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Distinct associations of insula and cingulate volume with the cognitive and affective dimensions of alexithymia

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ABSTRACT

Alexithymia ("no words for feelings") is a major risk factor for psychosomatic and psychiatric conditions characterized by affect dysregulation. The alexithymia personality construct comprises an affective dimension, the level of subjective emotional experience (emotionalizing and fantasizing), and a cognitive dimension, referring to the cognitive control of emotions (identifying, analyzing, and verbalizing feelings). These two dimensions may differentially put individuals at risk for psychopathology, but their specific neural bases have rarely been investigated. Therefore, the aim of the present study was to find out whether the two alexithymia dimensions are associated with discriminable neural correlates. By means of voxel-based morphometry (VBM), differences in gray matter volumes were compared between 20 (10 male) high-scorers and 20 (9 male) low-scorers on the Toronto Alexithymia Scale (TAS-20), reflecting the cognitive alexithymia dimension. In a subset of 32 subjects, the impact of the affective alexithymia dimension was tested in addition, as assessed with the affective subscale of the Bermond–Vorst Alexithymia Questionnaire (BVAQ). Analysis 1 (cognitive alexithymia dimension) revealed significantly larger gray matter volumes in the right posterior insula in high-scorers compared to low-scorers on the TAS-20. Analysis 2 (affective alexithymia dimension) revealed that the affective alexithymia dimension, specifically the emotionalizing factor indicative of low emotional reactivity, was associated with larger gray matter volumes of the right cingulate cortex. These results suggest that the two alexithymia dimensions are associated with distinct structural correlates.

1. Introduction

With a prevalence rate of ten percent in the general population, alexithymia ("no words for feelings") is a major risk factor for a range of medical and psychiatric disorders (Taylor, Bagby, & Parker, 1997), including somatoform (Waller & Scheidt, 2004) and panic disorders (Parker, Taylor, & Bagby, 1993). In general, men seem to exhibit higher levels of alexithymia than women, though gender differences are small (Levant, Hall, Williams, & Hasan, 2009). Although alexithymia has long been thought of as a unidimensional construct, it is now acknowledged that it comprises two dimensions, an affective and a cognitive one (Vorst & Bermond, 2001). The cognitive dimension refers to the processing of emotions at the cognitive level and comprises low abilities to identify, analyze, and verbalize one's feelings. These three cognitive alexithymia facets are traditionally assessed with the TAS-20 Toronto Alexithymia Scale (Bagby, Parker, & Taylor, 1994a; Bagby, Taylor, & Parker, 1994b), which comprises the three subscales 'difficulty identifying feelings', 'difficulty describing feelings', and 'externally oriented thinking'. For the TAS-20, a clinical cut-off score has been established that classifies a score equal to or higher than 61 as a clinically relevant alexithymia score (Taylor et al., 1997). The affective alexithymia dimension refers to the level of subjective emotional experience and comprises low degrees of emotional arousal in response to emotion-inducing events (emotionalizing factor), and reduced imaginative capabilities (fantasizing factor). While these affective factors are not part of the TAS-20, they can be assessed by means of the Bermond–Vorst Alexithymia Questionnaire (BVAQ, Vorst & Bermond, 2001).

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Based on these two dimensions, different subtypes of alexithymia have been proposed (Bermond et al., 2007). Individuals with type 1 alexithymia are characterized by high scores on both alexithymia dimensions (i.e., the cognitive processing of emotions as well as the level of subjective emotional experience is reduced) and may be perceived as 'cold-blooded' personalities as they experience little emotional arousal. This type has been proposed to underlie schizoid personality (Moormann et al., 2008) and psychopathy, in which physiological reactions to emotional stimuli are low (Levenston, Patrick, Bradley, & Lang, 2000) and the cognitive processing of emotions is impaired (Lander, Lutz-Zois, Rye, & Goodnight, 2011). In contrast, individuals with type 2 alexithymia may experience emotional arousal to a normal or even heightened extent, but have difficulty regulating their feelings at the cognitive level (i.e., the cognitive processing of emotions is reduced while the subjective experience of emotions is unaffected). Individuals with type 2 alexithymia tend to be emotionally labile as seen in patients with borderline personality disorder (Moormann et al., 2008). This subtype has also been linked to schizophrenia (van der Meer, van't Wout, & Aleman, 2009), which is in line with the theory of the emotional paradox stating that these patients do experience emotions but are unable to show them (Aleman & Kahn, 2005). Taken together, type 1 and type 2 alexithymia might differentially put individuals at risk for psychopathology. However, the neural correlates of the cognitive and affective dimensions underlying the alexithymia subtypes are still poorly understood.

