Looking on the bright side
van der Velde, Jorien

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Dissociative morphometric profiles of the affective and cognitive dimensions of alexithymia

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ABSTRACT

BACKGROUND: Alexithymia ("no words for feelings") is a psychological construct that can be divided in a cognitive and affective dimension. The cognitive dimension reflects the ability to identify, verbalize and analyze feelings, whereas the affective dimension reflects the degree to which individuals get aroused by emotional stimuli and their ability to fantasize. These two alexithymia dimensions may differentially put individuals at risk to develop psychopathology. However, their neural correlates have rarely been investigated. The aim of the current study was to investigate whether the cognitive and affective alexithymia dimension are associated with unique anatomical profiles.

METHODS: Structural MRI scans of 57 participants (29 males; mean age: 34) were processed using a voxel-based morphometry (VBM) - Diffeomorphic Anatomical Registration Through Exponentiated Lie Algebra (DARTEL) approach. Multiple regression analyses were performed to examine the common and specific associations between gray and white matter volume and alexithymia subdimensions.

RESULTS: The results revealed that the cognitive dimension was related to lower dorsal anterior cingulate volume. In contrast, the affective alexithymia dimension was associated with lower gray matter volume in the medial orbitofrontal cortex and lower white matter volume in the superior longitudinal fasciculus near the angular gyrus. No relationship between corpus callosum volume and alexithymia was observed.

CONCLUSION: These results are consistent with the idea that there are two separable neural systems underlying alexithymia. This finding might encourage future research into the link between specific alexithymia subtypes and the development of psychopathology.
INTRODUCTION

With a prevalence rate of ten percent in the general population (Salminen et al., 1999), alexithymia (“no words for feelings”) is considered a risk factor for a range of neurological and psychiatric disorders (Taylor et al., 1997). Alexithymia is a dimensional psychological construct that is characterized by difficulties identifying and describing one’s feelings as well as a difficulty in distinguishing them from bodily sensations of arousal. Alexithymia has further been associated with a lack of imagination and an externally oriented thinking style with reduced capacities of introspection (Sifneos, 1973; Vorst and Bermond, 2001).

However, it is suggested that alexithymia is not a uniform construct, but may instead comprise of an affective and a cognitive dimension (Vorst and Bermond, 2001). The affective dimension refers to the level of subjective emotional experience and consists of the factors emotionalizing (the degree to which someone is emotionally aroused by emotion-inducing events) and fantasizing (the degree to which someone is inclined to imagine, day-dream etc.). The cognitive dimension refers to the processing of emotions at a cognitive level and consists of the factors identifying, analyzing and verbalizing feelings. Based on these dimensions, Bermond et al. (2007) proposed to distinguish subtypes of alexithymia which seem to be differentially associated with psychopathology. Type-I alexithymia is characterized by high scores on both the affective and the cognitive dimension (i.e. both emotional experience and the cognitions accompanying the emotions are impaired) and has been suggested to relate to schizoid personality disorder and psychopathy (Moormann et al., 2008a). Type-II alexithymia is characterized by intact or even heightened levels of emotional experience, while cognitive emotion processing is reduced, and is associated with Borderline Personality disorder and schizophrenia (Moormann et al., 2008a; van der Meer et al., 2009). Thus, the two alexithymia dimensions might put individuals at risk for developing psychopathological disorders in different ways.

