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The ability to understand emotions is associated with interoception-related insular activation and white matter integrity during aging

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Abstract

Cerebral small vessel disease (SVD) is a major cause of cognitive impairment in elderly people. While most research focuses on the role of the classical vascular risk factors in SVD, a description of the psychophysiological mechanisms leading to the age-related brain damage may open new possibilities for prophylaxis. In the current study, we evaluated the associations between emotional abilities, interoception, and age-related vascular white matter degeneration. The work was influenced, first, by multiple studies recognizing alexithymia as a cardiovascular risk factor; second, by theories of emotions linking body's allostasis and emotional regulation; and third, by neuroimaging data highlighting the shared role of the insular cortex in interoceptive and emotional processing. In a sample of older female adults ($N = 30$), we performed the Mayer–Salovey–Caruso Emotional Intelligence Test, functional MRI using the heartbeat detection task, and evaluation of white matter microstructural integrity using diffusion weighted imaging. The ability to understand and analyze emotions—one of the four components of emotional intelligence—was found to be associated with higher interoception-related activation of the right anterior insula and preserved white matter microstructure. We interpret these results in light of the concept of Embodied Predictive Interoception Coding, which proposes that emotional processing, interoception, and allostasis (antecedent top-down regulation of the body's internal milieu) may rely on the shared neural mechanisms of predictive coding. The study demonstrates feasibility of the investigation of cerebrovascular diseases form a psychophysiological perspective and calls for future research.

KEYWORDS

DWI (diffusion weighted imaging), emotions, female, fMRI, Small vessel disease (SVD), neuroscience, interoception

1 | INTRODUCTION

Cerebral small vessel disease (SVD) is a major cause of dementia and disability in aging populations (Hachinski & World Stroke Organization, 2015). During the time course of SVD, abnormalities of the smaller cerebral vessels (i.e., perforating arteries, arterioles, and capillaries) lead to progressive vascular brain damage with predominant involvement of the white matter, which, in turn, results in cognitive impairment (Pantoni, 2010). Several vascular risk factors are linked to the pathogenesis of SVD, including arterial hypertension and smoking (Das et al., 2019). However, the prophylaxis of SVD targeted at correcting these "traditional" factors is of limited efficacy (SPRINT MIND Investigators for the SPRINT Research Group et al., 2019) and, thus, the investigation of "nontraditional" vascular risk factors is appropriate (Bairey Merz et al., 2002). Aberrant emotional processing is increasingly recognized as a factor linked to cardiovascular diseases. Several studies demonstrate higher rates of alexithymia and lower emotional awareness in patients with primary, but not secondary, arterial hypertension (Consoli et al., 2010; Gage & Egan, 1984; Jula, Salminen, & Saarijarvi, 1999; Todarello, Taylor, Parker, & Fanelli, 1995). Emotional regulation has been found to moderate the association between chronic stress and a composite score of cardiovascular disease risk (Roy, Riley, & Sinha, 2018). At the same time, the possible relation between the efficacy of emotional processing and SVD has not been investigated directly.

From a fundamental point of view, cerebrovascular regulation may represent a particular case of allostasis (i.e., antecedent top-down visceromotor regulation of the body's internal milieu), which is known to be linked to emotional processing (Kleckner et al., 2017). The interrelated nature of emotional and interoceptive processing is widely recognized, starting from the early theories of emotion (Cannon, 1927; James, Burkhardt, Bowers, & Skrupskelis, 1981), continuing with the description of the shared brain systems supporting bodily perception and emotional experience (Caseras et al., 2013; Critchley, Wiens, Rotshtein, Öhman, & Dolan, 2004; Pollatos, Gramann, & Schandry, 2007; Terasawa, Fukushima, & Umeda, 2013; Zaki, Davis, & Ochsner, 2012) and leading to recent integrative neuroscientific theories (Barrett, 2017; Kleckner et al., 2017). In recent years, the link between emotions and interoception is being discussed within the predictive model of psychological activity, which is reflected in the concept of Embodied Predictive Interoception Coding (Barrett & Simmons, 2015) and recent updates to the Theory of Constructed Emotion (Barrett, 2017). The brain is thought to continuously anticipate the next external and internal states on the basis of action plans (inner models). Predictions regarding social situations prepare upcoming perceptions of emotions, and predictions regarding the body's state are used for the allostasis (Kleckner et al., 2017). Cerebral vascular regulation is also thought to be based on predictive coding: the hemodynamic response anticipates neural firing in order to prevent a mismatch in blood supply and demand (Das & Sirotin, 2011; Philips, Chhabria, & Chakravarthy, 2016; Sirotin & Das, 2009). Thus, common mechanisms may support emotional perception, interoception, and bodily and cerebrovascular regulation (Barrett & Satpute, 2019).

In summary, we propose that the brain circulation may represent a neurally mediated process intrinsically linked to the social activity of the human and, thus, the SVD may be linked to aberrant emotional–interoceptive processing. This hypothesis is indirectly supported by the existing clinical and physiological research. In the current study, we investigate emotional and interoceptive processing in a sample of older adults with preclinical signs of SVD. The different aspects of emotional processing are assessed within the Mayer–Salovey–Caruso model of emotional intelligence, which is defined as "the ability to perceive and express emotion, assimilate emotion in thought, understand and reason with emotion, and regulate emotion in the self and others" (Mayer, Salovey, Caruso, & Cherkasskiy, 2011). Previously, we had shown that the Mayer–Salovey–Caruso Emotional Intelligence Test (MSCEIT) is a significant predictor of the subjective measure of the rubber hand illusion, which characterizes the multisensory processing of bodily signals (Perepelkina, Boboleva, Arina, & Nikolaeva, 2017). The efficacy and brain-level correlates of interoceptive processing are evaluated during a classical heartbeat detection task, while a commonly utilized technique, diffusion weighted magnetic resonance imaging (DWI MRI), is used to assess the integrity of the white matter, which is predominantly affected by SVD (Lyoubi-Idrissi, Jouvent, Poupon, & Chabriat, 2017).