Three brain regions seem to be particularly implicated in emotion processing deficits associated with alexithymia: the anterior cingulate cortex (ACC), the amygdala, and the insula. The ACC is involved in the awareness and monitoring of one's emotional experiences (Heinzel et al., 2010a; Medford & Critchley, 2010) and has been proposed to be a key region in alexithymia (Lane, Ahern, Schwartz, & Kaszniak, 1997). Given its involvement in both emotional experience and cognitively demanding emotional tasks, the ACC could be implicated in both alexithymia dimensions (Bermond, Vorst, & Moormann, 2006; Lane et al., 1997; Larsen, Brand, Bermond, & Hijman, 2003; Wingbermühle, Theunissen, Verhoeven, Kessels, & Egger, 2012). The amygdala is an essential structure for the processing of emotions as it is involved in the evaluation of emotional significance, fear conditioning, emotional reactivity, and general salience detection (Adolphs, 2008, 2010; Sergerie, Chochol, & Armony, 2008). The insula takes part in the cognitive processing of emotions as well as in the generation of emotional states (Medford & Critchley, 2010; Phillips, Drevets, Rauch, & Lane, 2003), and is a key region in the subjective experience of feelings derived from bodily states and emotional arousal (Critchley, Wiens, Rotshtein, Ohman, & Dolan, 2004; Diekhof, Geier, Falkai, & Gruber, 2011). In addition, the insula regulates autonomic activity in reaction to salient stimuli (Menon & Uddin, 2010), is directly involved in pain perception (Craig, Chen, Bandy, & Reiman, 2000; Ostrowsky et al., 2002), and lesions to the insula may cause deficits in balance, light touch, proprioception, pain, taste (Cereda, Ghika, Maeder, & Bogousslavsky, 2002), and heartbeat perception (Khalsa, Rudrauf, Feinstein, & Tranel, 2009). The amygdala and the insula are thought to relate to both alexithymia dimensions, given their involvement in empathy, emotionalizing as well as analyzing emotions (Wingbermühle et al., 2012). Functional imaging studies have reported altered functioning of the ACC (Berthoz et al., 2002; Frewen et al., 2008; Heinzel et al., 2010a; Huber et al., 2002; Moriguchi et al., 2007), the amygdala (Goerlich-Dobre et al., 2013b; Kugel et al., 2008; Miyake, Okamoto, Onoda, Shirao, & Yamawaki, 2012; Reker et al., 2010; Zotev et al., 2011) as well as the insula (Frewen, Pain, Dozois, & Lanius, 2006; Heinzel et al., 2010b; Kano et al., 2003; Kano, Hamaguchi, Itoh, Yanai, & Fukudo, 2007; Moriguchi et al., 2007; Reker et al., 2010; Silani et al., 2008) in relation to alexithymia (for a meta-analysis, see van der Velde et al., 2013). However, all these studies used the TAS-20 scale for alexithymia assessment, which assesses only the cognitive alexithymia dimension. To date, only one functional imaging study took the affective alexithymia dimension into account and found that low emotional reactivity was linked to hyperactivity of the dorsal ACC in response to fearful faces (Pouga, Berthoz, de Gelder, & Grezes, 2010).

Supplementing functional studies, structural imaging studies have begun to reveal changes in cerebral morphology associated with the cognitive alexithymia dimension. Initial studies using manual tracing techniques focused on the ACC as a region of interest (ROI), based on Lane's hypothesis of a core deficit in emotional self-awareness in alexithymia. The first study of this kind found a positive correlation between the cognitive alexithymia dimension and the surface area of the right ACC (Gündel et al., 2004), whereas a second study reported a negative correlation between alexithymia and gray matter volumes of the right rostral ACC (Paradiso, Vaidya, McCormick, Jones, & Robinson, 2008). Subsequent studies using automated Voxel-Based Morphometry (VBM) methods reported reduced ACC volumes (Borsci et al., 2009; Ihme et al., 2013; Sturm & Levenson, 2011) or no volume differences of the ACC in relation to the cognitive alexithymia dimension (Heinzel et al., 2012; Kubota et al., 2011; Zhang et al., 2011). Besides the ACC, structural differences of the insula were observed in some studies (Borsci et al., 2009; Ihme et al., 2013; Zhang et al., 2011), but not in others (Heinzel et al., 2012; Kubota et al., 2011; Sturm & Levenson, 2011). Regarding the amygdala, one study reported smaller amygdala volumes in high-scorers on alexithymia compared to gender-matched low-scorers (Ihme et al., 2013). In addition to the ACC, insula, and amygdala, structural differences in other regions have sporadically been found in relation to the cognitive alexithymia dimension, including middle temporal gyrus (Borsci et al., 2009; Ihme et al., 2013), superior temporal sulcus (Borsci et al., 2009), orbitofrontal gyrus (Borsci et al., 2009), ventral striatum, ventral premotor cortex, and supramarginal gyrus (Kubota et al., 2011). All of these previous studies used the TAS-20 for the assessment of alexithymia, and therefore previous findings can only be related to the cognitive alexithymia dimension, while the impact of the affective alexithymia dimension on morphometric differences has not been investigated yet.

Taken together, results of previous structural studies are equivocal, and no clear picture has yet emerged regarding the morphological underpinnings and the directionality of differences in gray matter volume in relation to alexithymia. Conclusions with respect to gray matter volume differences are further complicated by the fact that such differences may be interpreted in the light of recruitment of additional (compensatory) processing resources, or in the light of a positive relationship between the regular use of a brain region and its size (Maguire et al., 2000). Discrepancies between previous structural alexithymia studies may be due to variance in the range of alexithymia scores between studies (below or above the clinical threshold score on the TAS-20), differences in analysis strategies (region of interest versus whole brain approach), and finally, the fact that all previous structural studies considered only the cognitive alexithymia dimension, despite findings indicating that also the affective alexithymia dimension modulates emotion processing (Bermond, Bierman, Cladder, Moormann, & Vorst, 2010; Goerlich, Aleman, & Martens, 2012; Moormann et al., 2008; Pouga et al., 2010).

