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Ana Manuel Macedo Veiga Gomes

Insular Cortex Structural Variability and Individual Differences in Empathic Traits

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Insular Cortex Structural Variability and Individual Differences in Empathic Traits

Dissertação de Mestrado
Mestrado Integrado em Psicologia

Trabalho efectuado sob a orientação da
Professora Doutora Ana Seara Cardoso

e coorientação da
Professora Doutora Adriana Sampaio

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Mestrado Integrado em Psicologia da Universidade do Minho

Insular cortex structural variability and individual differences in empathic traits

Ana Manuel de Macedo Veiga Gomes

Orientador: Professora Doutora Ana Seara Cardoso

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Abstract

This study aims to investigate associations between individual differences in empathy and structural variations in the insular cortex, particularly in the anterior insula (AI). A normative sample of 31 male subjects was selected from the community, ranging from the ages of 20 to 40 years old. Individual differences on empathy were assessed through the *Questionnaire of Cognitive and affective Empathy* (QCAE). Measures of grey matter volume, area, cortical thickness and white matter volume were extracted from T1-Wheighted structural MRI scans with FreeSurfer, and analysed in *Statistical Package for the Social Sciences* (SPSS). Hierarchical Regression analyses showed that variance in anterior insula grey matter area and insula white matter volume is positively significantly associated with individual differences in empathy.

Keywords: empathy, MRI, insular cortex, brain structural variability.

Mestrado Integrado em Psicologia da Universidade do Minho

Insular cortex structural variability and individual differences in empathic traits

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Resumo

Este estudo pretende investigar associações entre diferenças individuais ao nível da empatia e variações na estrutura da insula, particularmente ao nível da insula anterior (AI). Uma amostra normativa de 31 sujeitos do sexo masculino foi selecionada da comunidade, com idades compreendidas entre os 20 e 40 anos. Diferenças individuais ao nível da empatia foram medidas através do *Questionnaire of Cognitive and affective Empathy* (QCAE). Medidas de relativas ao volume, área e espessura cortical da substância cinzenta e medidas do volume da substância branca foram extraídas de *scans* de MRI estruturais, *T1-Wheithed*, com o programa FreeSurfer e analisadas no *Statistical Package for the Social Sciences* (SPSS). Análises de regressão Hierárquica revelaram variações significativas na área da substância cinzenta da insula anterior e volume da substância branca da insula, positivamente, associadas com diferenças individuais na empatia.

Palavras-chave: empatia, MRI, córtex insular, variabilidade estrutural do cérebro.

1. Introduction

1.1. Empathy

The understanding of empathy mechanisms in the brain has great significance for clinical and public health domains. Deficits in empathy are associated with numerous clinical conditions, such as, frontotemporal lobar degeneration, autistic spectrum disorders, - squizophrenia disorder, borderline personality disorder, psychopathy and antisocial personality disorders and conduct disorders (Decety, 2011; Decety & Meyer, 2008; Decety & Moriguchi, 2007; Mutschler, Reinbold, Wankerl, Seifritz, & Ball, 2013; Rankin et al., 2006; Reniers, Corcoran, Drake, Shryane, & Vollm, 2011; Shamay-Tsoory, Aharon-Peretz, & Perry, 2009). As such, empathy has been a phenomenon vastly studied for many years now (Eres, Decety, Louis, & Molenberghs, 2015).

Empathy can be described as the ability to experience and thus understand the emotional states of others (Eres et al., 2015; Gallese, 2003; de Waall, 2008; Singer & Lamm, 2009). It is a process that provides emotional understanding (Shamay-Tsoory et al., 2009) and enables us to show care and concern as a response to manifestations of distress (Decety, 2011), thus playing a crucial role in healthy social functioning (Decety & Meyer, 2008; de Waall, 2008; Eres et al., 2015; Fan, Duncan, Greck, & Northoff, 2011; Fan & Han, 2008; Jackson, Brunet, Meltzoff, & Decety, 2005; Jackson, Meltzoff., & Decety, 2006; Mutschler et al., 2013; Seara-Cardoso, Sebastian, Viding, & Roiser, 2016; Shamay-Tsoory et al., 2009).

Empathy implies the sharing of others' emotional experiences and understanding of others' emotions while keeping perspective of ones' self-emotional state. The empathic processing entails perspective-taking skills and facilitates emotional awareness and identification with another's emotional state (affective sharing) (Decety, 2011; Eres et al., 2015; Singer & Lamm, 2009).