2 | METHOD

2.1 | Participants

Volunteers were enrolled among nonphysician healthcare workers in Moscow according to the following inclusion criteria:

- age from 40 to 65 years;
- female;
- no history of cardiovascular events, such as stroke or myocardial infarction; and
- no severe white matter hyperintensities according to structural MRI—modified Fasekas score of 2 or less (Fazekas, Chawluk, Alavi, Hurtig, & Zimmerman, 1987).

The participants were interviewed in order to access the presence of known health-related conditions, personal and family history of cardiovascular diseases, and drug use. They were also screened for common syndromes of emotional dysregulation with the use of the Beck Depression Inventory

(Beck, Ward, Mendelson, Mock, & Erbaugh, 1961), the Spielberger State-Trait Anxiety Inventory (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983), and the Screening for Somatoform Symptoms II scale (Rief, Hessel, & Braehler, 2001) and the level of alexithymia was evaluated with the use of Toronto Alexithymia Scale 20 (TAS-20) (Bagby, Parker, & Taylor, 1994). The participant also underwent a 24-hr ambulatory blood pressure monitoring; mean and variability were calculated for the of the 24-hr, day and night systolic and diastolic pressure.

Thirty-two participants were initially enrolled into the study; one participant was excluded due to severe white matter hyperintensities revealed on the MRI, and another participant canceled the participation. The resulting sample consisted of 30 females aged 51 ± 5.7 years. Among health-related conditions, 10 subjects reported primary hypertension (8 of them received antihypertensive drugs), 5—gastrointestinal diseases, 3—autoimmune thyroiditis, and 2—type 2 diabetes mellitus (controlled by oral hypoglycemic agents). Only one participant had mild depression, while other had minimal or no depressive symptoms; three participants met the criteria for somatoform disorders. The Spielberger State-Trait Anxiety Inventory revealed high trait anxiety in 60%, moderate in 36.7%, and low in 3.3% of participants; and high state anxiety in 13.3%, moderate in 53.3%, and low in 33.3% of participants.

The study protocol was approved by the Ethics Committee and the Institutional Review Board of the Research Center of Neurology, and all participants gave informed consent for participation. The procedure consisted of an emotional intelligence test, structural MRI, and functional MRI.

2.2 | Evaluation of emotional intelligence

Emotional intelligence was evaluated with the use of a Russian adaptation of the MSCEIT v. 2.0, which was well validated on an original sample of 638 respondents and in several subsequent studies (Sergienko & Vetrova, 2010; Sergienko, Vetrova, Volochkov, & Popov, 2010). The MSCEIT has a four-factor structure and consists of eight sections, two for each subscale. During the test, the participant is required to complete a variety of tasks reflecting different emotional abilities as described below.

- The ability to perceive and express emotions (Perceiving Emotions subscale) is measured during the identification of emotions in facial expressions (Section A) and in pictures, such as a landscape (Section E).
- The ability to assimilate emotions in thought, such as using them during judgment (Facilitating Thought subscale), is measured in tasks targeted at selecting the emotions that are most effective in a given situation (Section B) and at finding the verbal description for an emotional state (Section F).
- The ability to understand and analyze emotions, including the relations between emotions and their natural dynamics (Understanding Emotions subscale), is measured in tasks requiring an understanding of emotional reactions and their dynamics in complex interpersonal situations (Section C) and analysis of the emotional components of complex feelings such as love or hope (Section G).
- Finally, the ability to regulate emotions reflectively (Managing Emotions subscale) is measured in tasks requiring the evaluation of the efficacy of certain actions in the regulation of one's own emotions (Section D) and of others' emotions (Section H).

The evaluation, lasting for about an hour, was provided by a psychologist blinded to the data of structural and functional MRI. Processing of the data with calculations of the raw and IQ scores was performed by specialists of the Institute of Psychology of Russian Academy of Sciences, authors of the Russian version of the MSCEIT. According to the recommendations on the analysis of the MSCEIT data, raw scales were used for computations (Sergienko & Vetrova, 2010), while for illustrative purposes IQ scores were displayed on the diagrams.

2.3 | MRI data acquisition

MRI was performed with a Siemens MAGNETOM Verio 3T scanner (Erlangen, Germany) located at the Research Center of Neurology. A three-dimensional structural image consisted of a sagittal T1-weighted 3D-MPRAGE sequence (TR 1900 msec, TE 2.47 msec, voxel size 1 × 1 × 1 mm, FOV 250 mm). In addition, T2-weighted (TR 4000 ms, TE 2.5 ms, voxel size 1 × 1 × 1 mm^3, FOV 250 mm), T2 fluid-attenuated inversion recovery (FLAIR, TR 9000 ms, TE 113 ms, voxel size 0.9 × 0.9 × 5 mm, FOV 220 mm) and diffusion-weighted imaging (DWI; TR 6600 ms, TE 100 ms, voxel size 1.1 × 1.2 × 4 mm^3, FOV 220 mm) sequences were applied in order to evaluate the white matter. The magnetic field was registered for further correction of images with the use of a double-echo gradient field map sequence. Functional images were acquired using T2*-gradient echo imaging sequences (TR 2000 ms, TE 21 ms, voxel size 3 × 3 × 3 mm, FOV 192 mm). Four extra functional volumes were acquired at the start of the session and discarded by the scanner software in order to prevent the usage of artifactual data obtained before the magnetic equilibrium could be reached.