The present VBM study investigated the impact of the cognitive ($_c$) alexithymia dimension on gray matter volume in 40 female and male age- and education-matched individuals with either low scores (Low ALEX$_c$ group) or scores equal to or higher than the clinical cut-off score on the TAS-20 alexithymia scale (High ALEX$_c$ group), in keeping with previous studies. In addition, we tested

the impact of the affective alexithymia dimension (i.e., difficulty emotionalizing and fantasizing) on gray matter volumes as assessed with the affective subscales of the BVAQ (Bermond–Vorst Alexithymia Questionnaire) (Vorst & Bermond, 2001) in a subset of 32 subjects. We hypothesized gray matter volume differences in emotion-related brain areas previously suggested to alter in structure and function in alexithymia, particularly the ACC, amygdala, and insula. We further hypothesized that the affective and cognitive alexithymia dimensions would be associated with distinct structural correlates.

2. Methods and materials

2.1. Participants

A total of 1128 individuals filled out the TAS-20 questionnaire online through the community-based study pool run by the Department of Psychology at Harvard University (TAS-20 score range 20–80, mean 44.52 ± 11.81). The cut-off score of 61 on the TAS-20 was used as the minimum score for the group of participants scoring high on the cognitive alexithymia dimension (High $ALEX_c$). As there is no established cut-off score for low alexithymia, a TAS-20 score of 35 (i.e., the 25th percentile) was used as the maximum score for the group of participants scoring low on the cognitive alexithymia dimension (Low $ALEX_c$).

Individuals with TAS-20 scores above 61 or below 35 were then contacted and screened for eligibility via a phone interview. Potentially eligible individuals were invited to the lab and interviewed by trained graduate students with the M.I.N.I. neuropsychiatric interview (Sheehan et al., 1998, Journal of Clinical Psychiatry). Thus, only healthy individuals without a psychiatric condition participated in the study. Further exclusion criteria were: substance abuse or dependence, loss of consciousness resulting from head injury, significant vision problems, and MR contraindications.

The final sample consisted of 40 right-handed, fluent English speaking, healthy individuals aged between 18 and 40 years. Twenty participants with TAS-20 scores equal to or higher than 61 formed the High $ALEX_c$ group, twenty participants with TAS-20 scores below 35 formed the Low $ALEX_c$ group. TAS-20 scores in the Low $ALEX_c$ group (n=20, 9 male) ranged from 20 to 35 (mean 27.65 ± 3.82), TAS-20 scores in the High $ALEX_c$ group (n=20, 10 male) ranged from 61 to 77 (mean 67.20 ± 7.48). The study comprised two sessions: A scan session including the anatomical scan used for the present VBM analyses and two functional MRI tasks (which will be reported elsewhere), and a behavioral session, in which the BVAQ was to be filled out amongst other questionnaires not used for the present study.

Each participant gave informed consent prior to the study. The study protocol was approved by the International Review Board (IRB) of Harvard University and conducted in compliance with the Declaration of Helsinki. The participants received monetary compensation for participation.

2.2. Alexithymia questionnaires

2.2.1. Toronto Alexithymia Scale (TAS-20)

The TAS-20 (Bagby et al., 1994a; 1994b) is currently the standard measure of alexithymia and has a demonstrated validity, reliability, and stability. This self-report scale consists of 20 items rated on a 5-point Likert scale. It comprises three subscales assessing the cognitive dimension of alexithymia: (1) difficulty identifying feelings (DIF), (2) difficulty describing feelings (DDF), and (3) externally oriented thinking (EOT). Possible scores range from 20 to 100, higher scores indicate higher degrees of alexithymia. Individuals with TAS-20 scores lower or equal to 51 are considered non-alexithymic, a score from 52 to 60 indicates moderate alexithymia, and a score of 61 or higher indicates clinical alexithymia.

Analysis 1 (High $ALEX_c$ group versus Low $ALEX_c$ group) was based on TAS-20 scores in order to analyze differences in gray matter volumes in relation to the cognitive alexithymia dimension.

2.2.2. Bermond–Vorst Alexithymia Questionnaire (BVAQ)

In order to assess the affective alexithymia dimension, the Bermond–Vorst alexithymia questionnaire (BVAQ) was used (Vorst & Bermond, 2001). The BVAQ consists of 40 items rated on a 5-point Likert scale, and has five subscales. The subscales (1) identifying, (2) analyzing, and (3) verbalizing feelings assess the cognitive alexithymia dimension. The sum score of these three cognitive BVAQ subscales overlap substantially with the TAS-20 sum score (r=.80), indicating that these scales measure the same features of alexithymia (Berthoz, Ouhayoun, Perez-Diaz, Consoli, & Jouvent, 2000; Vorst & Bermond, 2001). The additional BVAQ subscales (4) fantasizing (the degree to which someone is inclined to imagine, daydream, etc.) and (5) emotionalizing (the degree to which someone is emotionally aroused by emotion-inducing events) assess the affective dimension of alexithymia. Higher scores on the cognitive alexithymia dimension indicate lower abilities to interpret, analyze, and verbalize one's feelings. Higher scores on the affective alexithymia dimension indicate diminished fantasizing ability and reduced emotional reactivity.

