The Dorsolateral Prefrontal Cortex Presents Structural Variations Associated with Empathic Capacity in Psychotherapists.

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Abstract

Empathic capacity has been shown to be correlated with brain structural variations. This study investigates how this is the case in a group of psychotherapists who have a constant demand to modulate their empathic response. Eighteen psychotherapists and eighteen healthy controls underwent 3-Tesla MRI scanning and completed empathy-related psychometric assessments. Cortical thickness (CT) measures were estimated for each participant. We evaluated how these measures differed between groups, and if they were associated with individual empathy scores at a series of regions of interest. Our analysis shows that psychotherapists display a significantly greater CT at the left dorsolateral prefrontal cortex (dlPFC; $p < 0.05$, FDR corrected). Moreover, psychotherapists' CT in this region is correlated with the tendency to feel empathically concerned for others ($p < 0.01$, FDR corrected). This finding is relevant because this dlPFC region participates importantly in emotion regulation and perspective taking processes. Thus, our findings support the idea that empathic capacity is reflected by brain structural variations, recruiting for the first time a sample of subjects for whom empathic responding is crucial in their jobs.

Key words: empathy, cognitive empathy, cortical thickness, psychotherapy, emotion regulation, dorsolateral prefrontal cortex

Introduction

Empathy is defined as an umbrella term that encompasses all processes through which an organism—generally a mammal—can understand others' affective states through the activation of their own representations of such states (Bernhardt & Singer 2012; De Waal & Preston 2017; Preston & De Waal 2002). These processes are generally classified into two categories. Affective empathy phenomena are bottom-up processes which depend on the coupling of perception and action, and engage brain regions associated with first-hand affective experiencing and sensori-motor activity—like insula, amygdala, somatosensory and motor cortices and ventromedial prefrontal cortex (vmPFC). Meanwhile, cognitive empathy phenomena are said to be top-down, executive processes engaging brain structures that participate in mentalizing and working memory—such as dorsolateral prefrontal cortex (dlPFC), ventral medial prefrontal cortex (vmPFC) and posterior cingulate gyrus (pCC). (Bernhardt & Singer 2012; De Waal & Preston 2017; Engen & Singer 2013)

Such segregation of empathic processes, however, does not mean that they happen independently. On the contrary, they remain functionally integrated and a real-life empathic experience will engage both affective and cognitive empathic phenomena (De Waal & Preston 2017; Zaki & Ochsner 2012). Accordingly, Decety (2011) and his colleagues have proposed that an experience of empathy consists of three consecutive components: affective arousal, emotion awareness and emotion regulation. While the first component represents the bottom-up ("affective") aspect of empathy, the emotion regulation component characterizes its top-down ("cognitive") aspect and permits to effectively engage in helping behavior (Decety 2011; Elliot et al. 2011; Lamm et al. 2007a).

Emotion regulation refers to the modulation of ongoing affective states through conscious or unconscious processes. (Etkin, Büchel & Gross 2015; Ochsner & Gross 2005). A distinction is commonly made between behavioral and cognitive emotion regulation processes (Ochsner & Gross 2005). While the former refer to inhibition of expressive behavior (i.e. expressive suppression), the latter point to top-down mechanisms aimed to modulate the intensity of the emotional experience or change the emotion itself (e.g. attentional deployment away from, or cognitive reappraisal of, the eliciting stimuli). (Etkin, Büchsel & Gross 2015; Gross 2002; Ochsner & Gross 2005)

Psychotherapists might suppress the expression of their emotions during a session as a first resource, as not to display their full blown emotional response to the patient (for instance, when the therapist becomes angry; Prikhidko & Swank 2018). However, there is evidence that this type of inhibition tends to impair some aspects of cognition, such as memory about the emotion-eliciting stimuli, and also has negative effects on the ongoing social interaction (Gross, 2002). It is thus suggested that, in general, expressive suppression is not a desirable emotion regulation strategy for psychotherapists (Pletzer, Sanchez & Scheibe 2015; Prikhidko & Swank 2018).