A classical technique for the assessment of interoception, the heartbeat detection task, was used in the functional MRI (fMRI) setting (Critchley et al., 2004). Multiple variants of the heartbeat detection task exist; the common point is that an interoceptive condition (attending to one's own heartbeat) is compared with an exteroceptive condition (usually, attending to audial tones) (Schulz, 2016). There is controversy regarding the optimal procedure of response collection: some researchers evaluate accuracy in heartbeat detection using a button press task, where the participant has to make a press for each heartbeat (Caseras et al., 2013; Zaki et al., 2012), while others prefer a task requiring the calculation of one's own heartbeats (Pollatos, Schandry, Auer, & Kaufmann, 2007; Wiebking & Northoff, 2015). In the current study, which to our knowledge is the first fMRI investigation of interoception targeted at aging subjects, we used a simple design with minimum distractors and straightforward instructions. Since our participants with a medical professional background had an a priori knowledge about the usual heartbeat rate, we decided to use button press responses. All participants watched a standard video instruction outside of the scanner, which included training in attending to heartbeats under audio taped fMRI noise. Then, immediately before the task, the instruction was repeated in a presentation inside the scanner.

The protocol of the heartbeat detection task consisted of sixteen blocks with alternating eight interoceptive (Heart) and eight exteroceptive (Sound) conditions (see Figure 1). Each task consisted of an attending phase (20 s), a response phase (6 s), and a rest phase with a fixation cross (6 s). The Heart/Sound phase was indicated on the screen by an ECG/note sign, and at the start of the response phase a finger on a button sign appeared nearby. During the Heart condition, participants were asked to listen to their own heartbeat and, during the response phase, to press a button each time they felt a heartbeat. During the Sound task, "beep" tones were presented at the individual rate of heartbeats with a similar random variance. Before the task, the level of sound was individually adjusted to the minimum that the participant was able to discriminate from the noise of the scanner. The participants were instructed to attend to the tones and, during the response phase, to press a button each time they heard a tone.

The presentation of the task and collection of responses was performed with the use of the Cogent Matlab Toolbox (http://www.vislab.ucl.ac.uk/cogent_2000.php, RRID:SCR_015672). Pulses were recorded with a pulse oximeter by the Siemens Physiological Monitoring Unit, and TAPAS PhysIO Toolbox (https://www.tnu.ethz.ch/en/software/tapas/documentations/physio-toolbox.html) was used for artifact correction, peak detection, and the extraction of interbeat intervals.

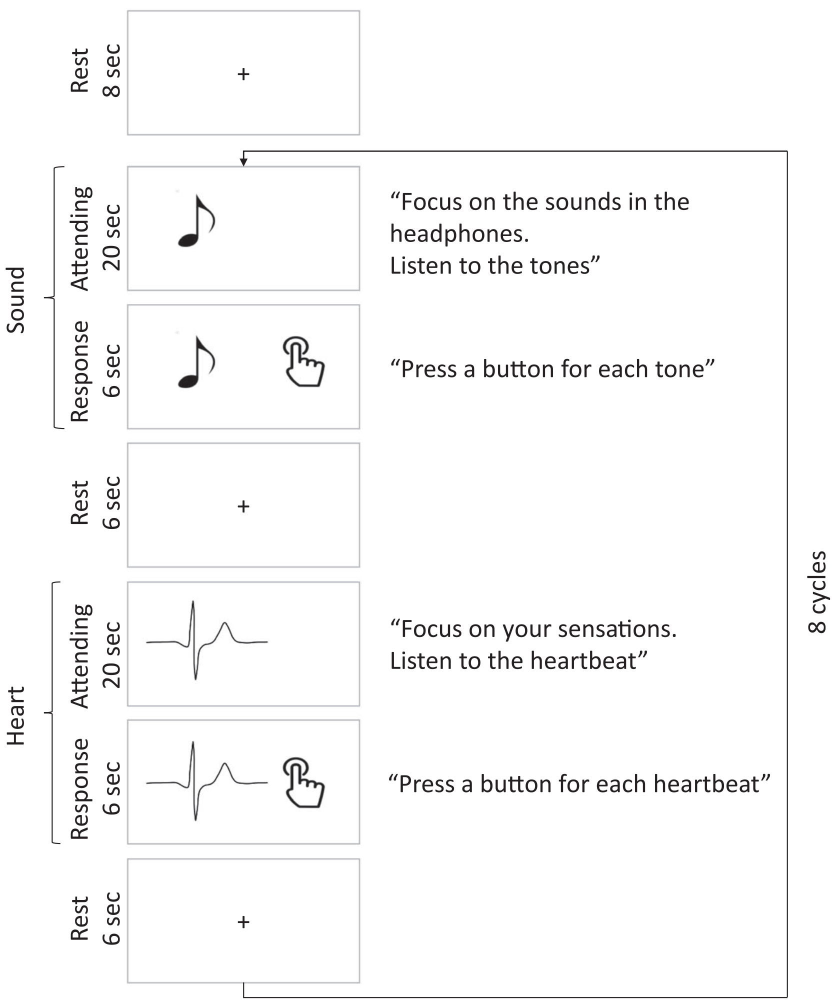

FIGURE 1 The implementation of the interoceptive task used in the fMRI setting. The heartbeat detection (Heart condition) task was repeated eight times, alternating with a control exteroceptive condition—the sound detection (Sound) task. Each condition consisted of an attending phase, when the participant was focusing on the heartbeats or "beep" tones, and a response phase, when a button press was required for each signal. During the Sound condition, the "beep" tones were played through the headphones with a mean rate corresponding to the individual's heart rate and a variance of 50 ms (normal distribution)

2.4 | Analysis of the structural MRI data

In order to exclude participants with severe white matter abnormalities, the T2-weighted and FLAIR images were visually inspected for the presence of white matter hyperintensities and rated in accordance to the Fasekas criteria (Fazekas et al., 1987). One participant was excluded from the study due to a Fasekas score exceeding 2.