Although the precise definition of empathy is still a matter of debate amongst researchers (Batson, 2008), most seem to agree on the division of empathic processes into two distinct dimensions: (1) Cognitive empathy, characterized as the ability to understand others' emotional states and associated with advanced perspective taking processes; and (2) Affective empathy, characterized by the vicarious sharing of others' emotions and associated with emotional contagion processes (Decety, 2011; Eres et al., 2015; Reniers et al., 2011; Shamay-Tsoory et al., 2009).

Cognitive empathy is frequently allied to *Theory of the Mind* (ToM) process, but these are two distinctive concepts. ToM is characterized as an attributional process of another's mental state (ranging from the attribution of desires, intentions and beliefs). Because the failure to succeed in these attributions is often linked to poor perspective-taking (i.e. the ability to differentiate ones' perspective from another's), which is also important for empathy, it is likely that the skills required for ToM overlap with the ones required for cognitive empathy as both designate attributional processes. However, cognitive empathy consists only on the attribution of emotions and not general cognitions, partaking in affective and cognitive mentalising functions (Eres et al., 2015; Reniers et al., 2011).

In affective empathy, emotional contagion enables us to share and understand emotions through the synchronization with others' emotional state (Gallese, 2003; Singer & Lamm, 2009). Evidence indicates that the perception of others' emotions triggers mechanisms related to the generation of emotions in oneself (Decety & Moriguchi, 2007; Decety, 2011; Fan & Han, 2008; Jackson et al., 2006; Sassi & Soares, 2001).

Both cognitive and affective empathy require functions related to self-awareness (recognition of oneself as an individual separate from the environment and other individuals) and a sense of agency (recognition of oneself as the agent of a specific behavior). Self-awareness and sense of agency enables the differentiation between self and others' feelings and affective representations, promoting selflessness concern rather than selfish avoidance regarding others, which in turn allows for healthy social functioning (Lamm & Decety, 2006).

1.2. Empathy-related Brain Regions

The understanding of the neural bases involved in empathy is of significant relevance since it will allow for the identification of structural brain correlates and its association with either cognitive or affective empathy (Shamay-Tsoory, 2011). Numerous investigations have been developed trying to associate different brain regions with components of empathy (Eres et al., 2015). A wide network of regions has been associated with empathic function, for example, the cingulate cortex, insular cortex, amygdala, cerebellum, brainstem, thalamus, ventral striatum, bilateral precuneus, temporal-parietal junction (TPJ), occipital frontal cortex (OFC), dorsolateral and ventromedial prefrontal cortex (dlPFC/vmPFC), frontal gyrus, parahippocampal gyrus, bilateral parietal cortex, and medial and lateral premotor areas (Banissy, Kanai, Walsh, & Rees, 2012; Carr, Lacoboni, Dubeau, Mazzlotta, & Lenzi, 2003; Chakrabarti, Bullmore, & Baron-Cohen, 2007; Dazinger, Faillenot, & Peyron, 2008; Decety, 2011; Fan et al., 2011; Fan & Han, 2008; Gu et al., 2012; Jackson, Brunet, Meltzoff, & Decety, 2006; Jackson et al., 2005; Lamm, Batson, & Decety, 2007; Lamm, Decety, & Singer, 2011; Marsh et al., 2013; Mercadillo, Díaz, Pasaye & Barrios, 2011; Moll et al., 2005;

Mutschler et al., 2013; Seara-Cardoso et al., 2016; Singer, Seymour, O'Doherty, Kaube, Dolan & Frith, 2004; Wiech et al., 2010).

Most studies, though, have consistently referred the involvement of the insula cortex in empathy processes (Banissy et al., 2012; Carr et al., 2003; Chakrabarti et al., 2007; Dazinger et al., 2008; Eres et al., 2015; Fan et al., 2011; Gu et al., 2012; Jackson, et al., 2006; Jackson et al., 2005; Lamm et al., 2007; Lamm et al., 2011; Mutschler et al., 2013; Seara-Cardoso et al., 2016; Singer et al., 2011; Wiech et al., 2010). In fact, two recent meta-analyses (Fay, Dunca, de Greck, & Northoff, 2011; Lamm & Decety, 2011) indicate the anterior insula, in particular the left anterior insula, as the region most consistently activated during empathic processing.

The anterior insular cortex (AIC) has been noted to be the only region of the brain with consistent associations with all emotional, attentional, cognitive, intentional, perception, sensation awareness and motor perception, empathy-related tasks leading to the formulation of a domain general region for empathy in the AIC (Mutschler et al., 2013).