Cognitive emotion regulation mechanisms do not seem to have such detrimental effects on cognition and social interaction, probably because the intensity of the emotional experience itself is directly modulated (Gross, 2002). This makes cognitive emotion regulation more suitable for psychotherapists' empathic responding (Pletzer, Sanchez & Scheibe 2015; Prikhidko & Swank 2018). There is consistent evidence that this kind of regulation is mediated by prefrontal dorsolateral regions (Etkin, Büchel & Gross 2015; Ochsner & Gross 2005), especially on the left hemisphere (Ochsner et al. 2004), and involving to a lesser extent ventrolateral prefrontal and parietal cortices (Etkin, Büchel & Gross 2015).

Thus, empathy (especially its cognitive aspect) has an important role in psychotherapy (Elliot et al. 2011). When psychotherapists effectively modulate their empathic responding and reflect an emotional response that is congruent with the one of the patient, it is more likely that the patient feels understood and cared about, and even that they become more aware of their own affective state (Pletzer, Sanchez & Scheibe 2015). The relevance of this is to such an extent that the level of empathy during the psychotherapy session, as perceived by the patient, has been found to be a robust predictor of therapeutic success, independently of the theoretical system (Elliot et al. 2011; MacFarlane et al. 2017).

This suggests that there might be a pressure for therapists to be more empathic through continuously modulating their empathic response. The hypothesis that psychotherapists have an increased empathic capacity has been tested by some research groups, finding evidence that, even though therapists show similar levels of bottom-up emotional reactivity as nontherapists (Hassentab et al. 2007; Pletzer et al. 2015), they display a significantly higher cognitive empathy capacity as measured through behavioral tasks and psychometric scales (Hassentab et al. 2007; Olalde-Mathieu et al. 2020).

A further reason for the need of psychotherapists to be especially empathic is that they tend to experience strong emotions of anger, guilt and anxiety as a result of their professional practice. Due to these intense emotions psychotherapists are in constant risk of vicarious traumatization and, consequently, professional impairment. Thus, the constant monitoring of their own affective state, and the use of strategies to regulate it is even a matter of ethical responsibility (Prikhidko & Swank 2018). This means that psychotherapists are required to reliably modulate their emotional response even after work, whether this means down-regulating intense emotions or up-regulating desirable emotional states (Prikhidko & Swank 2018). Accordingly, some studies have found that psychotherapists are better at regulating their emotions than nontherapists (Pletzer et al. 2015), and that they tend to draw less often upon suppression as a strategy to modulate their affective state (Olalde-Mathieu 2020).

That said, the assumption that the healthy adult human brain is susceptible to local plasticity through repeated exposure to certain kinds of stimuli and environmental demands is strongly supported by empirical evidence (Banks, Sreenivasan, Weintraub et al. 2016; Bermudez & Zatorre 2005; Delon-Martin, Plailly, Fonlupt et al. 2013; Maguire, Gadian, Johnsrude et al. 2000). These variations are detectable through structural MRI analysis techniques such as voxel-based morphometry (Ashburner & Friston 2000) and cortical thickness analysis (Lerch & Evans 2005; Lerch, Van Der Kouwe, Raznahan et al. 2017).

Such methods have yielded evidence that certain brain structures tend to structurally vary as a function of various empathic measures. While affective empathy measures tend to correlate with structural variation in bilateral insula (Banissy et al. 2012; Eres, Decety & Louis 2015), left anterior cingulate cortex, left precuneus and left somatosensory cortex (Banissy et al. 2012), cognitive empathy measures correlate with structural variations in structures that comprise dorsolateral prefrontal cortex (Banissy et al. 2012; Uribe, Puig-Davi, Abos et al. 2019), left cingulate cortex (Banissy et al. 2012; Eres, Decety & Louis 2015; Uribe, Puig-Davi, Abos et al. 2019), and superior medial prefrontal cortex (Eres, Decety & Louis 2015; Uribe, Puig-Davi, Abos et al. 2019).