DWI data were available for 25 participants. The apparent diffusion coefficient (ADC) was measured manually with the use of individual DWI images. The analysis was performed by an experienced neuroradiologist, who was blinded to the behavioral and fMRI data. The ADC was extracted from eighteen regions of interest (ROI, 4–5 mm in diameter) in the white matter with subsequent averaging (mean ADC). The choice of the white matter integrity measure was influenced by the high sensitivity of the mean ADC: increased diffusivity precedes the appearance of classical ischemic lesions, and along with the fractional anisotropy it is a commonly used marker of early vascular injury (Helenius, Soinne, Salonen, Kaste, & Tatlisumak, 2002; Lyoubi-Idrissi et al., 2017; Mascalchi et al., 2002). The algorithm of ROI selection was based on data about the common localizations of vascular lesions of the white matter (Kim, MacFall, & Payne, 2008) and showed high sensitivity in our previous studies (Dobrynina, Gnedovskaya, Sergeeva, Krotenkova, & Piradov, 2016). An axial slice through the lateral ventricle based above the subcortical structures was chosen (see Figure 2a). The ADC was measured in the anterior, medial, and posterior parts of the white matter on three levels of deepness: periventricular, deep white, and juxtacortical (see Figure 2b). This division follows the classification of Kim et al. (2008), with an exclusion of the juxtaventricular white matter, which we did not evaluate due to the high rate of artifacts originating from cerebrospinal fluid pulsation and the risk of overestimation of the values due to accidental inclusion of voxels from the ventricle. The measurement was performed in the normal appearing white matter: if the ROI included a white matter hyperintensity, an adjacent area was chosen.

Absolute gray matter volume and total intracranial volume were estimated on the base of T1-weighted images with the use of voxel-based morphometry analysis (Ashburner & Friston, 2005) implemented in the Computational Analysis Matlab Toolbox (http://www.neuro.uni-jena.de/cat/). In order to correct for the individual head size, the relative gray matter volume was calculated as the ratio of absolute gray matter volume to total intracranial volume.

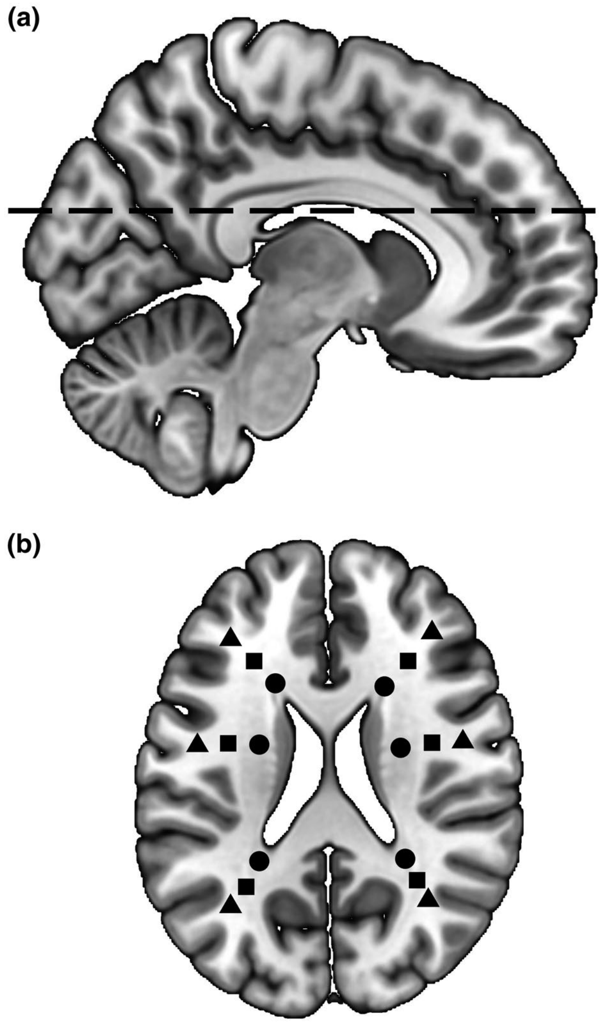

FIGURE 2 Algorithm of the calculation of the mean apparent diffusion coefficient. Measurement of the ADC was performed manually with the use of individual diffusion-weighted images. The algorithm of the ROI selection was based on data about common localizations of vascular brain lesions (Kim et al., 2008) and underwent approbation in our previous studies (Dobrynina et al., 2016). (a) An axial slice was selected at the level of the lateral ventriculi above the subcortical nuclei. (b) Virtual lines of radial orientation were constructed from the anterior horn, pars centralis and the posterior horn of both lateral ventricles. On each of these lines, the ADC was measured in the periventricular (circle), deep white (square), and juxtacortical (triangle) white matter. The resulting 18 values were averaged in order to calculate the mean ADC

2.5 | Analysis of the functional MRI data

Analysis of the fMRI data was performed with the use of Statistical Parametric Mapping (SPM) 12 package (www.fil.ion.ucl.ac.uk/spm, RRID:SCR_007037). The preprocessing included slice-timing correction, calculation of the voxel displacement map, realignment and unwrapping, coregistration of the structural and functional images, spatial normalization into standard Montreal Neurological Institute (MNI) space, and spatial smoothing using a Gaussian kernel of 8 mm full width at half maximum. Physiological noise resulting from central hemodynamics was estimated with the use of the TAPAS PhysIO Toolbox on the basis of the

RETROICOR algorithm (Glover, Li, & Ress, 2000; Kasper et al., 2017). During the first-level analysis, the attending phases of the two conditions (Heart and Sound) entered the model. Realignment parameters and physiological noise regressors were entered as covariates. Individual activation maps were calculated with the use of the "Heart versus Sound" contrast.

