



Individualized Prediction of Females' Empathic Concern from Intrinsic Brain Activity within General Network of State Empathy

Dongfang Zhao^{1,2} · Rui Ding^{1,2} · Huijuan Zhang^{3,4} · Nan Zhang^{1,2} · Li Hu^{3,4} · Wenbo Luo^{1,2}

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Abstract

Empathy can be measured based on behavioral tasks and self-report scales, which have been used to characterize the state and trait empathy, respectively, in previous studies. The neural correlates of state empathy have been deeply investigated, whereas the association between trait empathy and brain activity remains unclear. Thus, this study employed multiple variate pattern analysis (MVPA) to explore whether intrinsic brain activity (IBA) within state-empathy-related regions was associated with trait empathy. Meta-analysis of empathy-related fMRI experiments identified a general network underlying state empathy, which is located in the bilateral supplementary motor area (SMA) extending to the middle cingulate cortex (MCC) and left anterior insula (AI) and extending to the inferior frontal gyrus (IFG). The subsequent MVPA found that empathic concern can be predicted through the IBA of the general network at the female individual level (i.e., the fractional amplitude of low-frequency fluctuations and regional homogeneity). Based on the resting state fMRI (rs-fMRI), these results further support the involvement of SMA/MCC and AI/IFG in empathy. Meanwhile, the significant predictive association between IBA and trait empathy offers new insights into the general component of empathy, which may indicate the potential of using rs-fMRI to achieve the objective measurement of empathic ability.

Keywords Meta-analysis · Multiple variate pattern analysis · Resting-state fMRI · State empathy · Trait empathy

Introduction

When we see someone hurt, we feel sad too. We experience this feeling, because human beings have a unique psychological ability, namely empathy, which allows us to share and understand the affective states of others (Batson, 2009; Bernhardt & Singer, 2012; Hillis, 2014). Moreover, empathy

can smoothen social interactions and contribute to prosocial behaviors as well as moral judgments (Decety & Cowell, 2014; Eisenberg & Eggum, 2009; Eisenberg & Miller, 1987; Eisenberg & Morris, 2001; Gleichgerricht & Young, 2013; Hoffman, 2007; Li et al., 2013; Reniers et al., 2012).

Researchers measure empathy in various ways. Currently, there are three commonly used research methods: self-reporting, behavioral measures, and neuroscientific methods (Neumann et al., 2015), which can be utilized to assess two forms of empathy: trait empathy and state empathy. Trait empathy describes the extent of cognitive and emotional characteristics of everyday empathy, representing one's general ability to show empathy and is measured using self-report scales (Van der Graaff et al., 2016; Zhao et al., 2021). State empathy refers to responses depending on the immediate context toward empathized targets, which are measured using behavioral tasks (Van der Graaff et al., 2016; Zhao et al., 2021). Self-reporting usually takes the form of a verbal report or questionnaire survey (Anastassiou-Hadjicharalambous & Warden, 2007; Balconi & Bortolotti, 2014; Michaels et al., 2014), such as the Interpersonal Reactivity Index (Davis, 1983), the Empathy Quotient (Baron-Cohen

Dongfang Zhao and Rui Ding contributed equally to this work.

✉ Li Hu
huli@psych.ac.cn

✉ Wenbo Luo
wenbo9390@sina.com

¹ Research Center of Brain and Cognitive Neuroscience, Liaoning Normal University, Dalian, China

² Key Laboratory of Brain and Cognitive Neuroscience, Dalian, China

³ CAS Key Laboratory of Mental Health, Institute of Psychology, Beijing, China

⁴ Department of Psychology, University of Chinese Academy of Sciences, Beijing, China

& Wheelwright, 2004), the Basic Empathy Scale (Jolliffe & Farrington, 2006) and the Questionnaire of Cognitive and Affective Empathy (Reniers et al., 2011). Due to their well-built structure and easy implementation, self-report questionnaires are most commonly used to measure empathy at the individual level. Meanwhile, many behavioral tasks can be used to evaluate empathy, and related paradigms in the literature have gradually improved. Among these tasks, picture viewing paradigms (PVP) are used most frequently and are most effective (Neumann et al., 2015). The images show whether individuals are in certain negative (e.g., injury) or positive (e.g., win the lottery) situations. Participants view the images and response accordingly (Westbury & Neumann, 2008). With the advancement of cognitive neuroscience measurement technology, the emergence of functional magnetic resonance imaging (fMRI) has provided a new opportunity for measuring empathy. Combined with behavioral tasks and fMRI, neural activity for state empathy can be detected. Previous studies, using various tasks, have revealed a comprehensive brain region involved in empathic responses (i.e., state empathy), including the anterior/middle cingulate cortex (A/MCC), supplementary motor area (SMA), bilateral anterior insula (AI), inferior frontal gyrus (IFG), inferior parietal lobule (IPL), and temporoparietal junction (TPJ), etc. (Bernhardt & Singer, 2012). Using fMRI meta-analysis, the core network of empathy was calculated. Fan et al. (2011) found that dACC, aMCC, SMA, and bilateral AI were consistently activated by empathy tasks regardless of automatic and instructed responses. Moreover, the signal changes of the above empathy-related regions were demonstrated to be correlated with individual-level of empathy measured by self-report scales (e.g., IRI). However, recent studies have focused on associations between intrinsic brain activity (IBA) (i.e., brain activity at rest, IBA) and trait empathy. Cox et al. (2012) successfully revealed that trait empathy (i.e., measured by self-report scales) was significantly associated with the fractional amplitude of low-frequency fluctuations (fALFF) within the bilateral AI, putamen, and amygdala. Based on previous findings, task-based (i.e., state empathy) and task-free (i.e., trait empathy) fMRI showed potential for the objective measurement of empathy. However, it remains to be answered whether the IBA of brain regions involved in state empathy also supports trait empathy. Meanwhile, in a very recent study, trait empathy can be significantly predicted through functional connectivity (i.e., patterns of control and resonance networks) at rest (Christov-Moore et al., 2020). Whether regional features of IBA allow similar predictions needs further consideration.