On this basis, it is here hypothesized that psychotherapists, who are in constant demand of modulating their empathic response, will display brain cortical variations in regions associated with empathic social processing; and that these variations be associated with empathic capacity. In this study we aimed to test this by investigating a group of psychotherapists who embrace, and have training on, generating *alliance* as a psychotherapy tool. *Alliance* is defined to be the kind of bonds and synchrony between user and psychotherapist that is achieved through empathic efforts and commitment to the therapeutic process (Horvath 2001; Koole & Tschacher 2016) and which has been consistently associated with therapeutic success (Goldsmith et al. 2015; Klein et al. 2003; McLeod 2011; Webb et al. 2010).

Methods

Participants

Thirty-six participants were recruited for the study, 18 of whom were person-centered psychotherapists (TA; 9 female; age mean 54.9 ±7.6) and 18 were the non-psychotherapists control group (NT; 9 female; age mean 54.7 ±7.6). All psychotherapists had post-graduate studies of psychotherapy, as well as at least six years of professional clinical experience. All of them were professionally active at the moment of this study. All The control group participants were healthy professionals from the different fields specified in the national classification of occupations. All of them

had approximately the same amount of studies, socioeconomic status and professional working experience as the psychotherapists group. All participants were right handed, reported no neurological or psychiatric history, and were not taking any psychotropic medication. All participants signed a written informed consent to take part in the study. This project was approved by the ethics committee of the Neurobiology Institute (UNAM), following the Declaration of Helsinki guidelines.

Questionnaires

Empathic skills were assessed through the interpersonal reactivity index (IRI; Davis 1983), which is subdivided into four independent dimensions: *Fantasy* (that evaluates the tendency to identify with fictitious characters and situations, e.g. from a book), *Perspective Taking* (measures the tendency to actively adopt another person's point of view in orders to understand how they feel), *Empathic Concern* (evaluates the tendency to react emotionally to the suffering of the others, with sentiments of compassion, care and concern), and *Personal Distress* (which measures the tendency to experience distress in stressful interpersonal situations, including emergencies) (Carrazco-Ortiz et al. 2011; Davis 1983; Escrivá et al. 2004).

Emotion regulation was assessed by the Emotion Regulation Questionnaire (ERQ). Specifically, this questionnaire evaluates the tendency to adopt *expressive suppression* and *cognitive reappraisal* as emotion modulation strategies.

The Toronto Alexithymia Scale (TAS-20; Bagby et al. 1994) was also completed by all participants, the score of which was used as an exclusion criterion if it suggested pre-clinical or clinical alexithymia.

MRI acquisition

Structural MR imaging was performed on a 3 Tesla scanner (General Electric, Waukesha, WI), with a 32-channel array head coil. A whole brain three-dimensional high resolution T1 weighted image was acquired from each participant through a spoiled gradient recalled echo sequence (SPGR) with the following parameters: repetition time (TR) = 8.1ms, echo time (TE) = 3.2 ms, flip angle = 12°, isometric voxel = 1.0 x 1.0 x 1.0 mm^3 , image matrix = 256 x 256, FOV = 256, acquisition plane = Sagittal.

Preprocessing

A qualitative quality control was performed on each raw MRI volume by trained observers, evaluating four criteria: image sharpness, presence of ringing artifact, contrast to noise ratio (CNR) on subcortical structures, and CNR around the cortex (Backhausen et al. 2016). Hence, one volume pertaining to the nontherapists group was excluded from further analyses. Noise and magnetic field inhomogeneities were corrected using Advanced Normalization Tools (ANTs; Tustison et al. 2010). Finally, a binary mask was generated for each brain image using the online volBrain 1.0 pipeline (Manjón & Coupé

2016). The resulting masks' quality were also qualitatively controlled, and small manual corrections were applied when needed.