Overall, the Insular Cortex is thought to be implicated in both affective and cognitive processes, from the recognition of stimuli within the body (interoceptive awareness), to the formulation of emotional responses and empathic responses (Menon & Uddin, 2010). The insula is sensitive to salient events and directs stimuli for additional processing and is responsible for initiating control signals that will aide to guide human behaviour alongside with the cingulate cortex (Menon & Uddin, 2010). The interactions between the posterior and anterior regions of the insula allows for modulation of autonomic reactivity to salient stimuli (Menon & Uddin, 2010).

1.3. Individual Differences in Empathy

The ability to empathize with others shows individual variance (Mutschler et al., 2013) and reveals a tendency to stabilize over time, once adulthood is reached (Eisenberg, Cumberland, Guthrie, Murphy, & Shepard, 2005; Mutschler et al., 2013). Contributing for individual differences in empathy factors, such as, the background affective state of the individuals, the affective disposition towards or relationship/attachment with others, the past experiences with similar events, the contextual appraisal and the ability to cope with distress should be taken into account given their impact on the experience of the phenomena whether on a perception level, recognition or expression of emotions (Lamm & Decety, 2006; Singer & Lamm, 2009). For example in a study by Gleichgerrcht and Decety (2013) with both male and female certified practicing physicians, revealed that burnout and distress, known as negative aspects of empathy relating to compassion fatigue, can undermine empathy in caregiving settings. Results have shown an association between alexithymia (i.e. difficulty in verbalizing emotions and describing feelings as well as corporal sensations) and compassion fatigue (Gleichgerrcht & Decety, 2013).

Individual differences in empathy can also vary according to different neural substrates, an example of this can be found in a study led by Seara-Cardoso et al. (2016), who showed that individuals with elevated psychopathic traits (i.e. lack of empathy), whose results indicated less activation in anterior insula and amygdala (Seara-Cardoso et al., 2016). Additionally, structural MRI studies have been showing a consistent association between anterior insula structural variations and empathy (Banissy et al., 2012; Eres et al., 2015; Mutschler et al., 2013).

A structural MRI study (sMRI) by Muschler et al (2013), on healthy adult woman (N=101), showed correlates between gray matter (GM) density, in the AI, and individual empathy scores. Empathy results were assessed with the E-Scale (Leibetseder et al, 2001) and structural analyses consisted on the Voxel-Based Morphometry (VBM) analyses method (Mutschler et al., 2013).

A more recent VBM study performed with a healthy adult male sample (N=176), showed that greater GM density in the bilateral insular cortex was associated to affective empathy while greater GM density in the midcingulate cortex and dorsal-medial prefrontal cortex was associated to cognitive empathy. Empathy results were measured with the Questionnaire of Cognitive and Affective Empathy (Eres et al., 2015). These studies hold evidence to support the relation between volume variance in the insula and individual variance in empathy.

Taking into account these studies showing structural and functional brain variances associated with empathy measures, it is the aim of the present study to investigate AI morphometric variance and empathy measures, using an automated segmentation method that allows the morphometric measurement of GM and white matter (WM) volumes' area and GM thickness and test how they associate with individual differences in empathy on a healthy male adult population. This study also aims to test whether insula structural variances are limited to gray matter (GM) changes or do they manifest in white matter (WM) as well. In order to assess volumetric measurements, the FreeSurfer (FS), an automated MRI structural analysis program, provides a much better matching of cortical regions than volumetric techniques while allowing access to data for both the surface area and cortical thickness, separately (http://surfer.nmr.mgh.harvard.edu/, Center for Biomedical Imaging, Charlestown, MA).

Of note, volumetric measures, regarded as one of the first and most known brain structure measurements, have been found to be susceptible to effects of interindividual variability (Mills & Tamnes, 2014).

2. Materials and Methods

2.1. Participants

Data from 32 male subjects, previously collected for a comprehensive research project conducted at University College London were analysed. One participant was excluded from the analyses due to excessive motion inside the scanner, leaving 31 participants in the analyses study (mean age = 26.9; range = 20-40). The mean estimated Intelligence Quotient (IQ) was of 110 (range = 85-125), assessed by the Matrix Reasoning subscale of the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999). Recruitment took place in the community and only right-handed males were included in the selection. This study was approved by UCL Division of Psychology and Language Sciences Ethics Committee. All participants provided written informed consent. Participants received a modest compensation for their involvement.

2.2. Materials

Questionnaire of Cognitive and Affective Empathy (QCAE; Reniers et al., 2011):

As described in the literature above the main components of empathy differentiate into two classifiable domains: Cognitive and Affective Empathy. The *Questionnaire of Cognitive and Affective Empathy* (QCAE) provides a more accurate measure of the intended phenomena than previous attempts of developed self-report tests, indicating correlations of $r = .62$, $p < .001$ associated to cognitive empathy, and $r = .76$, $p < .001$ associated to affective empathy (Reniers et al., 2011).

