel-based morphometry, insula, cingulate cortex, dorsomedial prefrontal cortex

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1 Introduction

To successfully navigate our social environment it is integral to understand and experience the emotional states of others, a process typically referred to as empathy. Empathy involves an affective component, subjective experiences of the emotions of others, and a cognitive component, the ability to understand others' motivation (Bernhardt & Singer, 2012; Decety, 2011; Shamay-Tsoory, 2011). The aim of this study is to investigate whether individual differences in affective and cognitive empathy are subserved by differences in brain anatomy.

When considering the affective component of empathy, emphasis is typically placed on experiencing the emotional states of others consciously, which implies a self-other distinction, as well as an understanding of where the emotional experience originates from (Bernhardt & Singer, 2012; Decety & Jackson, 2004). Affective empathy is different from emotion contagion (the automatic adoption of another person's emotions; Hatfield et al., 2009) and mimicry (the synchronisation of emotional expressions and behaviours; Preston and De Waal, 2002) which act as automatic responses to another person's emotional state but not necessarily self-other distinction. Affective empathy is also differentiated from sympathy or empathic concern, as the latter represents an internal state of emotion and motivation driven by the concern for another person's welfare but not necessarily a sharing of emotions (Bernhardt & Singer, 2012; Decety & Chaminade, 2003; Decety & Cowell, 2014; Singer & Lamm, 2009). Note that we do not argue that these processes (for example empathic concern) are unrelated to affective empathy, but rather that affective empathy can be thought of as an umbrella term that encompasses multiple dimensions.

Initial neuroimaging studies on affective sharing suggested that the, emotional components are shared vicariously but not the sensory components (Jackson et al., 2006; Singer et al., 2004). For example, when experiencing pain first-hand, activity in the

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somatosensory cortex occurs as a response to the sensory stimulation received, whereas the insula and anterior cingulate cortex activate for the affective components of pain (Morrison et al., 2004; Singer et al., 2004). In contrast, when we observed another person in pain, initial findings suggested that only the affective components are vicariously experienced through activation of the insula and anterior cingulate cortex (Jackson et al., 2006; Singer et al., 2004; Lamm et al., 2011). More recent evidence suggests that somatosensory cortex may also be activated in response to perceiving another person in pain (Avenanti et al., 2005; Chen et al., 2012; Fox, et al., 2013; Marsh et al., 2013).

The degree of overlap between first-hand and second-hand emotional experienced for the affective components is controversial (Decety, 2010; 2011). For example, the anterior insula appears to activate more so with vicarious experiences of pain (Jackson et al., 2006), while for first-hand experiences of pain the posterior insula is implemented (Decety & Lamm, 2006). The insula also responds to affective sharing outside empathic pain. Specifically, greater activation in the anterior insula occurs when observing videos of people with disgusted faces (Wicker et al., 2006) as well as when vicariously observing others experience unpleasant food (Jabbi et al., 2007), and in response to positive emotions such as pleasure (Small et al, 2001). Menon and Uddin (2010) identify the insula as a fundamental brain region involved in integrating visceral and autonomic information with salient stimuli, which provides infrastructure for the representation of subjective bodily feelings of positive and negative emotions. This representation ultimately intensifies our emotional awareness. It should be noted that here we have focused primarily on the insula for processing vicarious emotions, however there is ample evidence to suggests that some emotions are vicariously processed in different regions; for example, fear in the amygdala (Askew & Field, 2007; Olsson & Phelps, 2007; Phelps, 2006).