Brain regions that are thought to underlie alexithymia include both (sub)cortical regions and white matter tracts. One of the oldest theories regarding the anatomical correlates of alexithymia suggests that abnormal corpus callosum morphometry may hamper interhemispheric communication subserving cognitive processing of emotions (Gazzaniga and LeDoux, 1978), thereby contributing to the cognitive dimension (Larsen et al., 2003) and type-II alexithymia (Houtveen et al., 1997). Besides the corpus callosum, several gray matter regions are thought to be related to alexithymia. It has been proposed that dysfunction of the anterior cingulate cortex (ACC) relates to both cognitive and emotional aspects of alexithymia (Bermond et al., 2006; Lane et al., 1997; Larsen et al., 2003; Wingbermühle et al., 2012) given its involvement in emotional experience (Milad et al., 2007) and cognitive demanding emotional tasks (Phan et al., 2002). However, results relating ACC volume to alexithymia are ambiguous. For example, positive correlations between alexithymia and ACC surface have been reported (Gündel et al., 2004), while others reported lower volume in this area (Borsci et al., 2009; Ihme et al., 2013; Koven et al., 2011; Paradiso et al., 2008; Sturm and Levenson, 2011) or were unable to find a significant association (Heinzel et al., 2012). Furthermore, previous studies associated alexithymia with lower gray matter in the orbitofrontal cortex (OFC), insula, and amygdala (Borsci et al., 2009; Ihme et al., 2013), whereas another study reported increased volume in the insula associated with alexithymia (Zhang et al., 2011). These regions are involved in primary emotion identification and in the generation of emotional states (Adolphs, 2002a; Phillips et al., 2003; Vuilleumier, 2005) and are thought to underlie both the affective and cognitive alexithymia dimension (Wingbermühle et al., 2012). However, it has also been proposed that dysfunctioning of specifically the medial OFC would be associated with solely the affective dimension.
As reported above, previous studies on the structural correlates of alexithymia have produced equivocal results. One explanation for this might be that all these studies used the Toronto Alexithymia Scale (TAS-20), which assesses the cognitive alexithymia dimension only. As previously suggested by Koven et al. (2011), assessing specific dimensions of emotional constructs, including alexithymia, instead of examining it as a unitary construct, can provide a more nuanced view and can indicate whether there are separate neural correlates underlying different alexithymia dimensions. Furthermore, a recent study revealed that the two alexithymia dimensions may indeed be related to different gray matter (GM) volumes (Goerlich-Dobre et al., 2013). It was shown that cognitive alexithymia, as examined by the TAS-20, might be more associated with larger insula volume, while affective alexithymia seemed to be related to larger cingulate volume. This together with the suggestions that the affective alexithymia dimension may differentially affect the processing of emotions and seems to be related to separate neural correlates (Bermond et al., 2010; Goerlich et al., 2012; Moormann et al., 2008b; Pouga et al., 2010), indicates that the lack of controlling for scores on the affective dimension may have confounded previous findings. Furthermore, the impact of this alexithymia dimension on brain morphology, especially white matter (WM), remains unknown.

The aim of the present study was to examine whether the affective and cognitive dimensions of alexithymia are associated with different anatomical profiles. To this extent, gray and white matter volume in relation to the affective and cognitive dimensions of alexithymia was examined using voxel-based morphometry (VBM). Based on previous literature, we hypothesized that corpus callosum volume would be specifically related to the cognitive alexithymia dimension, whereas medial OFC volume was thought to be related to solely the affective alexithymia dimension. Furthermore, we predicted to find structural differences in the ACC, insula and amygdala associated with both the alexithymia dimensions.

| METHODS |

Participants

Structural T1-weighted MRI scans of 60 right-handed healthy subjects (30 male and 30 female matched for age and education level, age range 18-55) were selected from one previous neuroimaging study (van der Meer et al., 2013) and two ongoing neuroimaging studies of our group. From these previous studies, 86 unique T1-weighted MRI-scans from healthy controls (excluding siblings of patients with schizophrenia and subjects at ultra-high risk for schizophrenia) were available from studies with identical scan parameters in which the BVAQ was administered. Of these 86, 26 scans were excluded based on the following exclusion criteria: 1) older than 55 (n=2), 2) left-handed (n=15), 3) subject did not finish high school (n=1), 4) reports of present or past psychiatric or neurological problems (n=6), and 5) incomplete BVAQ (n=2). All participants gave written informed consent and the studies were approved by the local medical ethical committee. Demographic characteristics are presented in Table 3.1.

Behavioral measurements

Bermond-Vorst Alexithymia Questionnaire

The Bermond-Vorst Alexithymia Scale (BVAQ) is a 40-item self-report scale used to assess
alexithymia. The BVAQ consists of five subscales (eight items per scale), identifying, verbalizing, analyzing, emotionalizing and fantasizing as defined by Nemiah and Sifneos (Nemiah and Sifneos, 1970). Answers are rated on a 5-point Likert scale (1 = certainly does not apply to me, 5 = certainly does apply to me) with higher scores indicating more pronounced alexithymic characteristics. Previous studies have confirmed the five-factor structure of the BVAQ and have shown that the BVAQ has good psychometric properties (Berthoz et al., 2000; Vorst and Bermond, 2001).