Variables related to cognitive empathy consist of *Perspective Taking* and *Online Simulatio*n. Variables related to affective empathy consist of *Emotion Contagion*; *Proximal Responsivity*; and *Peripheral Responsivity* (Reniers et al., 2011).

2.3. Procedure

The FreeSurfer program was used to run analysis on the brain scans and obtain structural data on the total volume, surface area and thickness of the AI, as well as provide for white matter data on the overall insular cortex.The structural data was exported into excel to proceed to a series of hierarchical regression analysis with empathy results from the QCAE using the *Statistical Package for the Social Sciences, version 23* (SPSS-23), as further explained.

2.4. MRI Acquisition

MRIs were acquired using a Siemens Avanto 1.5 T MRI scanner at the Birkbeck-UCL Centre for Neuroimaging with a 32-channel headcoil. A high-resolution, 5.5 min 3D T1-weighted structural scan was acquired using a magnetization prepared rapid gradient echo (MPRAGE) sequence. Imaging parameters were: 176 slices; slice thickness = 1 mm; gap between slices = 0.5 mm; TR = 2730 ms; TE = 3.57 ms; field of view = 256 mm x 256mm^2; matrix size = 256 × 256; voxel size = 1 × 1 × 1 mm resolution).

2.5. MRI Processing

Analyses were completed using the standard FreeSurfer (5.1) processing stream (http://surfer.nmr.mgh. harvard.edu/), following the associated workflow procedures.

Data on volume, area, thickness and WM was obtained from high-resolution T1 MPRAGE volumes in DICOM format and then imported into the FreeSurfer image analysis environment. Semi-automated methods employing the default surface-based and volume-based pipelines were used, including registration with the Talairach and Aparc Destrieux atlas, intensity normalization, skull stripping, pial and white matter boundary determination (Churchwell & Yurgelun-Todd, 2013). To Label each voxel in a MRI volume it was required an automated registration procedure based on probabilities estimated from a manually labelled training set (Churchwell & Yurgelun-Todd, 2013).

Standard predefined region of interest (ROI) maps were used in the statistical analysis for the left and right insular cortex. The human insula most commonly appears as a trapezoidal shaped brain structure, composed by 3 short gyri (anterior) and 2 long gyri (posterior) (Chiarello, Vazquez, Felton, & Leonard, 2013). The FreeSurfer Program Label Map for the Insula delimits the region by its circular sulcus, consisting of the ***superior*** [S_circular_insula_sup, 49], ***anterior*** [S_circular_insula_ant, 47], and ***inferior*** [S_circular_insula_inf, 48] sulcus. The ***central sulcus of the insula*** runs antero-inferiorly from the superior circular insula sulcus and separates the anterior insula from its posterior part. The FreeSurfer Label for the anterior insula translates to the ***short insular gyri*** [G_insular_short, 18], while the posterior insula Label translates to the ***long insular gyrus***. Due to their small size, the central sulcus of the insula and the long insular gyri are presented grouped in the FreeSurfer under the same label [G_Ins_lg_and_S_cent_ins, 17] (Destrieux, Fischl, Dale, & Halgren, 2010).

2.6. Data Analysis

A first set of hierarchical regressions aimed to find associations between structural measurements and QCAE Total results, while a secondary set of hierarchical analysis were performed differentiating between affective and cognitive empathy. All assumptions were met for the hierarchical analysis, preventing error Type I and II and under-estimation of significance or effect size.

Additionally, structural MRI studies have found volumetric measures to vary according to age and Total Intracranial Volume (TIV). Volume measurements have been found to decrease with age and increase with TIV. The cortical thickness, similarly to volumes, was found to decrease with age, but no significant associations were found between thickness measures and TIV. White Matter (WM) volumes have been found to vary according to age and TIV, though there's some controversy as to decrease/increase patterns. Regarding surface area measurements, studies have found a negative correlation with age and a positive correlation with TIV (Barnes et al., 2010). Knowing this, the hierarchical regressions were controlled for age and TIV (except while correlating thickness measurements, where TIV was excluded from analysis).

3. Results

3.1. Correlation between GM AI and WM insula structural measurements and QCAE Total results, controlling for age and TIV

Hierarchical regressions were conducted in order to test the hypothesis whether right and left AI structural measurements and WM insula volume varied according to levels of empathy and how age and TIV could be impacting structural variance. AI structural measurements and WM insula were used as independent variables; age was inserted in Step1, then TIV (except in the analysis involving thickness measures), followed by the empathy results from the QCAE Total. Results (see table 1) showed that, after controlling for age and TIV, total scores on the QCAE presented a positive significant correlation with left anterior insula area ($t = 2.331$, $p = .027$), with an R^2 *change* of 9,8% (F *change* = 5.432).