In order to access individual performance in the interoceptive task, the widely utilized index Interoceptive Accuracy (IAc) was used (Brener & Ring, 2016). IAc was calculated according to the formula:

$$\text{IAc} = 1/8 \sum_{1}^{8} \left(1 - \frac{\text{Number Actual Beats} - \text{Number Responses}}{\text{Number Actual Beats}}\right).$$

The second-level fMRI data analysis was performed on the basis of the general linear model with the use of SPM. Age was included into all analyses as a covariate of no interest in order to account for the age-related changes in BOLD (blood-oxygen-level dependent)-signal variability (Garrett, Lindenberger, Hoge, & Gauthier, 2017). During the whole-brain analysis, individual activation maps ("Heart vs. Sound") entered the one sample *t* test; IAc was included into the model as a covariate of interest. The group map was thresholded at the voxel level at $p < .001$ uncorrected, with a subsequent cluster-level threshold at *p* family-wise error-corrected (FWE-corr) < .05. The resulting cluster of activation, located in the right aIns (see Figure 3), was extracted with the use of MarsBar SPM Toolbox (http://marsbar.sourceforge.net/, RRID:SCR_009605) for further higher level statistical analysis.

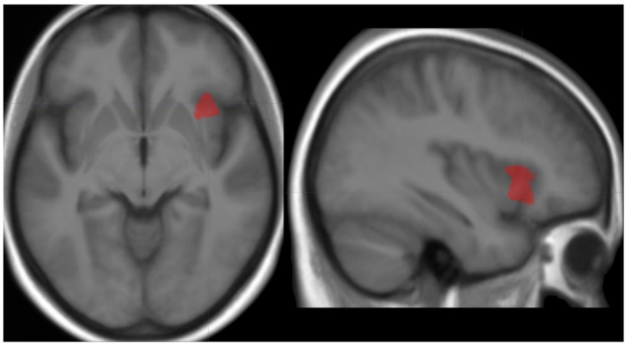

FIGURE 3 Brain activation related to interoceptive accuracy during the heartbeat detection task. One-sample *t* test with contrast "AllSubjects 0; IAc 1; Age 0" was applied to the activation maps calculated for the Heartbeat versus Sound conditions. The image is thresholded at $p < .001$, uncorrected. The mean group anatomical image is used for illustration. A cluster of 86 voxels is observed in the right dorsal anterior insula (cluster-level *pFWE-corr* = .041), which is consistent with other studies of interoceptive processing (Schulz, 2016)

2.6 | Higher level statistical analysis

On the basis of accumulating evidence about the shared nature of interoceptive and emotional processing (Barrett, 2017; Caseras et al., 2013; Terasawa et al., 2013; Zaki et al., 2012), we proposed that at least some components of emotional intelligence (MSCEIT scores) may be linked with the efficacy of heartbeat detection (IAc) and with the recruitment of the brain areas responsible for interoception (activation of the right aIns). Next, we proposed that the level of emotional abilities may correlate with the integrity of the white matter during aging. In order to test these hypotheses, we performed a multivariate general linear model analysis using SPSS software (IBM Corp.), where the IAc, right aIns activation, and mean ADC served as three dependent variables. Along with the four MSCEIT scores (independent variables), age, and relative gray matter volume were entered into the model as a covariates in order to control for their effects. Subsequently, we completed a path analysis to evaluate the pattern of relations between aging, interoception, emotional processing, and white matter integrity with the use of R Project package "Lavaan" (Rosseel, 2012).

3 | RESULTS

3.1 | Interoceptive processing: Brain activation related to the heartbeat detection task

In order to preview the results, we first performed a one-sample *t* test for the interoceptive (Heart vs. Sound) and exteroceptive (Sound vs. Heart) conditions without any covariates. As predicted, the control sound detection task (Sound vs. Heart, one-sample *t* test) was associated with activation in the superior temporal gyrus, predominantly on the right side—a cluster of 262 voxels with a peak at (69; −31; 8), *pFWE-corr* = .001. At the same time, there was no group activation for the interoceptive condition (Heart vs. Sound, one-sample *t* test). Manual analysis of the individual activation maps revealed very high variability, and the same tendency was seen in the IAc values, which ranged from 0.1 to 0.87 with an average of 0.49 ± 0.25. Since interoceptive abilities decline with age (Khalsa, Rudrauf, & Tranel, 2009), in order to reveal the interoception-related brain areas in aging participants it was essential to account for individual performance, which we did by adding the IAc covariate into the model. The resulting analysis of the activation related to the efficacy of heartbeat detection revealed a cluster of 86 voxels in the right aIns (cluster-level *pFWE-corr* = .041) with a peak at (36; 23; −10), belonging to the dorsal anterior insula subsystem (Deen, Pitskel, & Pelphrey, 2011) (see Figure 3). This pattern of activation is consistent with the results of other studies performed in younger subjects (Schulz, 2016).