Using the BVAQ, a second-order distinction can be made in which the factors emotionalizing and fantasizing are grouped into the affective dimension, and the factors identifying, verbalizing, and analyzing feelings into the cognitive dimension of alexithymia. The validity of this two-factor structure has been demonstrated and confirmed by several factor-analyses (Bailey and Henry, 2007; Bekker et al., 2007; Bermond et al., 2007), although not consistently (Bagby et al., 2009). Deborde et al. (2008) developed cut-off scores based on the BVAQ-B. The BVAQ-B is a shorter version of the BVAQ which is calculated by adding the scores on items 21 through 40 (Zech et al., 1999). The complete BVAQ scores were applied in all the analyses in the current study. However, to give an indication of severity of alexithymia in our sample, BVAQ-B scores were calculated. A score of 53 or higher indicates

|Table 3.1 Demographic variables, mean scores and standard deviations (SD) of alexithymia and affect scores, alexithymia comparisons between males and females and scanner sites (t-tests), and correlations between alexithymia, affect and demographic variables (n=57)

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Mean (SD)</th>
<th>Statistics Cognitive dimension</th>
<th>Statistics Affective dimension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male vs. female)</td>
<td>29 vs. 28</td>
<td>t = .94 p = .35</td>
<td>t = .46 p = .65</td>
</tr>
<tr>
<td>Age</td>
<td>34.1 (10.9)</td>
<td>r = -.12 p = .36</td>
<td>r = .17 p = .20</td>
</tr>
<tr>
<td>Education (in years)</td>
<td>17.2 (0.7)</td>
<td>r = .03 p = .82</td>
<td>r = -.12 p = .39</td>
</tr>
<tr>
<td>Scanner site</td>
<td>38 vs. 19</td>
<td>t = -.59 p = .56</td>
<td>t = .74 p = .46</td>
</tr>
<tr>
<td>BVAQ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total score</td>
<td>91.3 (16.5)</td>
<td>r = .85 p &lt; .01</td>
<td>r = .64 p &lt; .01</td>
</tr>
<tr>
<td>Cognitive dimension</td>
<td>49.9 (12.9)</td>
<td>r = .13 p = .34</td>
<td></td>
</tr>
<tr>
<td>Affective dimension</td>
<td>41.2 (8.8)</td>
<td>r = .13 p = .34</td>
<td></td>
</tr>
<tr>
<td>Identifying factor</td>
<td>14.7 (5.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verbalizing factor</td>
<td>19.8 (6.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Analyzing factor</td>
<td>15.5 (4.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotionalizing factor</td>
<td>19.9 (4.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fantasizing factor</td>
<td>21.3 (7.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PANAS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive affect</td>
<td></td>
<td>r = -.06 p = .65</td>
<td>r = -.04 p = .77</td>
</tr>
<tr>
<td>Negative affect</td>
<td></td>
<td>r = .16 p = .22</td>
<td>r = .05 p = .73</td>
</tr>
</tbody>
</table>

Abbreviations: BVAQ: Bermond-Vorst Alexithymia Questionnaire; PANAS: positive and negative affect scale; SD: standard deviation
high alexithymia, while participants scoring 43 or lower can be classified as low alexithymic (Deborde et al., 2008).

**Positive and Negative Affect Scale**

The positive and negative affect scale (PANAS) (Watson et al., 1988) was used to measure the current affective state. The scale consists of 10 positive affect items (reflecting the extent to which a person feels enthusiastic, active and alert) and 10 negative affect items (reflecting distress, anger, fear and guilt). Participants rated on a five-point scale to what extent they experienced certain mood states. The PANAS has been proven to be a reliable and valid measure of positive and negative affect (Crawford and Henry, 2004).

**Image acquisition**

Imaging data were acquired using 3.0 Tesla magnetic resonance imaging systems (Philips Intera, Best, NL) located at the University Medical Center Groningen and at the Academic Medical Center in Amsterdam. Both systems were equipped with an 8-SENSE head coil and anatomical images were obtained using a sagittal 3-dimensional T1-weighted sequence (176 slices; TR=9 ms; TE=3.5 ms; FOV=256 mm, voxel size=1 x 1 x 1 mm; slice thickness=1.0 mm).

**Statistical analyses**

Demographic data were analyzed using SPSS 20 (SPSS Inc, Chicago, Illinois). Pearson correlations were calculated to examine the associations between the two alexithymia dimensions and age, education and PANAS scores. Two-sample t-tests were calculated to examine possible alexithymia differences due to gender or scanner site. Significance was set at p<.05, two-sided.