Table 1

Coefficients for The Correlation Between Anterior Insula Area and Total Scores of QCEA, Controlling for Age and TIV

Anterior Insula Area							
	Left Anterior Insula				Right Anterior Insula		
Model	Beta	t	p	Model	Beta	T	p
1 (Constant)		11,179	,000	1 (Constant)		12,852	,000
Age	-,315	-1,784	,085	Age	-,492	-3,041	,005
2 (Constant)		1,065	,296	2 (Constant)		2,254	,032
Age	-,201	-1,361	,184	Age	-,407	-2,763	,010
TIV	,572	3,870	,001	TIV	,426	2,890	,007
3 (Constant)		-,109	,914	3 (Constant)		1,633	,114
Age	-,205	-1,493	,147	Age	-,408	-2,745	,011
TIV	,561	4,081	,000	TIV	,422	2,836	,009
QCAE Total	,314	2,331	,027*	QCAE Total	,100	,683	,501

Note. TIV = Total Intracranial Volume; QCAE Total = Total scores for the Questionnaire of Cognitive and Affective Empathy.
*p < .05. **p < .01.

Of note, total scores of the QCAE presented a positive, albeit at-trend, associations (table 2) with total volume in the same region (t = 1.853, p = .075), with an R^2 *change* of 5.4% (F *change* = 3.433).

Table 2

Coefficients for The Correlation Between Anterior Insula Volume and Total Scores of QCEA, Controlling for Age and TIV

Anterior Insula Volume							
	Left Anterior Insula				Right Anterior Insula		
Model	Beta	t	p	Model	Beta	t	p
1 (Constant)		11,960	,000	1 (Constant)		14,070	,000
Age	-,410	-2,418	,022	Age	-,575	-3,787	,001
2 (Constant)		1,071	,293	2 (Constant)		2,634	,014
Age	-,289	-2,169	,039	Age	-,492	-3,607	,001
TIV	,608	4,567	,000	TIV	,419	3,071	,005
3 (Constant)		,094	,926	3 (Constant)		2,311	,029
Age	-,292	-2,284	,030	Age	-,492	-3,541	,001
TIV	,600	4,694	,000	TIV	,419	3,017	,006
QCAE Total	,232	1,853	,075	QCAE Total	-,011	-,081	,936

Note. TIV = Total Intracranial Volume; QCAE Total = Total scores for the Questionnaire of Cognitive and Affective Empathy.
*p < .05. **p < .01.

It was also found (table 3) positive associations between the QCAE total scores and bilateral WM insula (left insula t = 3.360, p = .002, R^2 *change* = 18%, F *change* = 11,290; and right insula t = 2.313, p = .029, R^2 *change* = 14%, F *change* = 5,351).

Table 3

Coefficients for The Correlation Between White Matter Insula and Total Scores of QCEA, Controlling for Age and TIV

White Matter Insula							
	Left Insula				Right Insula		
Model	Beta	t	p	Model	Beta	T	p
1 (Constant)		12,787	,000	1 (Constant)		13,625	,000
Age	-,104	-,562	,579	Age	,035	,191	,850
2 (Constant)		1,629	,114	2 (Constant)		2,854	,008
Age	,020	,132	,896	Age	,117	,666	,511
TIV	,623	4,120	,000	TIV	,413	2,343	,026
3 (Constant)		,065	,948	3 (Constant)		1,587	,124
Age	,015	,114	,910	Age	,113	,688	,497
TIV	,608	4,697	,000	TIV	,400	2,436	,022
QCAE Total	,426	3,360	,002**	QCAE Total	,372	2,313	,029*

Note. TIV = Total Intracranial Volume; QCAE Total = Total scores for the Questionnaire of Cognitive and Affective Empathy.
*p < .05. **p < .01.

Of the controlled variables, only TIV revealed a significant effect on left anterior insula area (R^2 *change* = 31%), and bilateral WM insula (R^2 *change* = 37% for left WM insula and R^2 *change* = 16% for the right WM insula). No associations were found (table 4) between overall empathy results from the QCAE and AI cortical thickness measures (for the left AI t = .310, p = .159, R^2 *change* = .03%, F *change* = .096; and for the right AI t = -.843, p = .407, R^2 *change* = .02%, F *change* = .710).