Regions of interest (ROI) relevant to cognitive empathy were selected from the Human Brainnetome Atlas (BNA; Fan et al. 2016). This was done using BrainMap metadata associated with each region as available in the atlas. Namely, regions associated with the keyword *social cognition* were identified on the prefrontal and cingulate cortices. This selection was then further restricted according to the relevant previous literature. Next, the corresponding probabilistic maps were downloaded, thresholded and binarized to serve as ROI masks. The resulting ROIs are listed in Table 1.

region	hemisphere	location	centroid (MNI coord)	behavioral domains
A8dl	left	superior frontal gyrus	-18, 24, 53	Social cognition, emotion, ToM
A8dl	right	superior frontal gyrus	22, 26, 51	Social cognition, ToM
A9/46d	left	middle frontal gyrus	-27, 43, 31	Social cognition, action inhibition
A23d	left	anterior cingulate gyrus	-4, -39, 31	Social cognition, emotion
A23v	left	posterior cingulate gyrus	-8, 47, 10	Social cognition, explicit memory

Table 1. BNA ROI selection (Fan et al. 2016)

Cortical thickness measurement

CIVET 2.1.1 pipeline was used to extract brain surfaces and estimate cortical thickness on each brain image (Montreal Neurological Institute at McGill University, Montreal, Quebec, Canada). A 12-parameter affine transformation was applied to each individual preprocessed image, registering it to the MNI ICBM 152 model. Then a tissue classification was performed, that is, each voxel was assigned to represent white matter (WM), gray matter (GM) or cerebro-spinal fluid (CSF) based on signal intensity and *a priori* probabilistic models. The preprocessed T1-weighted volumes were fed to the pipeline with the individual volBrain masks for better segmentation. Next, deformable models were used to create and extract WM and GM surfaces for each hemisphere separately, yielding 40,952 vertices per surface. Then an estimation of the distances between the internal and the external cortical surfaces were estimated at each vertex, and smoothed using a 25 mm surface-based diffusion blurring kernel. For our study we extracted only cortical thickness data.

Statistical analysis

All statistical analyses were carried out using R (R Core Team, 2020). Cortical thickness (CT) data were analyzed with the RMINC package (Lerch et al. 2017). Using a linear model, vertex-wise comparisons were performed at each region of interest. Correction for multiple comparisons was made using false discovery rate (FDR; Genovese et al. 2002) at 5%. Age and sex were included in the model as covariates of no interest. Next, another linear model was used to determine whether the asymmetry measures (the difference between corresponding vertices of the two hemispheres) were different between groups. Finally, another linear model was used to explore if cortical thickness at the ROIs varied as a function of any of the psychometric scores. Sex and age were again included as covariates of no interest. The effect size for the first linear model was additionally calculated for the model (in terms of Hedges' g) at every vertex of the brain surface.

Results

Behavioral results

Psychometric results are listed in Table 1. Psychotherapists scored significantly higher than non-therapists on the two IRI subscales related to mentalizing capacity: *Fantasy* ($p < 0.01$) and *Perspective Taking* ($p < 0.05$). They also scored significantly lower on the ERQ *Expressive suppression* construct ($p < 0.05$; see Figure 1). This has been previously observed on a larger sample (Olalde-Mathieu et al. 2020).

	Fantasy	Perspective taking	Empathic concern	Personal distress	Reappraisal	Supression
Therapists						
average	19.17	22.72	22.61	8.06	4.70	1.89
s.d.	3.75	3.58	3.07	3.33	1.29	0.71
Nontherapists						
average	12.65	19.12	21.06	9.24	4.33	2.85
s.d.	5.36	4.94	5.56	5.09	1.83	1.29