Imaging data were analyzed with unified voxel-based morphometry (VBM) using Statistical Parametric Mapping (SPM8) (http://www.fil.ion.ucl.ac.uk) running under Matlab7 (The MathWorks Inc., Natick, MA, USA). Before processing the data, all images were checked for artifacts and the image origins were manually set at the anterior commissure. Subsequently, images were segmented into gray matter, white matter, and cerebrospinal fluid. The Diffeomorphic Anatomical Registration Through Exponentiated Lie algebra (DARTEL) approach was used for optimal registration of individual segments to a group mean template. DARTEL normalized and modulated gray and white matter segments were further normalized to the Montreal Neurological Institute (MNI) space and smoothed using an 8 mm full width half maximum (FWHM) Gaussian kernel. An 8 mm smoothing kernel is optimal for detecting morphometric differences in both large and small neural structures (Honea et al., 2005; White et al., 2001). However, with a smoothing kernel of 8 mm it is possible to miss differences in smaller structures such as the amygdala (Morawetz et al., 2008). Therefore, an additional analysis was performed to specifically investigate the amygdala with a smoothing kernel of 4 mm in order to ensure that differences in this structure were not overlooked.

To assess the effect of alexithymia on gray matter volume (GMV) and white matter volume (WMV), whole brain multiple regression analyses were conducted with the mean-centered cognitive and affective dimension of the BVAQ as covariates of interest. Both the effects of these dimensions separately, as well as the interaction between them were examined. An additional regression model was created including the total BVAQ score to
examine the effect of alexithymia irrespective of subtypes on brain volume. In all abovementioned analyses, sex, age and scanner site were entered as nuisance variables to adjust for their effect on regional brain tissue volumes. Whole brain volume (calculated as the sum of gray and white matter) was entered as a global by means of proportional scaling. A GM majority optimal threshold mask, created based on the whole sample, was applied to all analyses to eliminate voxels of non-GM for the GMV analyses while a white matter majority mask was applied in the WMV analyses (Ridgeway et al., 2009). To examine whether there was an interaction between the affective and cognitive dimension on GMV or WMV, additional analyses were performed by adding the interaction term (mean-centered affective dimension*mean-centered cognitive dimension) to the regression model. Follow-up analyses were performed to examine whether the observed correlations with the cognitive or affective alexithymia dimension were driven by specific BVAQ subscales. Individual volumetric measurements (extracted with masks based on the significant clusters) were entered into SPSS. These measurements were transformed into standardized residuals corrected for gender, age, scanner site, total brain volume, and the respective other alexithymia dimension to mimic the regression values of the SPM-model. For every significant cluster, a multiple regression was performed using a backward elimination procedure with a standard p-to-leave of .1. For significant clusters in association with the cognitive alexithymia dimension, the three subscales ‘Identifying’, ‘Analyzing’, and ‘Verbalizing’ were added into the regression model. For the affective dimension analysis, a regression model including the factor ‘Emotionalizing’ and ‘Fantasizing’ was created. To examine main effects of scanner site, a two-sample t-test was performed between the scanner sites in Groningen and Amsterdam in which whole brain volume (GM + WM) was entered as a global by means of proportional scaling.

The threshold for all whole brain analyses was set at p<.05 Family-Wise Error (FWE) corrected at the cluster level (corrected for non-stationary of smoothness characteristic for VBM data) with an initial voxel threshold of p<.001. For the GMV-analyses, effects occurring in our a priori-set ROIs [bilateral ACC, medial OFC, insulae, and amygdalae as defined by the Automated Anatomical Labeling system implemented in the WFU pickatlas (http://fmri.wfubmc.edu/software/PickAtlas)] had to meet p<.019 FWE corrected for the spatial extent of the ROI to be considered significant. This p=.019 was chosen to correct for the number of ROIs (i.e. 4) while taking into account their non-independency of the dependent measure [i.e. total GM volume of AAL masks: mean correlation r=.28, corrected for total brain volume (http://www.quantitativeskills.com/sisa/index.htm)]. For the WMV-analyses, only one a priori-set ROI was defined (corpus callosum, mask was manually created based on the average template of the whole sample). Effects for this ROI-analysis had to meet p<.05 FWE corrected for the spatial extent of the ROI to be considered significant.

To visualize the associations found with the alexithymia dimensions, individual volumetric measurements (extracted with masks based on the significant clusters) were entered into SPSS, corrected for gender, age, scanner site, total brain volume, and the respective other alexithymia dimension, and plotted against the alexithymia dimension of interest.