The validity of this two-factor structure of the BVAQ with an affective dimension versus a cognitive dimension has been demonstrated by factor-analyses in six languages and seven populations (Bermond et al., 2007). A validated English version of the BVAQ (Zech, Luminet, Rimé, & Wagner, 1999) was used to assess scores on the two affective BVAQ subscales (fantasizing and emotionalizing) in the present study, which were then included as regressors in analysis 2. This analysis aimed at testing the impact of the affective alexithymia dimension on gray matter volumes in a subset of participants (n=32).

2.3. Image acquisition and analysis

MRI data were acquired with a 3-T Siemens Magnetom TrioTim scanner at the Center for Brain Science (CBS) of Harvard University. A 32-channel RF head coil was used to acquire whole brain T1-weighted structural images for VBM analyses [1-mm^3 isotropic voxels, TR=2.53 s, TE=10.3 ms, flip angle=7°, FOV=256 mm, slice-thickness=1 mm].

2.4. VBM analysis

2.4.1. Preprocessing

Data were preprocessed using the SPM8 software (Wellcome Department of Imaging Neuroscience Group, London, UK; http://www.fil.ion.ucl.ac.uk/spm) running under MATLAB 2009b (The MathWorks, Natick, MA, USA) and the VBM8 toolbox (Gaser, 2009). That is, within the same generative model (Ashburner & Friston, 2005) images were reoriented to the intercommissural plane, corrected for field intensity inhomogeneities, and spatially normalized into standard space using the DARTEL default template of VBM8, which is based on 550 healthy control subjects and thus better suited to represent the healthy population than a study-specific template would have been. The images were segmented into gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF). The segmented tissue was then modulated with Jacobian determinants. Because normalization expands some brain regions and contracts others, modulation scales by the amount of expansion or contraction. Consequently, the total volume of gray matter in modulated images remains the same as in the original images. Finally, the modulated gray matter volumes were smoothed with a Gaussian kernel of 8 mm full width at half maximum (FWHM). An 8 mm smoothing kernel is optimal for detecting morphometric differences in both large and small neural structures (Honea, Crow, Passingham, & Mackay, 2005; White et al., 2001). Larger smoothing kernels (10–12 mm) are likely to miss group differences in small structures, whereas smaller kernels (4–6 mm) can produce false positive findings (Honea et al., 2005). Homogeneity check identified one outlier (>2SD from the mean), and the corresponding subject was excluded from subsequent analyses. The normalized, modulated, and smoothed gray matter segments of the remaining 39 (18 male) subjects were used to conduct the statistical analyses outlined below.

2.5. Statistical analysis

Whole brain voxel-by-voxel statistical analyses of gray matter volume were performed using the VBM8 software in SPM8 implemented in Matlab. Analysis 1 (cognitive dimension) was performed using a two-sample t-test with the factor group (Low $ALEX_c$ versus High $ALEX_c$), and gender and total brain volume (TBV, the sum of gray matter and white matter) included as covariates of no interest. This group analysis tested for gray matter volume differences in high-scorers versus low-scorers on the cognitive alexithymia dimension as assessed by the TAS-20 scale. Results were masked with a gray matter mask produced by averaging the GM-segmented anatomical images of the 39 subjects included in the analysis.

Scores on the affective dimension of the BVAQ (Bermond–Vorst Alexithymia Questionnaire) were available for a subset of 32 (13 male) participants, allowing for a further analysis specifically testing the impact of the affective alexithymia dimension on gray matter volume. The subset of analysis 2 (affective dimension) consisted of 18 high-scorers and 14 low-scorers on the TAS-20 alexithymia scale. Gray matter segments of these subjects were included in a multiple regression design with scores on the fantasizing factor and the emotionalizing factor of the affective alexithymia dimensions included as regressors. The design controlled for gender and TBV by including both as covariates of no interest. See Table 1 for a detailed characterization of the alexithymia groups included in analysis 1 (cognitive dimension) and analysis 2 (affective dimension).

The threshold for both whole brain analyses was set at $p<0.05$ Family-Wise Error (FWE) corrected at the cluster level (corrected for non-stationarity of smoothness) with an initial threshold of $p<0.001$ and an extent threshold of k=40 voxels.

Table 1
Characterization of alexithymia groups.

	Analysis 1: cognitive dimension		Analysis 2: affective dimension	
	Low $ALEX_c$ mean ± SD, range	High $ALEX_c$ mean ± SD, range	Low $ALEX_c$ mean ± SD, range	High $ALEX_c$ mean ± SD, range
TAS-20	26.8 ± 4.6, 20–34	67.2 ± 7.5, 61–77*	26.3 ± 3.5, 20–34	67.1 ± 4.7, 61–77*
DIF	11.05 ± 3.68, 7–19	23.43 ± 2.48, 19–28*	10.44 ± 3.86, 7–19	23.31 ± 2.52, 19–28*
DDF	9.01 ± 1.98, 5–14	17.35 ± 1.94, 14–21*	8.31 ± 1.62, 5–11	17.44 ± 1.97, 14–21*
EOT	17.36 ± 3.61, 8–22	24.29 ± 3.96, 19–34*	16.51 ± 3.54, 8–22	24.63 ± 3.85, 20–34*
BVAQ affective	–	–	54.7 ± 7.2, 43–70	43.3 ± 9.7, 20–56*
Emotionalizing	–	–	24.79 ± 6.51, 18–36	25.01 ± 7.89, 8–39
Fantasizing	–	–	29.93 ± 6.28, 17–40	18.23 ± 5.18, 11–28*
Age	26.8 ± 7.5, 19–47	23.7 ± 5.5, 18–41	28.0 ± 7.9, 19–47	23.4 ± 5.6, 18–41
Total brain Volume	1522.8 ± 66.1, 1422.5–1650.6	1504.8 ± 67.7, 1342.9–1632.1	1520.3 ± 78.5, 1342.9–1650.6	1514.5 ± 56.5, 1408.0–1604.0

* $p < 0.001$.