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The cognitive component of empathy relies heavily on attributing emotional states onto others and may partially call onto mechanisms underlying Theory of Mind (ToM; Decety, 2011). The dorsomedial prefrontal cortex (dmPFC) and temporoparietal junction (TPJ) are the two most common regions associated with theory of mind (Van Overwalle, 2009; Schurz et al. 2014). Considering the dorsal regions of the medial prefrontal cortex, there are a range of behaviours related to cognitive empathy that are recruited. A link to the dmPFC has been found for triadic relationships between two separate agents and a goal (Saxe, 2006), perspective taking (D'Argembeau et al., 2007) and direct and reflected self-knowledge (Ochsner et al., 2005). The TPJ on the other hand plays a role in several lower-level computational processes associated with a self-other differentiation and reorienting attention to salient stimuli, and as such plays a crucial role in higher-level cognitive process such as theory of mind and cognitive empathy (Decety & Lamm, 2007). There is also evidence to suggest that the TPJ can be broken into three separate sections, each interacting structurally and functionally with known areas of social cognition and attention (Mars et al., 2012).

However, neuroimaging and psychological research show that ToM and cognitive empathy are also distinct. Theory of mind involves taking on the perspective of another person and attributing to them particular cognitive states; while cognitive empathy is more involved in attributing emotional states (Reniers, 2011). That said, Perry and Shamay-Tsoory (2013) deconstruct cognitive empathy further by suggesting that it comprises higher order cognitive processes typically involved in ToM, including affective and cognitive mentalizing. The former surrounds beliefs about the emotional state of another, whilst the latter concerns beliefs about the beliefs of another person. Though both mentalizing processes are involved in cognitive empathy, Perry and Shamay-Tsoory (2013) suggest affective mentalizing may sustain a prioritised role in understanding and sharing the mental states of others. Völlm et al.

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(2006) investigated the overlap between neural correlates associated with cognitive empathy and theory of mind tasks using fMRI. The authors presented participants with static images that depicted a story but manipulated whether the story recruited theory of mind or cognitive empathy mechanisms. Both tasks involved the dmPFC and TPJ but the empathy condition also showed unique activation along the cingulate cortex.

Functional MRI evidence strongly suggests there are differences in the neural activity associated with the different sub-components of empathy. However, fMRI methods cannot identify whether these differences are subserved by individual changes in brain anatomy. To test whether volumetric differences in brain anatomy predict a functional difference in empathic expression presupposes a relationship between blood oxygen level dependence (BOLD) responses and anatomy. Indeed, there is evidence to suggest that this may be the case. For example, fMRI studies have shown greater BOLD activity in the hippocampus when completing tasks involving spatial navigation and the use of mental maps (e.g., Astur et al., 2005; Rosenbaum et al, 2004). Greater gray matter density in the hippocampus has also been found in London taxi drivers who frequently draw upon the hippocampus to navigate (Maguire et al. 2000). This suggests that functional activation, structural gray matter density, and behavior might be related.

Previous investigations looking at brain structure and its relationship with empathy have identified differences in several regions. Banissy and colleagues (2012) used VBM to infer a relationship between each of the sub-scales of the interpersonal reactivity index (IRI; Davis, 1980) and local gray matter density (local grey matter density here refers to the distribution of gray matter within each voxel to be compared across participants; Ashburner & Friston, 2000). They showed negative associations between gray matter density and the inferior frontal gyrus (IFG) and the empathic concern sub-scale, a sub-scale aimed at tapping into affective empathy. A second sub-scale tapping into affective empathy, the personal

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distress sub-scale, was positively associated with gray matter density in left insula. In addition, the anterior cingulate and dorsolateral prefrontal cortex were positively associated with scores on the cognitive empathy measure. In a different VBM investigation, Mutschler et al. (2013) similarly showed greater gray matter density in the left anterior insula to be associated with scores of affective empathy when using the Empathy Scale (E-Scale).

In a recent meta-analysis of 40 functional MRI studies, Fan et al. (2011) investigated the consistency of brain regions involved in affective and cognitive empathy, as well as the functional role they may play using a more comprehensive analysis. Multi-kernel density analysis (MKDA) was used to measure the peak coordinates in each statistical contrast map from each of the cognitive and affective empathy studies used in their meta-analysis. Fan et al. (2011) showed that the affective component of empathy was more associated with insula activity, whereas the cognitive component of empathy was more associated with the mid-cingulate cortex and adjacent dorsomedial prefrontal cortex (MCC/dmPFC). This highlights a consistent neural substrate for each component of empathy.