Table 2. mean psychometric scores and standard deviations

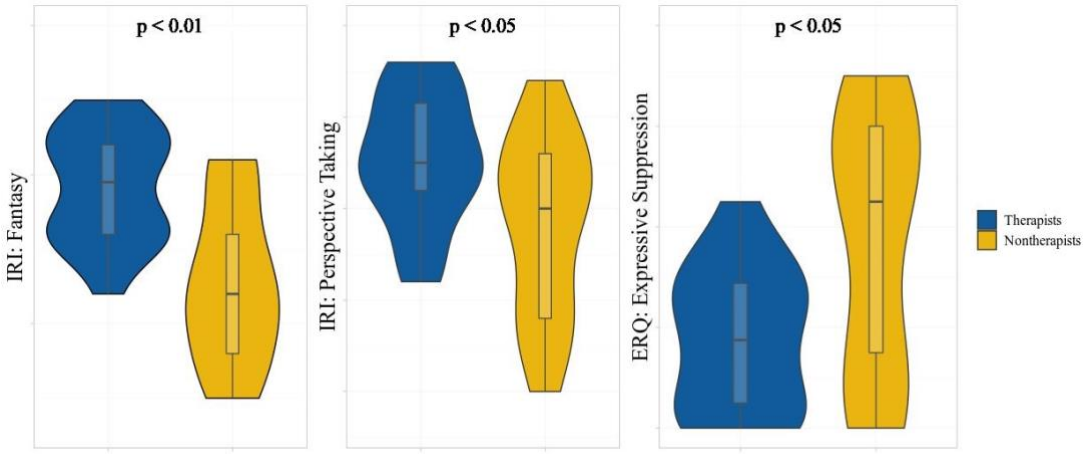

Figure 1. Scores in which significative inter-group differences were found

Cortical thickness results

Psychotherapists displayed a significantly thicker left dorsolateral prefrontal cortex on the A9/46d region than non-therapists ($q < 0.05$, FDR corrected). This region, located in the middle frontal gyrus, is represented in Figure 2. No significant cortical thickness differences were to be found between the groups in the cingulate regions. The therapists' cortical thickness in the dlPFC A9/46d region correlated with IRI's *Empathic Concern* score ($q < 0.01$, FDR corrected; see Figure 3), but not with any of the other measured psychometric scales.

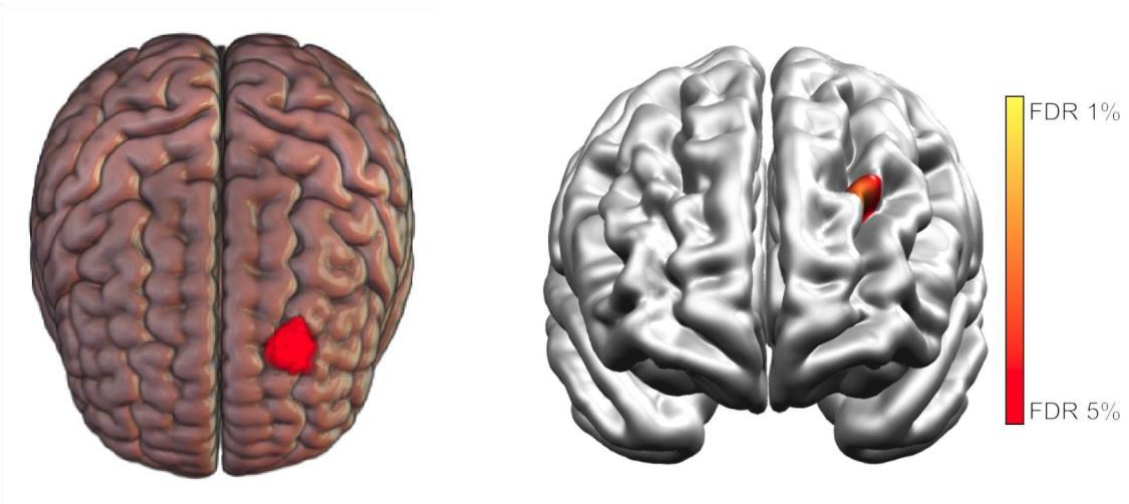

Figure 2. a) left A9/46d region; b) statistical map of left A9/46d region (therapists > nontherapists)