Table 4

Coefficients for The Correlation Between Anterior Insula Thickness and Total Scores of QCEA, Controlling for Age

Anterior Insula Thickness							
	Left Anterior Insula				Right Anterior Insula		
Model	Beta	t	P	Model	Beta	t	p
1 (Constant)		21,119	,000	1 (Constant)		16,827	,000
Age	-,163	-,891	,380	Age	-,099	-,537	,595
2 (Constant)		10,398	,000	2 (Constant)		9,313	,000
Age	-,164	-,878	,387	Age	-,098	-,530	,600
QCAE Total	,058	,310	,759	QCAE Total	-,157	-,843	,407

Note. QCAE Total = Total scores for the Questionnaire of Cognitive and Affective Empathy.
*p < .05. **p < .01.

3.2. Correlation between GM AI and WM insula structural measurements and QCAE results for cognitive and affective empathy (CE/AE), controlling for age and TIV

A secondary analysis of hierarchical regressions was performed for left and right AI structural measurements and WM insula volume in order to determine whether these presented different associations with affective or cognitive dimensions of empathy. AI structural measurements and WM insula were entered as independent variables; age was selected for Step1 correlation, followed by TIV (except for those analysis involving cortical thickness measurements) and lastly the affective and cognitive empathy results from the QCAE (QCAE AE/CE) correlated separately. Results (table 5 and table 6) showed positive, albeit at-trend, associations between the left anterior insula area and both cognitive (t = 2.004, p = .055, R^2 *change* = 7.6%, F *change* = 4.017) and affective (t = 1.876, p = .071, R^2 *change* = 6.8%, F *change* = 3.521) empathy.

Table 5

Coefficients for The Correlation Between Anterior Insula Area and QCAE Scores for Cognitive Empathy (CE), Controlling for Age and TIV

Anterior Insula Area							
	Left Anterior Insula				Right Anterior Insula		
Model	Beta	t	p	Model	Beta	T	p
1 (Constant)		11,179	,000	1 (Constant)		12,852	,000
Age	-,315	-1,784	,085	Age	-,492	-3,041	,005
2 (Constant)		1,065	,296	2 (Constant)		2,254	,032
Age	-,201	-1,361	,184	Age	-,407	-2,763	,010
TIV	,572	3,870	,001	TIV	,426	2,890	,007
3 (Constant)		-,040	,969	3 (Constant)		1,592	,123
Age	-,236	-1,666	,107	Age	-,419	-2,797	,009
TIV	,580	4,129	,000	TIV	,429	2,879	,008
QCAE CE	,278	2,004	,055	QCAE CE	,098	,668	,510

Note. TIV = Total Intracranial Volume; QCAE CE = scores for the Questionnaire of Cognitive Empathy.
*p < .05. **p < .01.

Table 6

Coefficients for The Correlation Between Anterior Insula Area and QCAE Scores for Affective Empathy (AE), Controlling for Age and TIV

Anterior Insula Area							
	Left Anterior Insula				Right Anterior Insula		
Model	Beta	t	p	Model	Beta	T	p
1 (Constant)		11,179	,000	1 (Constant)		12,852	,000
Age	-,315	-1,784	,085	Age	-,492	-3,041	,005
2 (Constant)		1,065	,296	2 (Constant)		2,254	,032
Age	-,201	-1,361	,184	Age	-,407	-2,763	,010
TIV	,572	3,870	,001	TIV	,426	2,890	,007
3 (Constant)		-,410	,685	3 (Constant)		1,921	,065
Age	-,177	-1,246	,223	Age	-,400	-2,670	,013
TIV	,550	3,873	,001	TIV	,420	2,800	,009
QCAE AE	,263	1,876	,071	QCAE CE	,074	,504	,619

Note. TIV = Total Intracranial Volume; QCAE AE = scores for the Questionnaire of Affective Empathy.
*p < .05. **p < .01.

Of note, as can be seen in table 7, measures of GM volume in the left AI were positively associated, albeit marginally, with QCAE CE scores (left AI t = 1.783, p = .086 R^2 *change* = 5%, F *change* = 3.179), but no associations were found (table 8) with QCAE AE scores (left AI t = 1.356, p = .186, R^2 *change* = 3%, F *change* = 1.840; right AI t = .146, p = .885, R^2 *change* = 0%, F *change* = .021).

Table 7

Coefficients for The Correlation Between Anterior Insula Volume and QCAE Scores for Cognitive Empathy (CE), Controlling for Age and TIV

Anterior Insula Volume							
	Left Anterior Insula				Right Anterior Insula		
Model	Beta	t	p	Model	Beta	T	p
1 (Constant)		11,960	,000	1 (Constant)		14,070	,000
Age	-,410	-2,418	,022	Age	-,575	-3,787	,001
2 (Constant)		1,071	,293	2 (Constant)		2,634	,014
Age	-,289	-2,169	,039	Age	-,492	-3,607	,001
TIV	,608	4,567	,000	TIV	,419	3,071	,005
3 (Constant)		,064	,949	3 (Constant)		2,396	,024
Age	-,317	-2,453	,021	Age	-,487	-3,484	,002
TIV	,615	4,791	,000	TIV	,418	3,011	,006
QCAE CE	,226	1,783	,086	QCAE CE	-,043	-,310	,759

Note. TIV = Total Intracranial Volume; QCAE CE = scores for the Questionnaire of Cognitive Empathy.
*p < .05. **p < .01.