In light of this, we aimed to identify whether the different components of empathy are associated with gray matter differences. We aim to provide convergent evidence for the reliability and validity of previous VBM outcomes by conceptually replicating previous studies to show individual differences in empathic ability are subserved by differences in gray matter density when using alternate methodologies. Conceptual replication is an important tool in psychological sciences as it helps determine the true effect between particular constructs. There are two methods commonly used to measure differences in gray matter across participants. The first, cortical thickness, measures a one-dimension scalar of cortical thickness at each voxel (surface analysis), whilst the other, voxel-based morphometry (volumetric analysis), measures the amount of tissue within each voxel (Hutton, et al., 2009). In line with previous studies that associated individual differences in empathy with gray

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matter density (Banissy et al., 2012; Mutschler et al. 2013), and in order to replicate their findings, we also opted for the VBM method.

Considering our aims, peak MNI coordinates for affective (i.e., insula) and cognitive (i.e., MCC/dmPFC) empathy were used as regions of interest based on the findings from Fan et al. (2011). We also used scores on the questionnaire of cognitive and affective empathy (QCAE; Reniers et al., 2011) as regressors for the VBM analysis. The QCAE is well established in terms of concurrent, ecological and construct validity as well as being a highly reliable measure of affective and cognitive empathy. For example, scores on the QCAE are associated highly ($r = .62$, $p < .001$ for the affective components and $r = .76$, $p < .001$ for the cognitive components) with scores on the basic empathy scale (BES; Jolliffe & Farrington, 2006). Internal consistencies have been shown to be of a high standard with Cronbach's alpha values up to .85 (Reniers et al., 2011). We hypothesised, that if empathy is subserved by gray matter differences, participants with higher scores on affective empathy will have greater gray matter density in the insula while participants who score higher on cognitive empathy will have greater gray matter density in the MCC/dmPFC. To test this hypothesis, we used voxel based morphometry (VBM) to investigate local gray matter density associated with scores on the QCAE measure.

2 Method

2.1 Participants

One hundred and seventy-six participants (females = 88, $M_{age} = 22.07$, $SD_{age} = 4.82$ years) completed the QCAE and a structural MRI scan. Participants were undergraduate psychology students recruited for a range of social neuroscience projects. All participants had no history of neurological illness or injury and provided full written informed consent. The current study was approved by the local Ethics Committee from the University of Queensland.

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2.2 Questionnaire for cognitive and affective empathy

The Questionnaire for Cognitive and Affective Empathy (QCAE; Reniers et al., 2011) was used to assess participants' level of cognitive and affective empathy. Within this measure are five subcomponents that constitute the two overarching factors of cognitive empathy and affective empathy. The first affective subcomponent, *emotion contagion*, involves items surrounding the automaticity of mirroring others' emotional states while the second, *proximal responsivity*, measures the responsiveness of affective situations in close social context. Finally, *peripheral responsivity*, involves measuring the responsiveness to affective situations that occur in a more detached context.

In relation to the cognitive factor, the subcomponent *perspective taking* involves intuitively placing oneself in the shoes of others whereas the *online simulation* component is a more effortful process of attempting to understand the emotional state of others by imagining how they feel. Each item was measured on a four point Likert Scale with the options comprising *Strongly Agree, Slightly Agree, Slightly Disagree,* and *Strongly Disagree*. An example item used to assess cognitive empathy included, "*Before criticising somebody, I try to imagine how I would feel if I was in their place*" and for assessing affective empathy, an example item was "*I usually stay emotionally detached when watching a film*" (R).

Total scores were calculated for the affective component by aggregating the scores for each of the three subscales; Emotion contagion, proximal responsivity and peripheral responsivity. Total scores were similarly created for cognitive component by summating the scores on the online simulation and perspective taking subscales. Higher scores on each component of the QCAE are associated with greater cognitive and affective empathy.