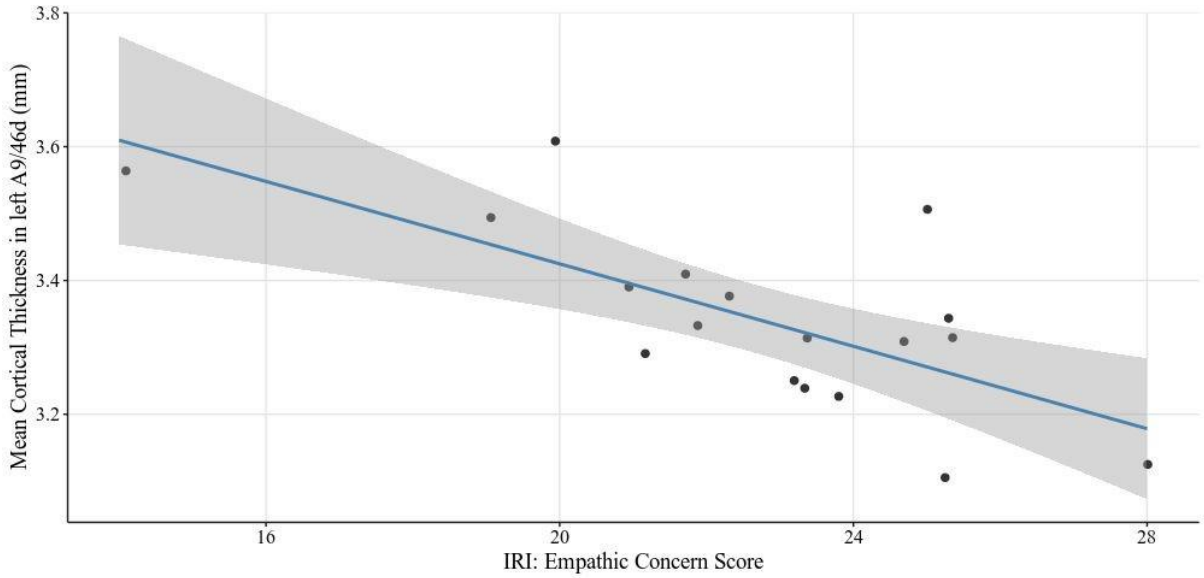

Figure 3. Representation of the significant linear model: Empathic Concern vs. left A9/46d mean cortical thickness

The asymmetry linear model also revealed a higher cortical thickness asymmetry at the A9/46d region in the therapists' brains (left > right), although with a higher FDR threshold ($q < 0.1$, FDR corrected).

Finally, a whole-brain effect size statistical map was computed for the first linear model (see Figure 4), showing that the dlPFC displays the highest effect size values. Although not directly related to this study's purposes, it is worth noting that sensorimotor regions, such as the inferior somatosensory cortex and paracentral gyrus, display a tendency to high effect sizes ($g > 8.0$).

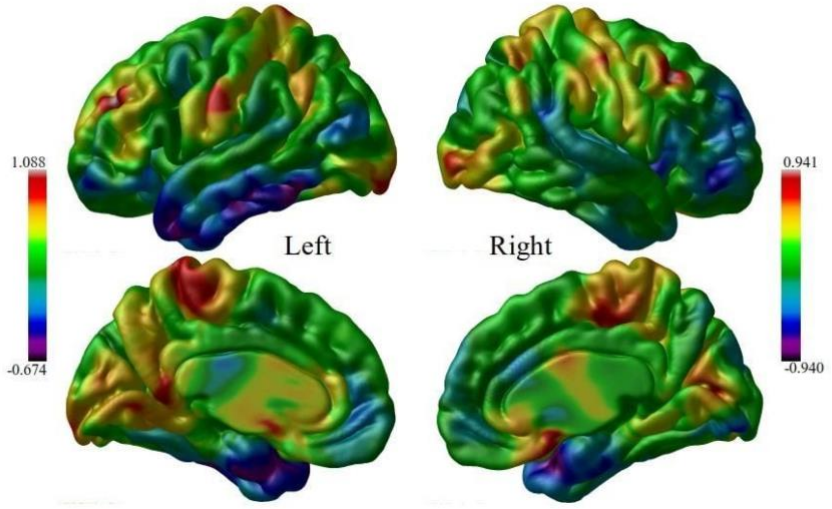

Figure 4. Whole brain effect size statistical map (Hedges' g)

Discussion

The aim of this study was to investigate the potential cortical thickness variations associated with the professional psychotherapeutic practice, and their relation with empathic capacities. Our findings reveal that a region in the left dorsolateral prefrontal cortex was significantly thicker in a group of psychotherapists than in the nontherapists control group. Also, the cortical thickness in this region negatively correlates with the tendency to feel empathically concerned about others, as measured by the corresponding IRI scale. Overall, these results suggest that expertise in such a profession that demands augmented empathic skills could be reflected in structural dorsolateral prefrontal variations.