Intrinsic brain activity can be scanned and recorded using resting-state functional magnetic resonance imaging (rs-fMRI), which is an effective method independent of experimental tasks to investigate the neural substrates of mental activity (Karoly et al., 2013; Lai & Wu, 2015; Pan et al., 2018;

Xu et al., 2015). Many researchers have used rs-fMRI in recent years to explore the neural correlates of dispositional traits (Bilevicius et al., 2018; Esménio et al., 2019; Wei et al., 2014). In the current study, we focused on two indicators of IBA: namely fALFF and regional homogeneity (ReHo). The fALFF measures the regional intensity of spontaneous fluctuations in the BOLD signal (Pan et al., 2018; Zou et al., 2008), and ReHo measures regional synchronization at the whole-brain level and spontaneous local neural activity (Liu et al., 2013; Zang et al., 2004). Both indicators of validated reproducibility have been approved as two regional brain features linking the brain and behaviors (Tian et al., 2012; Zuo & Xing, 2014).

In general, the current study was designed to investigate the associations between IBA located in brain regions underlying state empathy and trait empathy. Specifically, to address the above issues regarding empathy, the data of rs-fMRI and trait empathy (i.e., measured by IRI) were collected from Chinese college students. Given the gender effect on empathy (e.g., females generally behave more empathically than males) (Christov-Moore et al., 2014), only women were enrolled in the study. Then, a meta-analysis of task-based fMRI studies of empathy was conducted to define brain networks (i.e., regions of interest, ROIs) consistently activated by state empathy. The fALFF and ReHo maps of individuals were calculated within such an ROI. Finally, multiple variate pattern analysis (MVPA) was performed within the ROIs, which was expected to link trait empathy and the IBA of state empathy. The MVPA has successfully been used to decode neural information and discriminate cognitive states, connecting brain activity to behavior and clarifying the structure of neural representations (Norman et al., 2006; Peelen & Downing, 2007). Therefore, MVPA can be employed to address the question of whether IBA can predict trait empathy. Based on previous and existing evidence (Cox et al., 2012; Nummenmaa et al., 2008), we hypothesize that (1) there are repeat common patterns of neural activation-relevant empathy found through meta-analysis, including bilateral SMA, bilateral CC, bilateral insula, bilateral IFG, and so on; (2) the prediction model based on the neural structure could significantly predict trait empathy, and the values of ReHo and fALFF may be positively correlated with the behavioral scores. This study implicates and inspires the possibility of objective measurement of empathy using rs-fMRI, providing a new perspective for the evaluation of empathy.

Materials and methods

Participants

Given the significant effect of gender on empathy (Christov-Moore et al., 2014), only female subjects were recruited

in the current study. 115 females (mean age = 20.9 years, standard deviation [SD] = 2.16 years) participated in the experiment. All were healthy and with normal or corrected-to-normal vision. Before the experiment, participants signed a written, informed consent and got paid for their participation. Due to the excessive head movement during scanning (>1.5 mm translation or $>1.5^\circ$ rotation), 9 participants were excluded from the final analysis, which leads to final sample of 106 participants (mean age = 20.9 years, SD = 2.08 years, 3 were left-handed). The study was approved by the local ethics committee.

Measurement of trait empathy

To assess an individual's empathy capacity, participants completed the Chinese adapted version of Interpersonal Reactivity Index (IRI-C) (Davis, 1980, 1983; Zhang et al., 2010). The IRI questionnaire consists of four subscales: fantasy empathy (FS), perspective-taking (PT), empathic concern (EC), and personal distress (PD). PT and EC measure different aspects of empathy: the former measuring the tendency to take the perspective of others cognitively and the latter one reflecting the self-compassion and concern for others. The subscales PT and EC were frequently used to evaluate cognitive and affective empathy (i.e., emotional empathy), which also received the agreement of previous researchers (Davis, 1980, 1983; Rankin et al., 2006). By contrast, the other two (FS and PD) were not effective to measure empathy of individuals in terms of construct validity (Baron-Cohen & Wheelwright, 2004). In the domain of neuroscience, PD often was considered as the distinct mental processing from empathy. Additionally, Decety and Lamm (2011) argued that PD would be induced through the complete self-other overlap, which did not satisfy the empathy-evoking conditions raised by Vignemont and Singer (2006) and empathy towards target actually did not happen. Thus, only the scales of PT and EC were used in the current study.