2.3 Structural Scan Acquisition

All structural images were obtained with a 3T Siemens MRI scanner. Images provided were high-density T1 images (TR = 1900, TE = 2.32, FA = 9°, 192 cubic matrix,

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voxel size = 0.9 cubic mm, slice thickness = 0.9 mm) which were used in a voxel-based morphometry (VBM) analysis, comparing the gray matter density across participants.

2.4 Voxel-Based Morphometry

The VBM analysis conducted in the current study followed the procedures described in the VBM tutorial provided by Ashburner (2010). MATLAB (MathWorks, Natick, MA) was used in conjunction with statistical parametric mapping software (SPM8; Wellcome Department of Imaging Neuroscience, Institute of Neurology, London) to segment the images into gray matter, white matter and cerebral spinal fluid. To create a coregistered template from the gray matter images across participants, we used a diffeomorphic anatomical registration through exponentiated lie (DARTEL) algorithm (Ashburner, 2007). We used the DARTEL toolbox for the VBM analysis because it has recently been argued to be a more effective method for running morphometry analyses over standard and optimised VBM, as it creates an accurate segmentation of the different tissue classifications (Vovk et al., 2014). Absolute threshold masking was used at a threshold of 0.2 to help accommodate the proportional scaling corrections made; in addition to this we also used an explicit whole brain mask (O'Connor, 2010) to ensure clusters did not extend into the background and increase unwanted noise. Image modulation was conducted through the preserve amount function which creates flow fields that parameterize deformations automatically through the DARTEL algorithm. We then transformed this DARTEL template into MNI stereotactic space using non-linear spatial normalisation and then smoothed the images with a Gaussian Kernel (full-width at half-maximum, FWHM) of 10mm.

Once the data had been pre-processed we entered the pre-processed gray matter images into a regression model using SPM8 to measure correlations between cortical regions and scores on the cognitive and affective components of the QCAE. To regress any

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extraneous effects of age and gender we entered these variables as covariates of no interest into the regression model.

A regions of interest (ROI) approach was used based on coordinates provided by a recent meta-analysis (Fan et al., 2011; Table 1) which showed that the insula was most often associated with affective empathy (left insula; $x = -42$, $y = 18$, $z = 0$ and right insula; $x = 38$, $y = 24$, $z = -2$) and the MCC/dmPFC most often with cognitive empathy ($x = -2$, $y = 24$, $z = 38$). Specifically, we created a 10 mm sphere around these coordinates using the WFU Pickatlas (Maldjian, et al., 2003). Statistical significance was assessed using an FWE value of $p < .05$ corrected for the size of the ROIs. Outside these pre-defined regions, we used a FWE value of $p < .05$ corrected for the whole-brain volume.

3 Results

3.1 QCAE

Confirmatory factor analysis was used to assess the reliability and validity of the QCAE measure. Varimax rotations were used along with Kaiser Normalisation and eigenvalues above one were accepted. This analysis revealed two factors: cognitive empathy which contained two items: perspective taking and online simulation; and affective empathy which contained three items: emotion contagion, proximal responsivity and peripheral responsivity. Both factors contained high and clean factor loadings (Table 1). In total, the factor analysis accounted for 67.1% of the total variance.

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Table 1.

Factor loadings of the Questionnaire of Cognitive and Affective Empathy.

Item/Measure	Affective Empathy	Cognitive Empathy
AE Emotion Contagion	**.887**	-.191
AE Proximal Responsivity	**.705**	.523
AE Peripheral Responsivity	**.525**	.435
CE Perspective Taking	.016	**.843**
CE Online Simulation	.104	**.759**

3.2 Voxel-based morphometry analysis

Higher scores on the affective empathy scale were associated with significantly larger gray matter density in left (*r* = .27; -42, 11, 6; Z=3.12; extent = 609; *p* corrected = .035) and right (*r* = .23; 39, 24, 7; Z = 3.24; extent = 163; *p* corrected = .021) insula (Figure 1). Additionally, higher scores on the cognitive scale were associated with significantly larger gray matter density in the MCC/dmPFC (*r* = .16; -12, 24, 37; Z = 2.99; extent = 609; *p* corrected = .043; Figure 2). Whole brain analyses with the affective and cognitive scores yielded no additional significant regions.