3. Results

3.1. Behavioral data

Results of the alexithymia scale ratings and characteristics of the two $ALEX_c$ groups are presented in Table 1. Internal consistencies as indexed by Cronbach's α ranged from acceptable to excellent for the three subscales of the TAS-20 (DIF, $\alpha = .912$; DDF, $\alpha = .800$; EOT, $\alpha = .703$) and was good for the two affective subscales of the BVAQ (emotionalizing, $\alpha = .829$; fantasizing, $\alpha = .829$). The three TAS-20 subscales were significantly correlated with each other (DIF and DDF, $r = .895$, $p < 0.001$; DDF and EOT, $r = .675$, $p < 0.001$; DIF and EOT, $r = .552$, $p < 0.001$). The two affective BVAQ subscales, however, were not significantly correlated ($r = -.092$, $p = .309$). A two-sample *t*-test showed that the Low $ALEX_c$ group had significantly lower scores on the affective alexithymia dimension than the High $ALEX_c$ group, resulting from significantly better capacities to fantasize in low-scorers on cognitive alexithymia (see Table 1). Within-group correlations between TAS-20 scores and the affective BVAQ subscale further showed that the two measures did not correlate in either group (Low $ALEX_c$, $r = -0.331$, $p = 0.247$; High $ALEX_c$, $r = 0.165$, $p = 0.512$). Total brain volume and age did not differ between $ALEX_c$ groups in either analysis.

3.2. Imaging data

Analysis 1 (cognitive dimension) revealed significantly larger gray matter volumes in one cluster with peak GM differences in the right posterior insula ($p_{FWE} < 0.05$) for the contrast High $ALEX_c$ > Low $ALEX_c$, extending to the rolandic operculum, superior temporal gyrus, and Heschl's gyrus in the right hemisphere (Fig. 1, Table 2). This finding suggests that high scores on the cognitive dimension were associated with significantly larger gray matter volume of the right posterior insula (Fig. 1). There was no interaction between group and gender. The contrast Low $ALEX_c$ > High $ALEX_c$ revealed no significant differences at $p_{uncorr} < 0.001$.

Analysis 2 (affective dimension) revealed that the emotionalizing factor of the affective alexithymia dimension correlated with larger GM volume in the right posterior mid cingulate cortex (MCC) at $p_{FWE} < 0.05$, indicating that higher scores on the emotionalizing factor (i.e., less emotional reactivity) were associated with larger MCC volume (Table 2). This significant correlation ($r = .46$, $p < .001$) between the emotionalizing factor and mean gray matter volumes of the cingulate cluster at the peak coordinate is displayed in Fig. 2. No significant correlations of the fantasizing factor with GM volumes were observed.

GM volume differences in the amygdalae were not found in the above analyses. Due to the small size of the amygdalae and the resulting risk of missing amygdalar differences with a larger smoothing kernel, both analyses were repeated using a smaller kernel of 4 mm. However, also with the smaller smoothing kernel no GM volume differences in the amygdalae were found in relation to either alexithymia dimension.

Moreover, power analyses were performed by means of the recently developed tool PowerMap (Joyce & Hayasaka, 2012), which is specific to voxel-wise (mass-univariate) analyses of neuroimaging data as it corrects for multiple comparisons. For the insula cluster ($k = 1185$, analysis 1), PowerMap calculated that the required sample size to achieve a desired power of 80% (FWE corrected) was $n = 36$, suggesting that statistical power in analysis 1 ($n = 39$) was adequate. For the cingulate cluster ($k = 350$, analysis 2), the sample size required to achieve a desired power of 80% was calculated to be $n = 59$, suggesting that statistical power in analysis 2 ($n = 32$) was not sufficiently high. Thus, this finding should be considered preliminary.

4. Discussion

The present study aimed to find out whether the cognitive and affective dimensions of alexithymia are associated with distinct neural substrates in a group of female and male individuals with TAS-20 scores above the clinical threshold, compared to a group of individuals with low alexithymia scores. We found that the cognitive alexithymia dimension was related to significantly larger gray matter volumes of the right posterior insula, whereas the affective dimension was associated with larger gray matter volumes in the right posterior MCC. These results confirm our hypothesis that distinct neural substrates underlie the two alexithymia dimensions.