Data acquisition and processing

The image data were acquired using a 3.0 Tesla Discovery MR750 scanner (GE, Milwaukee, USA). First, structural images were acquired sagittal using the following parameters: repetition time (TR) = 1,900 ms; echo time (TE) = 2.52 ms; flip angle = 9° ; the field of view (FOV) = 256 mm $\times$ 256 mm; matrix size = 256 $\times$ 256; voxel size = 1 $\times$ 1 $\times$ 1 mm³; slice thickness = 1 mm and 176 slices. Then, a 10-min resting-state functional images were obtained using the echo-planar imaging (EPI) BOLD sequence with the following imaging parameters: repetition time (TR) = 2000 ms; echo time (TE) = 30 ms; flip angle = 90° ; the field of view (FOV) = 192 mm $\times$ 192 mm; matrix size = 64 $\times$ 64; voxel size = 3 $\times$ 3 $\times$ 3 mm³; slice thickness = 3 mm and 43

slices. During the resting state scanning, participants were instructed to close their eyes and stay awake, especially not to think or do anything.

The processing of resting-state fMRI images was performed using the Data Processing and Analysis of Brain Imaging (DPABI) toolbox (Yan et al., 2016). Preprocessing steps comprised the removal of the first 10 volumes; slice-timing correction; head motion estimation and correction; nonlinear normalization to the standardized Montreal Neurological Institute (MNI) space (3 $\times$ 3 $\times$ 3 mm³); detrending to remove the linear drift; spatial smoothing with a Gaussian Kernel filter of 4-mm full-width at half-maximum (FWHM); regression of nuisances, including signals of white matter, cerebrospinal fluid and Friston-24 head motion parameters (Friston et al., 1996); finally band-pass filter of signals at the frequency of 0.01–0.10 Hz.

Data analysis

Meta-analysis of empathy

To locate the brain regions consistently involved in state empathy, the meta-analyses based on activation likelihood estimation algorithm were performed (Eickhoff et al., 2012; Eickhoff et al., 2009). The reasons why previous meta-analytic result was not adopted in the current study were based on following considerations: (1) previous studies included much fewer original experiments because of the early publication date and thus synthesizing empathy network needs update; (2) previous meta-analyses did not differentiate the empathy towards physical pain and emotions, and new meta-analyses need to be performed to obtain domain-general empathy network. The task-based fMRI studies related to empathy were comprehensively searched in the PubMed database (<https://www.ncbi.nlm.nih.gov>) and the Web of Science (WOS) (<https://www.isiknowledge.com>). According to Lamm et al. (2010) and Ding et al. (2020), the searching keywords were set as (empathy OR empathic OR empathetic) AND (fMRI OR “magnetic resonance imaging”). The papers returned by above databases were screened according to defined exclusion criteria. The exclusion criteria were set as below: (1) the content of the experiment meets the definition of empathy (i.e., empathy is the ability which we can use to consciously share and infer the cognitive and affective state of other individuals) (Hillis, 2014; Vignemont & Singer, 2006); (2) the activation of the brain should be based on the contrast between different conditions; (3) the activation of the brain obtained by contrast should be based on whole-brain analysis; (4) the subjects of the included contrasts should be healthy. We extracted and inputted the activation coordinates of relevant contrasts into the software Ginger ALE 3.0.2 (<http://brainmap.org/ale>). The ALE maps were computed with a cluster-level

family-wise-error (cFWE) inference threshold at $p < 0.05$ as well as a cluster-forming threshold of $p < 0.001$, and 1,000 permutations were employed to calculate the minimum cluster-size threshold. It should be noted that, due to the stimuli influences (i.e., empathized targets) on the activations of empathic responses (Ding et al., 2020), the ROI of state empathy was defined through the overlap between neural correlates underlying empathy towards physical pain and emotion situations. Minimum conjunction analysis was used to locate the overlap between two separate meta-analyses (i.e., empathy towards physical pain and towards emotional situations) (Nichols et al., 2005). Except for overlapping regions, the differences of activation convergences between empathy towards physical pain and emotional situations also were provided using subtraction analysis (Eickhoff et al., 2012), the purpose of which was to offer the full view of the empathy network. Permutation procedures were adopted to obtain the statistically significant brain map of differences (*permutation times* = 5,000). All included contrasts were shuffled and then were randomly assigned into two groups (i.e., empathy of pain and emotion), in which assigned number of contrasts in each group were equal to the original experiments group. The ALE images of these permuted groups were calculated and subtracted to obtain the null distribution of ALE differences between permuted groups, which then was compared to the observed differences between two groups to calculate the p -values. The final subtraction results were thresholded at $p < 0.01$ and *cluster-extent* $\geq 200 \text{ mm}^3$.