Insert Figure 1 Here

Insert Figure 2 Here

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4 Discussion

Our findings show that individual differences in cognitive and affective empathy scores are associated with differences in MCC/dmPFC and insula gray matter, respectively. The insula has been implicated as an emotion processing hub involved in simulating the affective components of the emotions we observe in others (Carr et al., 2003; Danzinger et al., 2009; Singer et al., 2004). Menon and Uddin (2010) suggests that emotional awareness occurs because the insula creates a representation of positive and negative emotions by integrating salient environmental stimulation with autonomic and visceral bodily sensations. This is further supported by Wiech et al., (2010) who suggests that the role of the anterior insula in the saliency network is to process the importance of an impending stimulation and integrate this into a decision-making model.

Previously we highlighted that affective empathy can be differentiated from empathic concern. However, previous evidence has suggested that increased activation in the Anterior Insula and adjacent Inferior Frontal Gyrus (AI/IFG) is associated with greater empathic concern when measured by the Interpersonal Reactivity Index (IRI; Singer et al., 2004; Sessa et al., 2013) and empathy quotient (EQ; Chakrabarti et al., 2006). Further, evidence also shows that lesions to this area are associated with lower scores on the empathic concern measure (Shamay-Tsoory et al., 2004; 2009). Together with the findings from the current investigation, which showed affective empathy to be associated with the anterior insula, it can be suggested that empathic concern and affective empathy are subserved by similar regions which feasibly suggests that empathic concern and affective empathy may be related.

Functional MRI has been used to elucidate the mechanistic role of the insula in affective empathy, however to establish whether any brain region is necessary for behaviour we need to determine whether a reduction in this behaviour occurs subsequent a lesion. For example, Gu and colleagues (2012) showed that participants with an anterior insula lesion

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perceived painful stimulation to others slower than when perceiving people not experiencing pain which is antithetic with theoretical underpinnings suggesting pain stimuli are processed faster. Further, Shamay-Tsoory et al. (2009) showed that lesions in the medial prefrontal cortex extending into the cingulate cortex had more problems with cognitive empathy, while patients with damage to the inferior frontal gyrus and adjacent insula had more problems with affective empathy.

Voxel based morphometry studies can also show how brain structure relates to empathy. The current investigation is in line with a VBM study by Banissy et al. (2012) who also illustrated that higher scores on the affective empathy subscales (for example the personal distress subscale) of the IRI were associated with greater gray matter density in the insula. In further collaboration, the current study is in line with research by Mutschler et al. (2013) who conducted a similar study with the empathy scale and found a similar positive association between affective empathy and the insula. Parkinson and Wheatley (2014), using diffusion tensor imaging, also showed that fractional anisotropy measures in communicative white matter tracts are also related with individual differences in empathy scores.

We have shown consistent findings with previous work using empathy measures and voxel-based morphometry. The current study, however, used a novel measure to elucidate the generalizability and reliability of previous work. Recently, structural brain-behaviour studies have come under scrutiny with regards to non-replicability; as such we used the QCAE as regressors in the VBM analysis in attempt to conceptually replicate previous work. Conceptual replication, in this circumstance, is critical as it aids in identifying whether structural differences in anatomy truly underlie differences in the subcomponents of empathy. This was also exacerbated by the large sample size we recruited which further helped to ensure that we are ruled out spurious sample errors. Boekel et al. (2015) have illustrated the difficulty with replicating structural brain-behaviour studies; however, here we have been

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able to conceptually replicate previous work by maintaining similar VBM methods but changing the regressing measure.

To conclude, we have shown that volumetric differences in brain structure subserve differential expressions of empathy, involving affective and cognitive empathic components. Here we highlight consistencies between functional MRI investigations, as well as lesion based studies surrounding empathy areas, and link this with volumetric differences which underlie these processes. Taken together, the evidence provided here in the structural analysis of a large non-clinical sample further confirms that empathy is a multi-dimensional construct which elicits differential expressions of affective and cognitive abilities.