The cingulate cortex is assumed to be a key correlate of alexithymia based on Lane's 'blindfeel hypothesis', stating that the core deficit of alexithymia lies in the conscious awareness and experience of emotions (Lane et al., 1997). Initial structural studies on alexithymia found a positive correlation (Gündel et al., 2004) and a negative correlation (Paradiso et al., 2008) between alexithymia and gray matter volumes of the right ACC. Subsequent VBM studies reported either reduced ACC volumes (Borsci et al., 2009; Ihme et al., 2013; Sturm & Levenson, 2011) or no ACC volume differences in relation to alexithymia (Heinzel et al., 2012; Kubota et al., 2011; Zhang et al., 2011). These studies could not yet clarify whether (a) alexithymia is associated with smaller or larger cingulate volume, and (b) whether cingulate volume is associated with the cognitive or the affective alexithymia dimension, as all of these studies assessed only the cognitive alexithymia dimension without providing information as to how its affective dimension relates to differences in cingulate volume. Functional imaging studies frequently reported increased activity of the cingulate cortex in relation to the cognitive alexithymia dimension

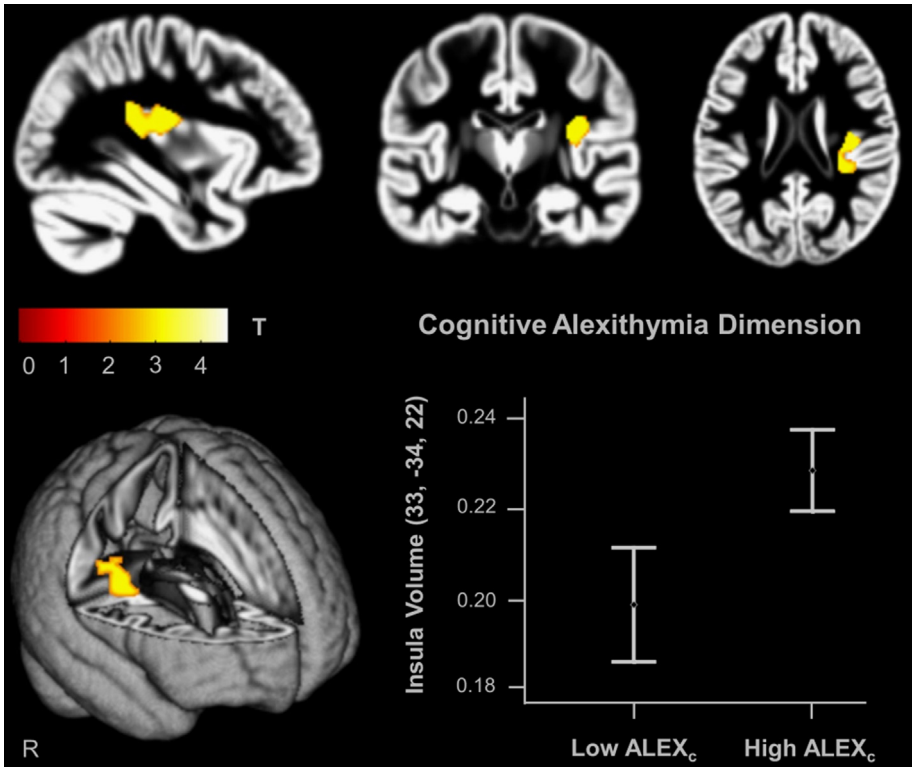

Fig. 1. Cognitive alexithymia dimension. Gray matter volume of the right posterior insula compared between the Low ALEX$_c$ and High ALEX$_c$ groups, created on the basis of the TAS-20. The *y*-axis of the boxplot shows the mean gray matter volume of the insula cluster at the peak coordinate. Error bars represent 95% confidence intervals. Results are displayed at $p_{uncorr} < 0.001$ and overlaid on a gray matter template created by averaging the segmented T1 images of all participants.

Table 2
Cognitive and affective alexithymia dimensions: gray matter volume differences.

	Area (aal)	*K* (cluster extent)	*x*	*y*	*z*	*T* score	P_{FWE} cluster level	P_{uncorr} peak level
Cognitive dimension	Insula *R*	1185	30	−34	22	4.78	0.05	0.001
			33	−16	21	3.89		
			36	−39	15	3.73		
			23	−37	19	3.51		
			26	−37	30	3.27		
Affective dimension	Cingulate *R*	350	9	−16	42	5.05	0.05	0.001
			20	−21	46	4.38		
			−6	−13	40	3.61		

(e.g., Berthoz et al., 2002; Frewen et al., 2008; Heinzel et al., 2010a; Mériau et al., 2006). The only functional study that investigated the relationship between the affective alexithymia dimension and cingulate activity found that dorsal ACC activity was significantly correlated with the emotionalizing factor of the affective alexithymia dimension during the viewing of fearful faces (Pouga et al., 2010).

Besides the anterior portion of the cingulate cortex, also its middle portion has been shown to be relevant for emotional processing. The MCC has been implicated in emotional awareness and valence evaluation (for meta-analyses, see Brown, Gao, Tisdelle, Eickhoff, & Liotti, 2011; Kühn & Gallinat, 2012). Recently, an association between the MCC and the alexithymia facet difficulty describing feelings has been reported (Lemche et al., 2013). In the present study, we found larger MCC volume in individuals scoring high on the emotionalizing factor of the affective alexithymia dimension, indicating low emotional reactivity. The regulation of emotional responses, specifically the attempted inhibition of arousal has been repeatedly associated with cingulate activity (Beauregard, Levesque, & Bourgouin, 2001). This may suggest a relation to the affective alexithymia dimension, particularly the emotionalizing factor that indexes emotional reactivity. Increased activity of the cingulate cortex may represent an effort of high-alexithymic individuals to down-regulate the arousal elicited by emotional stimuli, for example, by recruiting additional resources (Heinzel et al., 2010a). This would be in line with the observation that high-alexithymic individuals tend to suppress their emotions as their main strategy of emotion regulation (e.g., Goerlich-Dobre et al., 2013a; Swart, Kortekaas, & Aleman, 2009). The present result of larger MCC volume in relation to the affective alexithymia factor low emotional reactivity may be a consequence of the use of additional resources that are recruited when emotional arousal is down-regulated or suppressed. However, our interpretation of larger MCC volume observed here remains speculative, and the relation between the affective alexithymia dimension and cingulate volume needs to be investigated in future studies involving larger samples.