Calculations of fALFF and ReHo maps

The fALFF map was calculated for each participant. fALFF is calculated as the total power within the low-frequency range (0.01–0.10 Hz), divided by the entire frequency (0–0.25 Hz). Then, fALFF were transformed into Z-scores before statistical analyses to make sure the standardization of the data.

Individual ReHo map was described by calculating Kendall's coefficient of concordance for each voxel with its nearest 26 neighbors (Zang et al., 2004). To reduce the influence of individual variations, each ReHo map was divided by the whole brain mean ReHo for each subject. Similarly, the ReHo values were also transformed to Z scores before statistical analysis. The above calculations of both rs-fMRI indicators were conducted using DPABI toolbox. Finally, the brain maps of both indicators were smoothed with a Gaussian Kernel of 4mm FWHM.

ROI-based voxel-wise MVPA

Multivoxel pattern analysis (MVPA) is a powerful data-driven machine learning method and can be used in decoding

the neural activities. MVPA was applied to build the prediction model describing the association between trait empathy and fALFF/ReHo values within empathy-related ROIs. The Kernel Ridge Regression (KRR) algorithm was used to build prediction model in the present study. The KRR is the kernel version of Ridge Regression (RR), which is a linear least square regression with Tikhonov regularization (Chu et al., 2011; Jollans et al., 2019). For each subject, the fALFF maps of ROI were transformed into a column vector, and each value corresponded to a single voxel intensity. Then, the leave-one-out cross-validation (LOOCV) method was applied to estimate the optimal parameters and the performance of the prediction model. The correlation between the observed and predicted scores of trait empathy (predicted R) as well as mean square error (MSE) were calculated to assess the performance of the predictive model. At last, the permutation procedures were conducted to examine whether prediction R and MSE were significantly higher than the random level (1,000 permutations, $p < 0.05$). To provide the further evidence of the predictive associations between trait empathy and IBA, we also calculated the predictive model based on individuals' ReHo value of defined empathy regions.

Results

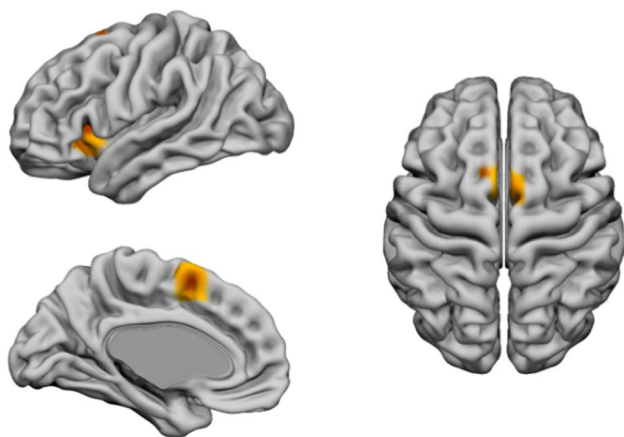
Meta-analysis of empathy

The current meta-analysis included a total of 100 studies, which recruited 2,980 subjects and consisted of 102 independent experiments/contrasts activating 1,515 foci. The included contrasts were also grouped into two datasets of coordinates according to the types of stimuli adopted, in which empathy for physical pain incorporated 65 studies (i.e., 1,807 subjects within 65 independent contrasts activated 1,013 foci) and empathy for emotional situations incorporated 35 studies (i.e., 1,171 subjects within 37 independent contrasts activated 502 foci.). The overall meta-analysis found the comprehensive brain regions activated by state empathy (voxel $p < 0.05$, cluster-forming $p < 0.001$), which included bilateral AI, bilateral MCC extended to ACC, bilateral supplementary motor area (SMA), bilateral IFG, bilateral IPL extending to TPJ, bilateral dmPFC, left thalamus, bilateral amygdala, and left middle temporal gyrus (STG/MTG) (see supplementary Fig. 1A). And the overlap between neural correlates underlying empathy towards physical pain and emotional situations was calculated and confirmed within two clusters of bilateral SMA/CC and left AI/IFG, which was set as ROI for the subsequent MVPA (Table 1; Fig. 1). It is noteworthy that the single meta-analysis of two sub-datasets needed to be performed before overlap analysis and the results were provided in

Table 1 Brain regions activated by state empathy regardless of physical pain and emotional situations as targets (cFWE correction, voxel $p < 0.05$, cluster-forming $p < 0.001$)

Volume	Talairach coordinates			ALE	Label
	x	y	z		
1008	-6	8	52	0.021	SMA/MCC
	4	4	64	0.020	SMA/MCC
720	-30	20	4	0.022	AI
	-34	22	-6	0.020	IFG

SMA, supplementary motor area; MCC, middle cingulate gyrus; AI, anterior insula; IFG, inferior frontal gyrus

**Fig. 1** Overview of general network (cFWE, $p < 0.05$; cluster-forming $p < 0.001$) engaged in state empathy.

[supplementary materials](#). For the full view of the empathy network, the meta-analytic subtraction analysis between neural convergences of empathy towards pain and emotions was also conducted, and the detailed results were provided in [supplementary materials](#).