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Figure 1. The left and right insula clusters found to have greater gray matter density associated with the affective component of the QCAE (A). Significant positive relationship between scores on the affective component of empathy and gray matter density scores for the peak voxel from the left (LI) and right (RI) insula clusters (B).

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Figure 2. The MCC/dmPFC cluster found to have greater gray matter density associated with the cognitive component of the QCAE (A). Significant positive relationship between scores on the cognitive empathy component and gray matter density scores for the peak voxel of the MCC/dmPFC cluster (B).

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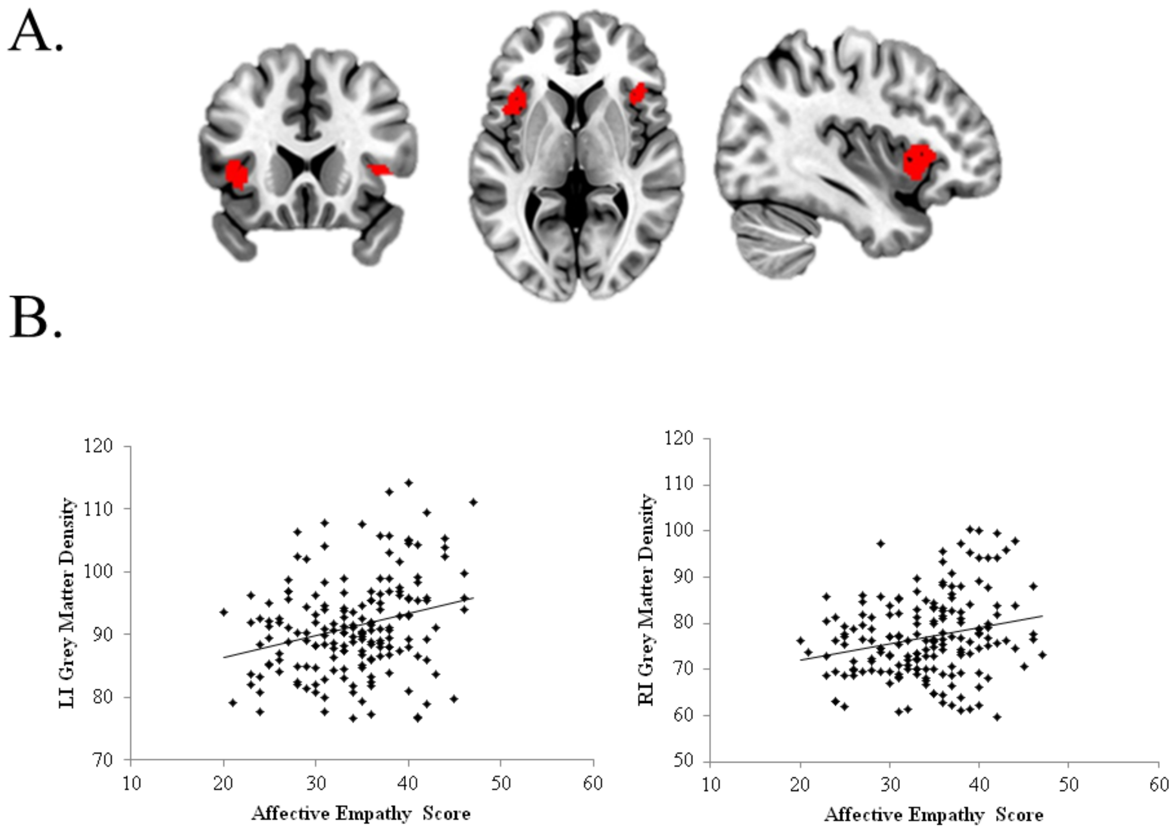