3.2 | The relation between emotional intelligence scores and interoceptive accuracy, right anterior insular activation, mean apparent diffusion coefficient

The study sample demonstrated an average level of emotional abilities as measured by the MSCEIT (Sergienko & Vetrova, 2010); the results are summarized in Table 1. According to the results of the general linear model analysis (see Table 2), the same component of emotional intelligence—the ability to understand and analyze emotions—was associated with the activation of the right aIns and with the mean ADC, and showed a tendency toward correlation with the IAc (see Figure 4). Other components of emotional intelligence appeared to be independent from the variables of interest. The gray matter volume was related to the mean ADC, while no significant effect of age was detected.

Path analysis revealed independent influence of the ability to understand emotions (coefficient –.68, $p = .001$) and of the gray matter volume (coefficient –.48, $p < .001$) on the mean ADC (see Figure 5). The same time, ability to understand emotions, right insular activation, and IAc appeared to be interlinked.

3.3 | Post hoc analysis

Due to the complex nature of the evaluated phenomena, we took several precautions in order to exclude the possible role of other factors that might better explain the revealed associations. First, in order to control for the influence of age, which in our sample varied from 42 to 62 years, we included it as a covariate into each of the performed analyses and found its effects to be insignificant. It was somewhat unexpected to find no association of age with the variables of interest,

TABLE 1 Results of the Mayer–Salovey–Caruso emotional intelligence test (IQ scores)

	Median	25% Percentile	75% Percentile
MSCEIT: total	96.0	90.0	105.0
MSCEIT: perceiving emotions	103.5	82.0	113.0
MSCEIT: facilitating thought	107.0	98.0	112.0
MSCEIT: understanding emotions	93.5	83.0	102.0
MSCEIT: managing emotions	98.0	82.0	109.0

TABLE 2 Relations between emotional intelligence scores and interoceptive accuracy (IAc), right anterior insular (rAIns) activation, and mean apparent diffusion coefficient (ADC); multivariate general linear model

Source	Dependent variable	*F* statistic	*p* value
Corrected model	IAc	2.406	.069
	rAIns activation*	3.977	.01
	Mean ADC*	5.117	.003
MSCEIT: perceiving emotions	IAc	0.969	.338
	rAIns activation	0.143	.710
	Mean ADC	1.543	.23
MSCEIT: facilitating thought	IAc	1.676	.212
	rAIns activation	1.733	.204
	Mean ADC	1.387	.254
MSCEIT: understanding emotions	IAc	4.349	.052
	rAIns activation*	11.978	.003
	Mean ADC*	15.438	.001
MSCEIT: managing emotions	IAc	0.240	.630
	rAIns activation	0.106	.749
	Mean ADC	0.627	.439
Age	IAc	1.115	.305
	rAIns activation	2.080	.166
	Mean ADC	0.104	.751
Gray matter volume	IAc	3.539	.076
	rAIns activation	1.191	.290
	Mean ADC*	8.518	.009

*stands for $p < .05$.

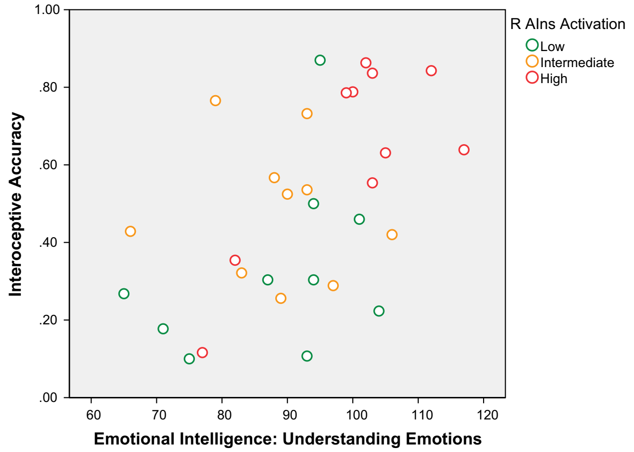

FIGURE 4 The relation between the MSCEIT understanding emotions score and the mean apparent diffusion coefficient. The raw data are displayed on the diagram: each circle corresponds to a single participant. On the horizontal axis, the MSCEIT score Understanding Emotions is represented in the standardized IQ (analogous to the Intelligence Quotient) scores, where 100 is the population mean. On the vertical axis, the mean ADC, which characterizes the microstructural damage of the white matter, is displayed in 10^{-6} mm^2/s. The color of the circle represents the activation of the right anterior insula during the heartbeat detection task (Heart vs. Sound condition), which was categorized into low (percentile below 33%), intermediate, and high (percentile above 66%) for purposes of illustration. The illustration demonstrates that participants with a higher ability to understand emotions have lower mean ADC and higher interoception-related insular activation