Descriptive statistics of demographic and behavioral data

The current study collected 106 female subjects in terms of empathy and rs-fMRI data. The ages of the participants fell into the range of 17–26 (mean value: 20.9 ± 2.08 years). Based on IRI scale, the averaged PT score of included females is 12.5 ± 3.11 , and the averaged EC score is 16.7 ± 4.17 . And the correlations between age and PT as well as EC demonstrated no statistical significance (Pearson's $r_{(\text{age}, \text{PT})} = 0.023$, $p = 0.82$; Pearson's $r_{(\text{age}, \text{EC})} = 0.086$, $p = 0.39$). It is worthy to note that two participants self-reported 3 standard deviations higher than the mean value of EC scores. However, their data were not excluded out of the final analysis based on three considerations: (1) after checking the IRI

data, we re-contacted the participants and reconfirmed that the data reflected their reality; (2) to double-check the validity of EC data from such two participants, we asked them to complete the Empathy Quotient Scale, in which they also scored low (both 3 relative to total scores 22) in terms of emotional reactivity sub-component; (3) in the final results of MVPA, the KRR model based on IBA also returned rather low predicted scores of EC for two participants (Fig. 2B).

ROI-based voxel-wise MVPA

Through LOOCV, we found that the regression model allowed the significant predictions of individuals' EC scores based on fALFF values of state-empathy-related ROI (i.e., bilateral SMA/MCC and left AI/IFG, Fig. 2A). This prediction was statistically significant relative to the random level ($R = 0.35$, permutation $p < 0.005$, Fig. 2B & C; MSE = 16.38, permutation $p < 0.005$, Fig. 2D). However, the PT-fALFF association is of no significant results.

Consistent with the above results, the predicted EC value of the regression model based on ReHo of state-empathy-related ROI is also significant. This prediction was statistically significant relative to random level ($R = 0.23$, permutation $p < 0.05$, Fig. 3B & C; MSE = 16.75, permutation $p < 0.05$, Fig. 3D). The PT-ReHo association built using KRR still remained non-significant.

Discussion

The main objective of this study was to explore the intrinsic brain activity of individuals toward predicting trait empathy, which was expected to link the IBA of state empathy to empathic traits. To date, no studies have focused on this topic. Using a combination of task-fMRI, rs-fMRI, and MVPA methods, we first verified the general brain network related to empathic responses, consisting of bilateral CC, bilateral SMA, left IFG, and AI. Moreover, the MVPA results showed that both the ReHo and fALFF values of the above general network can significantly predict the empathic trait (i.e., EC) of an individual. The above findings support the hypotheses we made in the introduction section, which indicate that IBA within state-empathy-related regions also underlies trait empathy and recognizes the potential of rs-fMRI to measure an individual's empathic ability.

General brain network for state empathy

Regardless of the targets, the current meta-analysis identified the general network of state empathy, including bilateral SMA, bilateral CC, left AI, and left IFG. Compared with Fan et al. (2011) and Timmers et al. (2018), the current study adopted different experiment-categorizing strategies