Figure 1

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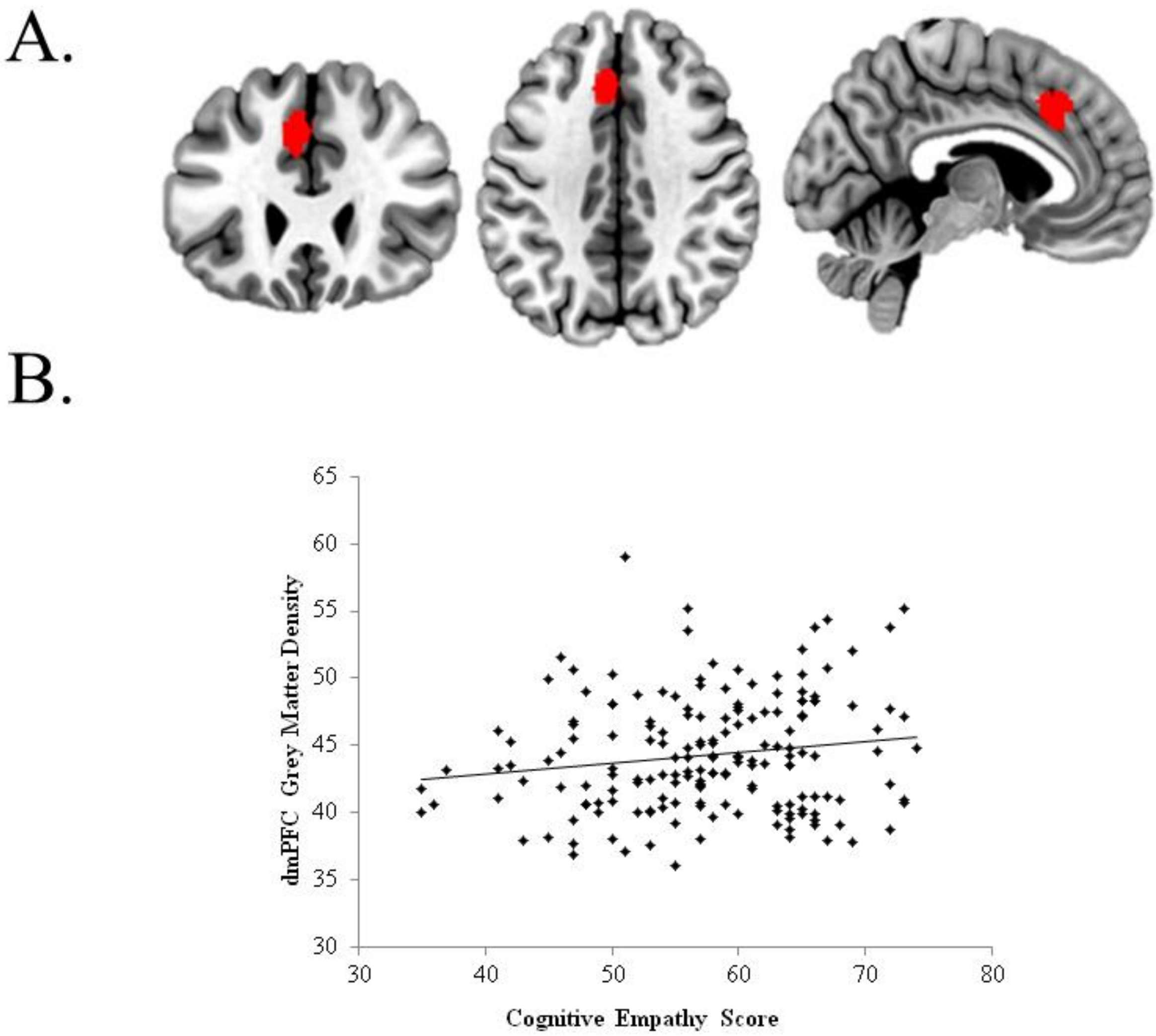

Figure 2

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Highlights:

- Voxel-based morphometry was performed with empathy scores of 176 participants
- Greater gray matter density in insula was associated with affective empathy scores
- Greater gray matter density in dmPFC was associated with cognitive empathy scores
- Empathy is a multi-component construct
- Individual differences in empathy are subserved by anatomical differences

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