The fact that the left middle frontal gyrus, in the A9/46d region was thicker in psychotherapists' brains is conceptually significant. This region, related to executive control, not only is strongly associated with perspective-taking skills (De Waal & Preston 2017; Völlm et al. 20016), but it is also deeply implicated in top-down emotion regulation processes (Enzi et al. 2016; Ochsner & Gross 2005). Moreover, activation in this region seems to negatively correlate to activity in limbic structures—including the amygdala—during the presentation of emotionally charged stimuli (Sang & Hamman 2007; Smoski et al. 2014; Urry et al. 2006). Thus, we speculate that the greater thickness of this region could reflect a greater tendency to regulate one's affective states.

In addition, the hypothesized partial lateralization of cognitive empathy-related processes (those preferentially engaged by therapists) can be supported by the tendency observed, that in psychotherapists the left A9/46d region seems to be thicker than the corresponding region in the right hemisphere when compared to nontherapists.

However, there seemed to be no correlation between the ERQ scores and left A9/46d cortical thickness. This suggests either that the psychotherapists engage in other cognitive emotion regulation mechanisms not measured here, or that the ERQ could not capture their higher tendency to engage in cognitive reappraisal to regulate their affective state. Any of these alternatives is supported by the fact that they scored significantly lower on the ERQ *Expressive Suppression* scale with respect to nontherapsits. Forthcoming research will be able to shed light on this issue.

Although we actually expected to find an effect of IRI's cognitive empathy constructs on this ROI's cortical thickness, it is meaningful that the correlation was with *Empathic Concern*. This construct has been repeatedly found to be IRI's strongest component—i.e. it represents the fundamental element of empathy as a global construct (Alterman et al. 2003; Cliffordson 2001). Moreover, its association with A9/46d is further supported by the previous finding that the tendency to feel empathically concerned for others is correlated with the ability to regulate one's affective states (Eisenberg, Spinrad & Morris

2013; Lamm et al. 2007b), a key function of this region. This suggests that variations in this region could be a reflection of an overall tendency to be differently empathic, not without help from efficient emotion modulation skills.

The middle frontal gyrus has also been identified to engage in moral decision making tasks, which tend to involve self-referential processes and the representation of others' intentions and affective states, as well as during emotion regulation related to morally charged stimuli (together with mPFC; Harenski & Haman 2006). These kinds of morally charged stimuli might be relevant to what psychotherapists might frequently encounter in session. However, there does not seem to be MRI studies of moral processing in psychotherapists yet, so this is a potential future research direction.

The subsequent, exploratory effect size statistical map confirmed that the A9/46d region indeed yields some of the highest effects from the model. Apart from that, it suggests that sensorimotor regions could play an important role in the presently studied phenomenon. Since this is in accordance with the perception-action theory of empathy (de Waal & Preston 2017; Preston & de Waal 2002) as well as with previous functional results (Gallo et al. 2018; Engen & Singer 2013), it would be worthwhile for future research efforts to address this issue.

A limitation of this study is that personality traits were not measured. This procedure might be important in future research in order to find out if the detected structural changes are related to personality differences. Longitudinal research is also needed to determine whether psychotherapists develop their increased empathic skills as a result of their professional training and experience, or whether they are drawn to the job because of their already higher empathic capacity.

Conclusions

Our results indicate that there is a difference in cortical thickness at a portion of the dorsolateral prefrontal cortex in a group of psychotherapists as compared to nontherapists, and that this variation is related to feeling empathically concerned for others. This in turn is suggested to be a good general indicator of empathy globally. In conclusion, these results suggest for the first time that a region in the dlPFC presents structural variations associated with empathic capacity in a group of professionals who are required to have a constant active modulation of their empathic response. This adds to the body of studies on neuroanatomical variations associated with different areas of expertise and sheds light to the problem of how the adult brain plasticity responds to environmental demands.

Declarations

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Conflicts of interest/Competing interests

The authors declare that they have no conflict of interest.

Ethics approval

This project was approved by the ethics committee of the Instituto de Neurobiología - National Autonomous University of Mexico (UNAM). The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

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