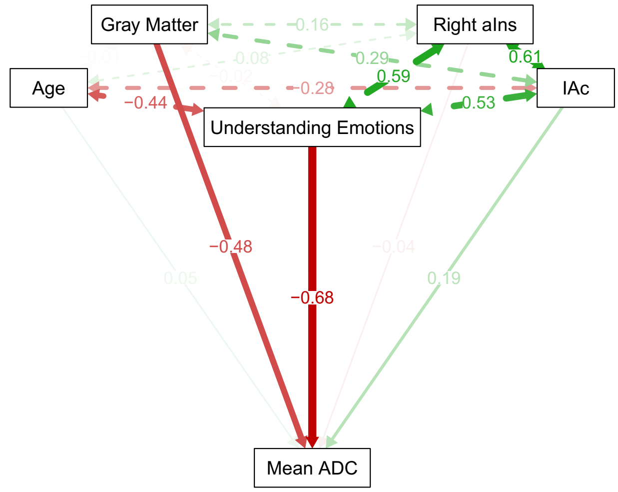

FIGURE 5 Path analysis of the relations between aging, emotional intelligence, insular activation, and white matter integrity. Path analysis was performed in order to evaluate the predictors of white matter integrity as measured by the mean Apparent Diffusion Coefficient (ADC). The MSCEIT score Understanding Emotions, Interoceptive Accuracy (IAc), activation of the right anterior insula (aIns) during the heartbeat detection task, age, and gray matter volume (Gray Matter) were entered into the model as covariates. The model is significant at $p < .001$. Positive relations are visualized as green, negative—as red lines, and estimated coefficients are indicated. The width of the line is proportional to the strength of the relationship, and dashed lines indicate nonsignificant paths. The Understanding Emotions score ($p = .001$) and gray matter volume ($p < .001$) show an independent influence on the mean ADC. Ability to understand emotions is linked with insular activation and IAc, forming a cluster of interrelated phenomena. A tendency toward negative influence of the age and positive influence of the higher gray matter volume on the variables characterizing emotional and interoceptive processing is observed

including the mean ADC (see Table 2). The latter findings may be explained by the absence of younger adults in our sample.

Second, we doubted whether affective disorders might mediate the link between emotional intelligence and white matter integrity. In our sample, there was a minor rate of depression and somatoform diseases, but clinically significant anxiety was frequent—high trait anxiety was detected in 60% of subjects, which is typical for women living in a megapolis (Gafarov, Gromova, Panov, & Gagulin, 2012). Trait anxiety did not correlate with the MSCEIT scores, mean ADC, IAc, and activation of the right aIns, suggesting no mediation. State anxiety, in contrast, positively correlated with the IAc ($R = .413$, $p = .023$), showing no significant correlation with the right aIns activation, MSCEIT scores, and mean ADC. The enhancement of interoceptive accuracy by anxiety is a previously described phenomena (Critchley et al., 2004) which was also present in our study; however, it had a minor or no influence on the dependences falling into the main scope of our investigation.

Third, we examined the role of the primary hypertension, which was present in one third of our participants—the rate common for the age group (Dorans, Mills, Liu, & He, 2018). The subjects with and without this diagnosis did not differ in IAc, MSCEIT scores, right aIns activation, and the mean ADC value. The latter unexpected lack of association (mean ADC 747 ± 38 vs. 734 ± 17, $p = .6$) may be explained by the use of antihypertensive drugs, which were received by 8 of the 10 hypertensive participants: lowering arterial blood pressure, this therapy alleviates the risk of vascular diseases (Das et al., 2019). Analyzing the role of the blood pressure level as measured by the 24-hr ambulatory blood pressure monitoring, we found a tendency toward correlation of the mean night diastolic pressure with the mean ADC ($R = .365$, $p = .087$). This finding is consistent with the results of our previous study on a larger sample of older adults with arterial hypertension and SVD, where we found a significant influence of the diastolic blood pressure level on the ADC (Dobrynina et al., 2019). The same time, none of the evaluated arterial blood pressure estimates correlated with the IAc, right aIns activation, or MSCEIT scores.

Finally, we examined whether the phenomena revealed by the MSCEIT test are close to the concept of alexithymia. According to the TAS-20 scale, five subjects from our sample were alexithymic, while nine had intermediate scores. The TAS-20 score had weak and insignificant correlation with the MSCEIT total and subscales scores, which is consistent with our previous observations (Perepelkina et al., 2017). The TAS-20 score correlated with the interoceptive accuracy ($R = -.412$, $p = .024$) but not with the right aIns activation or the mean ADC value. The major difference between the utilized instruments is that the TAS is a self-rating scale, and, thus, the results depend on the awareness of difficulties, self-esteem, self-concept etc., while the MSCEIT is a test that enables to measure actual performance. In a physiologically oriented study, the latter may be preferable, despite the much higher time consumption.

4 | DISCUSSION

The current study supports accumulating evidence about the interrelated nature of emotional and interoceptive processing (Caseras et al., 2013; Terasawa et al., 2013; Zaki et al., 2012). We showed that higher development of certain emotional abilities is related to stronger activation of the right aIns during the heartbeat detection task (see Table 2). Interestingly, only one subscale of the MSCEIT—Understanding Emotions—entered the results. According to the Mayer, Salovey, and Caruso hyperradical model, the ability to understand and analyze emotions reflects higher level information processing, in contrast with the lower level ability to perceive emotions in facial expressions and pictures (Mayer et al., 2011). Understanding emotions requires the use of complex, probably predictive concepts about the relations between different emotions. For example, in the MSCEIT tasks the participant must judge which emotion is going to follow shame (Section C), or which emotion includes both disgust and anger (Section G).

We propose that this interoception also required higher level processing of information on the basis of previous experience, which makes it similar to the understanding of emotions. First, let us analyze the intrinsic structure of the heartbeat detection task. On the basis of the verbal instruction "listen to the heartbeat," the participant is supposed to find inside the body a signal corresponding to the meaning "heartbeat," filter it from multiple others, integrate it in time and represent it in a form accessible for consciousness. Thus, this task includes multimodal processing of information—multiple distractors, a verbal prompt, body space, interoceptive perception—on the semantic level (finding the signal with a certain meaning). Second, from the neuroanatomical point of view, the area underlying interoception (the anterior insula) has widespread connections with associative brain areas (Ghaziri et al., 2017). Third, according to the Vygotsky Cultural-Historical Tradition, during human development the models underlying body perception and understanding of emotions are both interiorized as verbally mediated culturally governed objects; this view is in agreement with the neuroscientific Theory of Constructed Emotions (Barrett, 2017; Nikolaeva & Arina, 2003). Thus, in line with the Luria's framework, the ability to understand emotions and heartbeat detection may be based on a common operation that is supplied by the right anterior insula (Luria, 1980).