Regarding the cognitive alexithymia dimension, we identified larger gray matter volumes in the insula. This finding corroborates and extends the results of previous studies reporting differences in function (Bird et al., 2010; Kano et al., 2003; Karlsson, Naatanen, & Stenman, 2008; Moriguchi et al., 2007; Reker et al., 2010) and

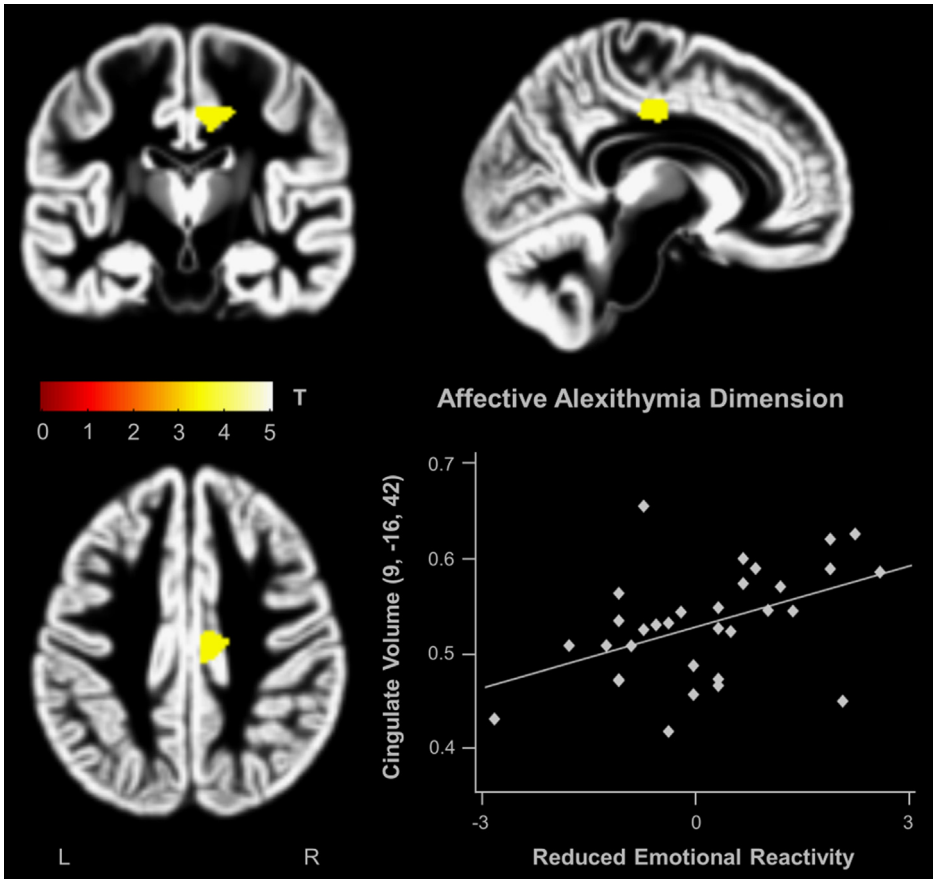

Fig. 2. Affective alexithymia dimension. Gray matter volume of the right posterior mid cingulate cortex in relation to the emotionalizing factor of the affective alexithymia dimension, assessed with the BVAQ. The *y*-axis of the scatterplot shows the mean gray matter volume of the cingulate cluster at the peak coordinate. Results are displayed at $p_{uncorr} < 0.001$ and overlaid on a gray matter template created by averaging the segmented T1 images of all participants.

structure (Ihme et al., 2013; Zhang et al., 2011) of the insula in relation to alexithymia. It is also in line with the finding that emotional intelligence, a construct closely and inversely related to alexithymia (Fukunishi et al., 2001; Parker, Taylor, & Bagby, 2001) has been associated with reduced gray matter density of the right insula (Takeuchi et al., 2010). Differences in insular cortex were not found for the affective alexithymia dimension, and thus these differences may be specific to impairments in the cognitive processing of emotions.

The insula has long been recognized as a relevant region for the processing of emotions (Adolphs & Damasio, 2000; Craig, 2009; Craig, 2002; Damasio, 1999; James, 1884). It is considered a central brain region in a network underlying emotional awareness of self and others, being at the transition of information about bodily arousal and physiological state into conscious awareness of feelings. The insula is critically involved in representing the degree of subjectively perceived emotions (Diekhof et al., 2011). Insular cortex functions as a center of multimodal convergence that relays information from unimodal sensory, visual, and auditory cortices to higher-order association cortex, allowing these regions to modify autonomic and visceral outflows (Mesulam & Mufson, 1985; Mufson & Mesulam, 1982). Posterior portions of the insula receive direct representations of homeostatic afferent information via thalamocortical pathways, and project this information onto the right anterior insula (Craig, 2002). The posterior insula is therefore directly involved in the representation of bodily states during emotional experience, in other words in psychosomatic function with autonomic regulation (see also Penfield & Faulk, 1955).