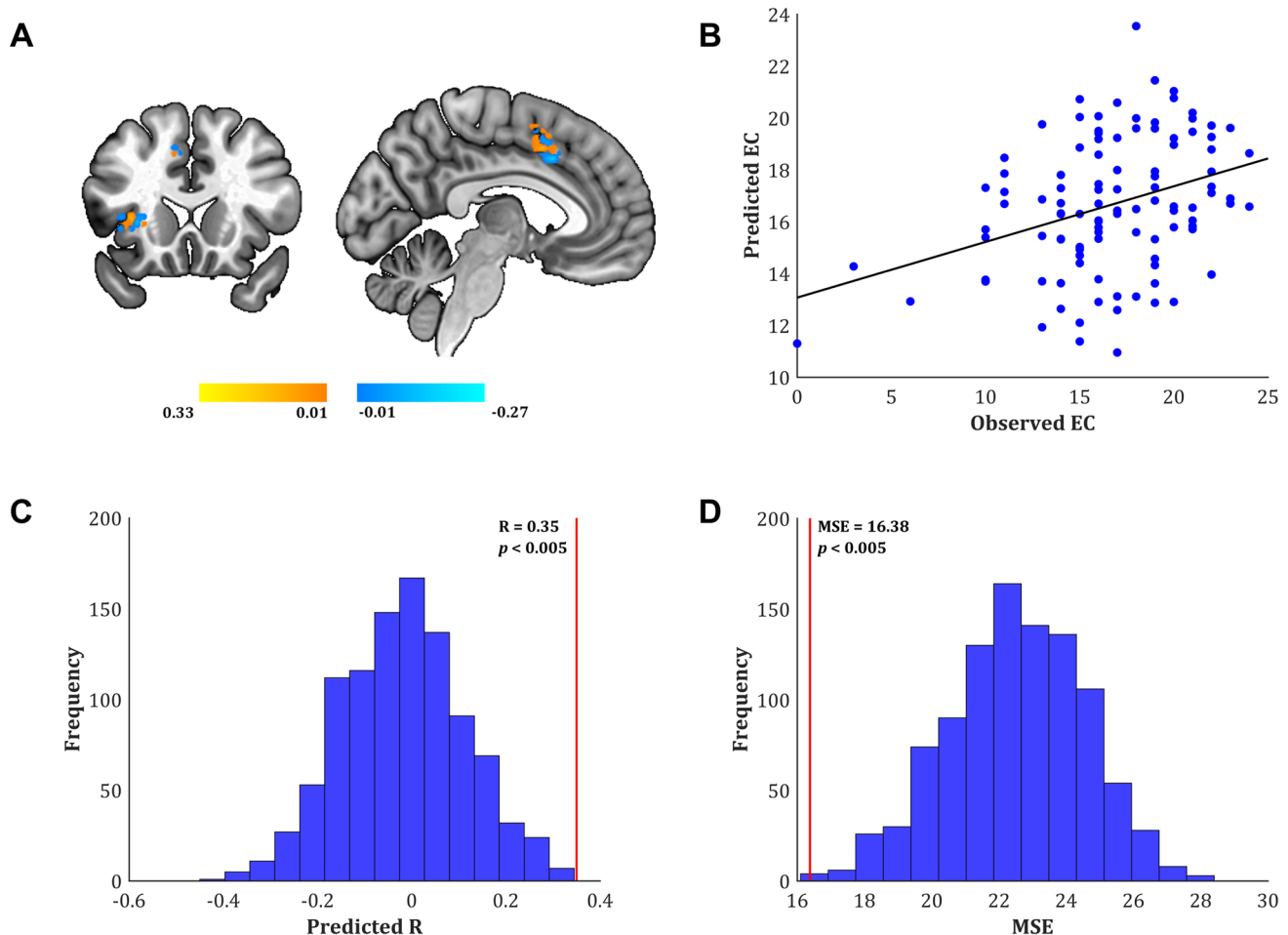


Fig. 2 Results of MVPA based on fALFF. **(A)** Brain regions contributing to the significant prediction of fALFF of individual females, in which color represents the contribution weights. **(B)** Scatter plots illustrating a significant correlation between predicted EC scores and

observed EC scores. **(C)** Distribution of predicted R obtained from the permutation statistic. **(D)** Distribution of MSE obtained from the permutation statistic. The red line indicates the predicted R and MSE derived from LOOCV analyses.

but arrived at similar convergences. Left AI was previously identified across task instructions (cognitive-evaluation empathy vs. affective-perceptual empathy), and the activations of the left MCC and left AI across stimulus types were also confirmed (Fan et al., 2011; Timmers et al., 2018), which offered further support for our defined domain-general network of empathy. In contrast, the current study expanded the general network to the bilateral SMA/MCC, which was partly because more original experiments were included than in Fan et al.'s study and a more precise experiment-categorizing method was employed than Timmers et al.'s. The interpretation and discussion of the role of this region can be found in the next paragraph. Finally, the current study reproduced the results of a previous study by our team (Ding et al., 2020). However, we excluded these studies which used facial expressions as empathized targets, since the lack of contextual information may have led to a lack of empathy toward targets (especially for those targets experiencing

negative feelings). In the current study, we also recruited more original studies in the meta-analysis, and both procedures made the empathy network more precise. This time, stimulus-independent activation of the left AI extending to the IFG was confirmed. Given the absence of similar activations within empathic responses for facial expressions (Ding et al., 2020), it could be speculated that AI/IFG may play an important role in attributing the targets' emotional states (Cerami et al., 2014; Haas et al., 2015). Additionally, the dominant role of AI/IFG in processing affective information has been suggested in previous empathy-related studies (Bernhardt & Singer, 2012), in which AI was preferentially engaged in affective empathy (Kanske et al., 2015; Krämer et al., 2010).

The SMA and A/MCC demonstrated close associations with emotion and pain processing, which is significantly supported by previous empirical studies (Lamm et al., 2007; Singer et al., 2004; Wager et al., 2013). The