Table 8

Coefficients for The Correlation Between Anterior Insula Volume and QCAE Scores for Affective Empathy (AE), Controlling for Age and TIV

Anterior Insula Volume							
	Left Anterior Insula				Right Anterior Insula		
Model	Beta	t	p	Model	Beta	T	p
1 (Constant)		11,960	,000	1 (Constant)		14,070	,000
Age	-,410	-2,418	,022	Age	-,575	-3,787	,001
2 (Constant)		1,071	,293	2 (Constant)		2,634	,014
Age	-,289	-2,169	,039	Age	-,492	-3,607	,001
TIV	,608	4,567	,000	TIV	,419	3,071	,005
3 (Constant)		,563	,578	3 (Constant)		2,385	,024
Age	-,273	-2,071	,048	Age	-,490	-3,516	,002
TIV	,594	4,509	,000	TIV	,417	2,995	,006
QCAE AE	,176	1,356	,186	QCAE CE	,020	,146	,885

Note. TIV = Total Intracranial Volume; QCAE AE = scores for the Questionnaire of Affective Empathy.
*p < .05. **p < .01.

It was also found (table 9) a significant correlation between scores from the QCAE CE with both left and right WM insula (left insula t = 2.494, p = .019, R^2 *change* = 12%, F *change* = 6.221; right insula t = 2.316, p = .028, R^2 *change* = 14%, F *change* = 5.365). Only TIV showed a significant effect on the model, with an R^2 *change* of 37% for the left WM insula and 16% for the right.

Table 9

Coefficients for The Correlation Between White Matter Insula and QCAE Scores for Cognitive Empathy (CE), Controlling for Age and TIV

	White Matter Insula						
	Left Insula				Right Insula		
Model	Beta	t	p	Model	Beta	T	p
1 (Constant)		12,787	,000	1 (Constant)		13,625	,000
Age	-104	-,562	,579	Age	,035	,191	,850
2 (Constant)		1,629	,114	2 (Constant)		2,854	,008
Age	,020	,132	,896	Age	,117	,666	,511
TIV	,623	4,120	,000	TIV	,413	2,343	,026
3 (Constant)		,279	,782	3 (Constant)		1,487	,149
Age	-,023	-,161	,873	Age	,071	,429	,672
TIV	,633	4,557	,000	TIV	,424	2,584	,015
QCAE CE	,343	2,494	,019*	QCAE CE	,375	2,316	,028*

Note. TIV = Total Intracranial Volume; QCAE CE = scores for the Questionnaire of Cognitive Empathy.
*p < .05. **p < .01.

Results (table 10) showed a significant correlation between scores from the QCAE AE with solely the left WM insula (t = 2.926, p = .007, R^2 *change* = 15%, F *change* = 8.563). Of the control variables, TIV revealed a significant effect on the model with an R^2 *change* of 37%.

Table 10

Coefficients for The Correlation Between White Matter Insula and QCAE Scores for Affective Empathy (AE), Controlling for Age and TIV

	White Matter Insula						
	Left Insula				Right Insula		
Model	Beta	t	p	Model	Beta	t	p
1 (Constant)		12,787	,000	1 (Constant)		13,625	,000
Age	-104	-,562	,579	Age	,035	,191	,850
2 (Constant)		1,629	,114	2 (Constant)		2,854	,008
Age	,020	,132	,896	Age	,117	,666	,511
TIV	,623	4,120	,000	TIV	,413	2,343	,026
3 (Constant)		,736	,468	3 (Constant)		2,218	,035
Age	,056	,412	,684	Age	,142	,825	,417
TIV	,591	4,388	,000	TIV	,390	2,268	,032
QCAE AE	,389	2,926	,007**	QCAE CE	,270	1,593	,123

Note. TIV = Total Intracranial Volume; QCAE AE = scores for the Questionnaire of Affective Empathy.
*p < .05. **p < .01.