Another important finding of the study is that in an aging sample we observed an association between the ability to understand emotions and white matter integrity (mean ADC), that is independent from the nonspecific effects of age and gray matter volume (see Figure 5). We believe that this finding is best explained in light of the concept of Embodied Predictive Coding (Kleckner et al., 2017). A hidden mediator—efficacy of the internal predictive models, which underlies all types of psychological activity, including interoception and emotions—may explain the study results. In favor of this hypothesis is the fact that the same MSCEIT score Understanding Emotions shows associations both with white matter integrity and with the activation of the right aIns during the heartbeat detection task. This task represents a perceptive activity in a complex multisensory environment targeted at construction of the dynamical heartbeat image on the basis of a semantic ("heartbeat") reference rather than a sensory one. Accomplishment of such an activity requires addressing the inner models of body image, developed during previous experience, that is, the use of predictive coding. The absence of associations between other MSCEIT scores and mean ADC may also be explained within this hypothesis. These components of emotional intelligence reflect lower order information processing (Perceiving Emotions), thinking and judgment (Facilitating Thought), and executive regulation of emotions in oneself and others on the basis of behavioral strategies (Managing Emotions)—all of these processes may be less connected with embodied predictive coding (Mayer et al., 2011).

Meanwhile, in light of the embodied predictive coding, it was surprising not to find a direct correlation between the parameters of interoceptive processing and the mean ADC. This lack of association may be explained either by the underpowered sample size or by the more complex nature of the emotional versus interoceptive processing. According to the study by Zaki and coauthors, the activation related to attending to emotion and attending to heartbeat tasks overlaps in the right aIns, but emotional perception is associated with wider recruitment of brain areas, including the medial prefrontal cortex and temporal lobes (Zaki et al., 2012). Brain correlates of allostasis also extend beyond the interoception-related areas: the regulation of bodily state requires participation of the large-scale salience and default mode networks (Kleckner et al., 2017). Thus, the ability to understand emotions, compared to interoceptive abilities, may better reflect the individual level of development of the neural mechanisms underlying allostasis (the hidden mediator).

There may be alternative explanations for the observed association between the ability to understand emotions and white matter integrity. First, within the behavioral model, it is proposed that emotional regulation mediates the effect of chronic stress on cardiovascular diseases risk (Roy et al., 2018). Individuals with a higher ability to understand and analyze emotions may better adapt in a demanding environment, which, in turn, may lead to a better health state. However, within this paradigm it is difficult to explain why the MSCEIT score for Understanding Emotions, but not others which are more relevant to the topic of self-regulation (such as Facilitating Thought or Managing Emotions) entered the results. Second, a correlational design does not allow us to make conclusions on the direction of the causal associations, and it is reasonable to suspect a biological explanation: what if vascular brain damage even at preclinical stages leads to a decreased ability to understand emotions? Again, this hypothesis fails to explain the different involvement of the four MSCEIT scores. Typical cognitive emotional consequences of SVD include apathy, depression, executive dysfunction and memory decline, but not the impairment of perception (Brookes, Herbert, Lawrence, Morris, & Markus, 2014; Dobrynina et al., 2018; Lohner, Brookes, Hollocks, Morris, & Markus, 2017), and thus, from this biological point of view, an association with emotional regulation rather than with the understanding of emotions would be more expected. Third, in the current study we took a general measure of white matter integrity derived from the regions most commonly involved in SVD, and did not investigate the integrity of the tracts originating from the insula. The insula has extremely widespread structural connections that only recently have fallen under the scope of research (Ghaziri et al., 2018, 2017). The description of age-related alterations in the insular structural connectivity is a complex research task that deserves separate studies. Nonetheless, a bidirectional link between decreased abilities for emotional processing and white matter abnormalities may also exist: a vicious circle which is common for various psychosomatic phenomena may exacerbate the effects of aging on the brain.

The study has notable limitations. Due to the known sex differences in emotional (Fischer, Kret, & Broekens, 2018; McRae, Ochsner, Mauss, Gabrieli, & Gross, 2008) and interoceptive (Grabauskaitė, Baranauskas, & Griškova-Bulanova, 2017) processing and, the same time, due to the prevalence of women among patients with SVD (de Leeuw et al., 2001), we did not include male subjects into the study. Thus, we can make no inference regarding the relations between the emotional and interoceptive abilities and white matter integrity in man, as well as in younger adults. In this pilot study with a relatively small sample, we aimed to avoid excessive heterogeneity of the data. Subsequent studies with wider demographic inclusion criteria are feasible. Another question that remains to be addressed is the potential modulatory role of the cognitive state in observed dependencies.

In conclusion, we have shown for the first time that only a certain component of emotional intelligence—ability to understand and analyze emotions—is related to interoceptive processing, while other components such as the perception of emotions, the use of emotions for facilitation of thinking, and emotional regulation seem to be independent. Importantly, a higher ability to understand and analyze emotions is associated with a lower risk of white matter microstructural damage during aging. The study results are of high practical significance, since the description of psychosomatic vascular risk factors brings new opportunities for prophylaxis, such as psychological or psychophysiological training (Bornemann & Singer, 2017; Shahbazi, Heidari, Sureshjani, & Rezaei, 2018). From a fundamental point of view, our findings fit into the emerging concept of Embodied Predictive Coding, which proposes that shared domain-universal predictive mechanisms under all types of higher order perception and allostasis—a continuous process of internal milieu regulation (Barrett, 2017; Kleckner et al., 2017). The study shows possibility of a psychosomatic view on the problem of age-related cerebrovascular disease and opens the field for subsequent research.

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CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.

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