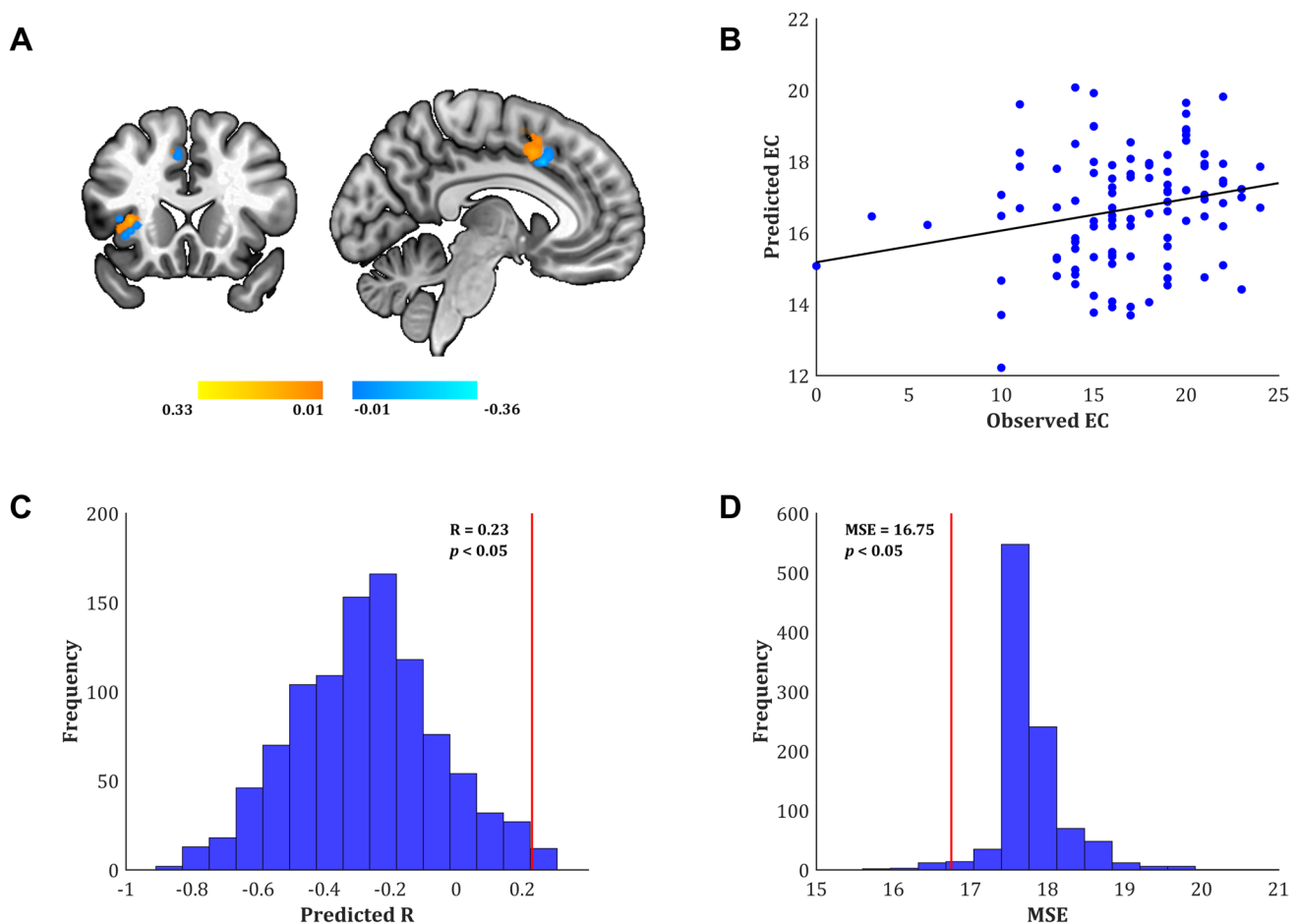


Fig. 3 Results of MVPA based on ReHo. **(A)** Brain regions contributing to the significant prediction of ReHo of individual females, in which color represents the contribution weights. **(B)** Scatter plots illustrating a significant correlation between predicted EC scores and

observed EC scores. **(C)** Distribution of predicted R obtained from the permutation statistic. **(D)** Distribution of MSE obtained from the permutation statistic. The red line indicates the predicted R and MSE derived from LOOCV analyses.

current meta-analysis focused on empathy involving the processing of pain and emotion and successfully located the shared convergences within the bilateral SMA extending to the bilateral MCC. Furthermore, SMA was significantly co-activated with the IFG, IPL, insula, CC, and thalamus, and such a co-activation pattern was associated with various behavioral domains (e.g., cognition, action, emotion). Combined with our findings regarding SMA, this suggests that SMA may play a critical role in linking and coordinating empathy-related regions to achieve empathic functions (Narayana et al., 2012). It should also be noted that MCC extending to the SMA might play a fundamental role in cue-triggered and target-oriented responses (Vogt et al., 2003; Vogt & Vogt, 2003). Such a role can also be applied to empathy, responses of which are triggered by cues and are represented by a series of mental manipulations that must orient toward certain targets. The shared activations in SMA/MCC can be interpreted as a motor-motivation component of empathy, yet such observations can also be caused by the

external orientations of the empathic tasks, as suggested by other studies (Golland et al., 2008). Thus, caution should be exercised when interpreting the results of the current meta-analysis.

Prediction of empathic trait based on IBA within brain regions underlying state empathy

We applied the MVPA method in an attempt to predict empathy traits based on ReHo and fALFF and found some interesting results. Both ReHo and fALFF within regions of state empathy can significantly predict the EC scores of individuals, but not the PT scores.