No associations were found (table 11) between QCAE scores for cognitive empathy and AI cortical thickness measures (left AI t = .165, p = .870, R^2 *change* = 0.1%, F *change* = .027; and right AI t = -1.274, p = .213, R^2 *change* = 5.4%, F *change* = 1.622), nor, as can be seen in table 12, between this measure and affective empathy (left AI t = .354, p = .726, R^2 *change* = 0.4%, F *change* = .125; and right AI t = -.237, p = .814, R^2 *change* = 0.2%, F *change* = .056).

Table 11

Coefficients for The Correlation Between Anterior Insula Thickness and QCAE Scores for Cognitive Empathy (CE), Controlling for Age

Anterior Insula Thickness							
	Left Anterior Insula				Right Anterior Insula		
Model	Beta	t	p	Model	Beta	T	p
1 (Constant)		21,119	,000	1 (Constant)		16,827	,000
Age	-,163	-,891	,380	Age	-,099	-,537	,595
2 (Constant)		10,823	,000	2 (Constant)		10,062	,000
Age	-,167	-,890	,381	Age	-,069	-,373	,712
QCAE CE	,031	,165	,870	QCAE CE	-,235	-1,274	,213

Note. QCAE CE = scores for the Questionnaire of Cognitive Empathy.
*p < .05. **p < .01.

Table 12

Coefficients for The Correlation Between Anterior Insula Thickness and QCAE Scores for Affective Empathy (AE), Controlling for Age

Anterior Insula Thickness							
	Left Anterior Insula				Right Anterior Insula		
Model	Beta	t	p	Model	Beta	T	p
1 (Constant)		21,119	,000	1 (Constant)		16,827	,000
Age	-,163	-,891	,380	Age	-,099	-,537	,595
2 (Constant)		12,635	,000	2 (Constant)		10,462	,000
Age	-,156	-,834	,411	Age	-,104	-,551	,586
QCAE AE	,066	,354	,726	QCAE CE	-,045	-,237	,814

Note. QCAE AE = scores for the Questionnaire of Affective Empathy.
*p < .05. **p < .01.

4. Discussion

In this study, the relation between GM AI and WM insula structural variations and empathy was investigated. Overall, variations in the left GM area of the AI, as well as variations in the WM insula volume were significantly associated with individual differences in empathy. Results were consistent with previously VBM studies showing associations between insula structural variances and empathy (Banissy et al., 2012; Eres et al., 2015; Mutschler et al., 2013).

In the current research, an investigation was conducted on whether volumetric measures related to empathy were driven by volume, surface area and/or cortical thickness. Results indicated a positive association between variance in the area of the left AI and overall empathy, with marginal associations with cognitive and affective empathy. A marginal association between the left AI volume and empathy was reported, whereas no associations were found between cortical thickness and empathy measures. Results from the present study suggest that it is the AI surface area, and not its cortical thickness, that holds an association with individual differences in empathy. Regarding these morphometric measures, researchers have found that surface area is associated cognitive functions (Schnack et al., 2015) rather than cortical thickness (Vuoksimaa et al., 2014), which suggest that surface area could be a more reliable morphometric measure to investigate with empathy measures.

This study also investigated whether there was an association between insula white matter variation and individual differences in empathy. Results showed a strong association between both left and right WM insula with total empathy scores, with stronger significance on the left insula. Further testing revealed that the WM in the overall insular cortex from the left hemisphere was significantly associated with both cognitive and affective empathy, although the association was stronger for the affective component. Additionally, the right WM insula was also associated with cognitive empathy. These results are in accordance with evidence showing a significant association between WM microstructural integrity in the insula and empathy (Nakagawa et al., 2015). However, no other studies have attempted to investigate a distinct association between WM insular structural changes, in the left and right hemispheres, and cognitive and affective empathy.

It is important to note that this is a preliminary study and these results are limited by its reduced sample size. Future investigations with a larger sample are necessary to confirm and extend these preliminary results concerning the variations in the AI GM area and empathy measures, as well as the insula WM association with empathy. Additionally, whether WM in the right hemisphere of the insula is associated solely to cognitive empathy while the left WM insula is more significantly associated to affective empathy should be also investigated.

Influential factors that might impact the results of the present study concerns the gender of the sample and the self-reported method used to assess empathy. Individual differences in empathy have been found to vary according to gender and women are known to present higher levels of empathy than men on self-report measures (Fan et al., 2011; Mutschler et al., 2013; Nanda, 2014; Rankin et al., 2006; Reniers et al., 2011). Some studies suggest that gender differences on empathy processing may not result from a difference in ability but simply that males are more reticent to report empathy than women due to gender stereotypes, particularly while reporting affective empathy (Nanda, 2014). Gender differences may also originate from gender differently-involved neural mechanisms and socially learned features (i.e. nurturing skills) (Mercadillo et al., 2011).

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