Alexithymia was originally discovered in patients with psychosomatic disorders (Sifneos, 1973). Difficulty identifying feelings and distinguishing them from bodily sensations is a defining characteristic of this condition. Alexithymic individuals fail to effectively regulate emotions at a cognitive level and tend to somatize their feelings instead, i.e., feelings find expression in bodily states. This becomes apparent in the alexithymic tendency to use somatic terms to describe their feelings (Taylor et al., 1997). Given this tendency to somatize emotions on the one hand, and the role of the insula as a direct representation of bodily states involved in psychosomatic processing on the other, it appears conceivable that the insula is a key region of emotion processing deficits associated with alexithymia. Indeed, Karlsson et al. (2008) suggested that bodily brain regions (i.e. the insula and somatosensory cortices) may be overactive during emotional processing in alexithymics, possibly reflecting the alexithymic tendency to experience physical symptoms when emotionally aroused. In the same line, Zhang et al. (2011) interpreted their finding of increased gray matter density in relation to alexithymia as indicative of a greater reliance on bodily sensations during the subjective experience of emotion. Kano et al. (2007) specifically tested the neural correlates of visceral hypersensitivity in alexithymia. They found that the right insula was hyperactive during colonic extension in individuals scoring above the clinical cut-off score on the TAS-20. In addition, the more alexithymic the individuals, the more anxiety they expressed during visceral stimulation, accompanied by higher blood levels of adrenaline. The authors concluded that high-alexithymic individuals may become more aroused by the experience of unpleasant feelings, thereby displaying more autonomous responses reflected in increased activity of the right insula.

Regular use of a brain region may correlate with its size as shown for taxi drivers whose posterior hippocampus, which stores

spatial representations of the environment, was larger than in control subjects, suggesting that the hippocampus expands regionally to accommodate elaboration of spatial representations in people with navigational expertise (Maguire et al., 2000). However, the present study identified larger gray matter volumes in the insula and cingulate cortex in individuals scoring high on alexithymia, a personality trait associated with pronounced difficulties, rather than expertise, in the processing and regulation of emotions. Thus, we interpret the present findings as more likely to reflect a recruitment of additional processing resources in order to accomplish emotion processing in alexithymia.

Besides structural differences in insular and cingulate cortex, we also predicted that amygdalar volume would be affected by the alexithymia dimensions based on reports of functional differences in the amygdala (Goerlich-Dobre et al., 2013b; Kugel et al., 2008; Miyake et al., 2012; Reker et al., 2010; Zotev et al., 2011) and reduced amygdalar volume in relation to alexithymia (Ihme et al., 2013). However, amygdalar volume differences were not observed in this study, in line with other studies, which also failed to find differences in amygdalar volume (Borsci et al., 2009; Heinzel et al., 2012; Kubota et al., 2011). Therefore, the involvement of the amygdalae as structural correlates of the alexithymia dimensions remains inconclusive and requires further investigation.

4.1. Limitations

Alexithymia shows comorbidity with several other emotional disturbances, such as depression and anxiety (Taylor, 2000). Though subjects with a psychiatric diagnosis were excluded from this study, subclinical levels of anxiety and depression were not specifically assessed, and we thus recommend controlling for these factors in future studies. Moreover, it could be worthwhile to investigate the specific relation between alexithymia, anxiety, and volumes of the right insular cortex in future research, as well as the relation between the alexithymic tendency to somatize and structure and function of insular cortex. Concerning the VBM method employed here, it should be kept in mind that the accuracy of automated VBM methods is limited, especially with respect to detecting differences in small structures such as the amygdala. Future studies could consider the additional use of manual tracing methods to confirm the accuracy of VBM.

Furthermore, it should be kept in mind that this is the first study investigating the structural correlates of the two alexithymia dimensions. While the sample size of analysis 1 was sufficiently high to achieve a statistical power of 80%, the sample size of analysis 2 was too small to achieve this power, and the present finding of larger cingulate volume in relation to the affective alexithymia dimension should thus be considered preliminary. The present sample size also precluded a sub-classification of participants into different alexithymia subtypes, which should be the next step in future research. Moreover, the present VBM data were smoothed with an 8 mm Gaussian kernel and FWE corrected at the cluster level. However, cluster correction for VBM data at small (6 mm) smoothing kernels may be more vulnerable to false positives compared to larger (12 mm) smoothing kernels and compared to voxel-wise correction methods (Silver, Montana, & Nichols, 2011). These limitations should be taken into account in future studies on the neural correlates of the alexithymia dimensions and their relationship to psychopathology.

4.2. Conclusions

In conclusion, the cognitive and affective alexithymia dimensions seem to be associated with distinct structural correlates. The right posterior insula may be a key correlate of the cognitive dimension of alexithymia, possibly reflecting tendencies to perceive feelings primarily as bodily sensations. The right cingulate cortex may be a key correlate of the affective alexithymia dimension and could be related to the recruitment of additional resources when down-regulating or suppressing emotional arousal. These findings may have important clinical implications as they emphasize that alexithymia is not a unitary construct and that the subtypes of alexithymia, which are based on the different alexithymia dimensions may differentially put individuals at risk for psychopathological conditions. Distinguishing between and, ideally, directly comparing individuals with type 1 and type 2 alexithymia in future research will help identify specific associations between alexithymia subtypes and psychopathology.

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