Although the ROIs (i.e., bilateral SMA/MCC and left AI/IFG) were detected during empathic responses, the regression models built with MVPA also successfully linked the IBA of ROIs and trait empathy. These findings are partly consistent with previous results obtained using univariate analysis (Cox et al., 2012), in which the fALFF of the SMA

was significantly associated with affective empathy (i.e., EC). The current study demonstrates the significant prediction of EC scores and offers robust evidence for the brain-empathy associations within bilateral SMA/MCC and left AI/IFG from the perspective of IBA. As discussed above, SMA/MCC may serve as the motor-motivation component of empathy. Behaviorally, EC could represent the extent to which empathizers are willing to approach the suffering targets. It is thus reasonable to derive the EC predictions based on the IBA of SMA/MCC. The left AI, as Singer et al. (2004, 2006), Singer, (2006) have revealed, may perform dual functions: helping with the subjective feeling of emotional stimuli and the evaluation of stimuli effects on empathized targets. Furthermore, EC, which is associated with signal changes of AI (Singer et al., 2004, 2006), mainly depicts the tendency and ability to show warmth and care for others, which could be improved by understanding the influences of stimuli on others (Gleichgerricht & Young, 2013). This relationship between EC and left AI was further evidenced in the current study, in which EC was predicted from the IBA of AI/IFG.

In this study, EC and PT were used to represent affective and cognitive processing in empathy, respectively (Davis, 1983; Rankin et al., 2006). Our findings offer some supplementary interpretations concerning the specific functions of the general brain network of state empathy, which was identified in the above meta-analysis. The IBA within target ROIs allows for the prediction of EC scores but not PT. This indicates that the functional relevance of the general network may preferentially correspond to the affective processing of empathy functioning. From another perspective, the robust EC-IBA relationship emphasized the important role of EC for empathy, based on which the affective reactions that resonated with the targets may represent a general component of empathy. This requires further investigation. PT, as a cognitive processing for self-other coupling and decoupling, may require more overt instructions and voluntary efforts, which are not necessarily involved in empathic tasks. This possibly led to the absence of PT-related regions in the current meta-analytic general network, which further caused the current MVPA to fail to identify PT-IBA associations within SMA/MCC and AI/IFG.

Finally, our research not only provides a more precise functional distinction for empathic brain regions, but more importantly, it provides a new perspective for measuring empathic ability. Although the high cost of fMRI has hindered the widespread use of this measurement method, it does not hinder the application of this technology in important fields. In particular, our research based on rs-fMRI will provide more objective and reliable evidence and reference for clinical diagnosis and treatment when evaluating the abnormality of empathy and other social functions in patients with mental disorders (Sui et al., 2020; Woo et al.,

2017). The combination of self-report questionnaires and IBA-based predictive models will measure empathic traits more scientifically and comprehensively, which, to some extent, can compensate for some of the drawbacks in traditional methods (i.e., confusing questionnaire results caused by individual subjectivity) and improve the accuracy of the measurement.

Limitations

The current study provides some compelling results; however, it has several limitations. First, due to the imbalance of gender, the experimental results are likely to be affected by gender. In terms of affective empathy, females show higher emotional responsiveness and better emotion recognition abilities (Christov-Moore et al., 2014). Even so, our research illustrates that the above neural representations have an undeniable effect on females' affective empathy. Later studies could add male subjects to verify these results. Second, several previous studies have shown that the concept of empathy is diverse (Batson, 2009; Gerdes et al., 2010; Preston & de Waal, 2002). Although it can be broadly divided into cognitive and emotional empathy (Hoffman, 2007), each aspect includes more specific empathy content. Our research only selected a part of this content for research and the results obtained are also limited in terms of the scope of empathic functions. Subsequent research can expand the predictive effect of neural patterns on empathy to a more comprehensive range of empathy.

Conclusions

Using meta-analytic and MVPA methods, the current study identifies the general brain network related to state empathy, consisting of bilateral CC, SMA, left IFG, and AI, which were activated across different empathic situations (i.e., physical pain and emotional situations). For the first time, we found that the IBA of state empathy allowed for the prediction of trait empathy (i.e., EC) at the individual level. From the perspective of IBA, such a robust association further emphasizes the importance of SMA/MCC and AI/IFG for empathy functioning. Also, it offered new insights regarding affective reactions in empathy, which may represent the general component of empathy. Finally, the significant predictions from the IBA indicated the potential of the objective measurement of empathic ability using rs-fMRI.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.3758/s13415-021-00964-z>.

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Availability of data and materials (data transparency) Data or materials for the experiments reported here is available upon the request to correspondence authors, whereas none of the experiments was preregistered.

Code availability (software application or custom code) Not applicable.

Declarations

Funding and/or Conflicts of interests/Competing interests The authors have no relevant financial or non-financial interests to disclose.

Ethics approval Approval was obtained from the ethics committee of Liaoning Normal University.

Consent to participate and/or Consent to publish Informed consent was obtained from all individual participants included in the study. The participant has consented to the submission of the case report to the journal.

Open Practices Statement None of the data or materials for the experiments reported here is available, and none of the experiments was preregistered.

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