**RESULTS**

**Alexithymia scores**

The mean scores and standard deviations of the two alexithymia dimensions and the five subscales are presented in Table 3.1. Overall the BVAQ scale demonstrated satisfying internal
consistencies (see Table 3.2) apart from the subscale ‘Emotionalizing’ which showed lower internal consistency ($\alpha=.58$). The two alexithymia dimensions were not significantly related to any of the demographic variables, including sex, age, education and scanner site (see Table 3.1 for test statistics). Furthermore, the two alexithymia dimensions were not significantly correlated with each other nor with the positive and negative affect scores of the PANAS (see Table 3.1). Of our 60 participants, 14 participants could be classified as alexithymic and 26 as non-alexithymic as indicated by the cut-off scores of Deborde et al. (2008) based on the recalculated scores of the BVAQ-B (Zech et al., 1999).

**VBM-results**

One subject (low alexithymic) was excluded from the analyses because of poor data quality. Furthermore, two subjects (1 high alexithymic and 1 low alexithymic) were excluded because they were identified as outliers by the homogeneity check (VBM8 toolbox version 435, [http://dbm.neur.uni-jena.de/vbm](http://dbm.neur.uni-jena.de/vbm)). The final sample therefore consisted of 57 participants (for sample characteristics see Table 3.1). No significant correlations were identified between total brain volume and the cognitive dimension ($r=-.038$) nor the affective dimension ($r=-.059$).

**Gray matter volume results**

Whole brain MRI-analyses revealed no significant associations (positive nor negative) between GMV and the cognitive nor affective dimension. No significant associations (in both whole brain as well as ROI analyses) were found with the total BVAQ score and GMV. Voxel-wise analyses however, revealed that the cognitive alexithymia dimension was negatively correlated to GMV in the dorsal ACC ($p=.002; k=532; Z=4.09; (x=11 y=35 z=18); Z=3.75; (x=3 y=30 x=27), p<.019$ FWE corrected for the extent of the ROI) (see Figure 3.1). The follow-up analysis indicated that this effect was mainly driven by the factor analyzing feelings (see Table 3.3). With the affective dimension, the voxel-wise analysis only showed a marginally significant negative correlation with GMV in the right medial OFC and the affective alexithymia dimension ($p=.027$ which was above our significance level of .019; $k=59; Z=3.54$; $p<.019$ FWE corrected for the extent of the ROI).
No significant interaction of the affective and cognitive dimensions was observed for the GMV analyses. Furthermore, in both voxel-wise whole brain and ROI analyses, no significant GMV differences between the two scanner sites were found. The additional analyses with a smoothing kernel of 4 mm did not reveal any significant associations between amygdala volume and the alexithymia dimensions.

**White matter volume results**

No significant associations (positive nor negative) between WMV and the cognitive alexithymia dimension nor the BVAQ total scores were found in the whole brain analysis nor in the ROI-analysis on the corpus callosum. However, the whole brain analysis did reveal lower WMV in the right superior longitudinal fasciculus (SLF) near the angular gyrus in association with the affective dimension \([k=586; Z=4.51; (x=34 y=-55 z=42); Z=3.86; (x=36 y=-58 z=30)](\text{see Figure 3.1})\). This result was particularly driven by the factor fantasizing (see Table 3.3). No significant interaction of the affective and cognitive dimension on WMV was observed. Furthermore, no significant effect of the affective dimension on the corpus callosum was found nor any differences between the two scanner sites on WMV in the whole brain analysis and the ROI analyses.
In this study, we investigated the structural correlates underlying the affective and cognitive dimension of alexithymia. In addition to previous MRI studies, which mainly focused on the cognitive alexithymia dimension, we also examined the morphological correlates of the affective dimension. The present results indicate that the two dimensions of alexithymia show distinct anatomical profiles. The cognitive dimension was associated with lower gray matter volume in the dorsal ACC, while the affective dimension was associated with slightly lower gray matter volume in the medial OFC and lower white matter volume in the SLF near the angular gyrus. The total score of the cognitive and affective dimension together was not significantly related to gray or white matter.

The dorsal ACC is an area involved in various cognitive tasks, such as attention and interference (Bush et al., 2000), as well as emotional processing tasks (Etkin et al., 2011). More specifically, the dorsal ACC monitors and evaluates the emotional meaning of stimuli (Etkin, 2010; Etkin et al., 2011) and gets activated when emotion processing tasks require some form of cognitive control (e.g. emotion regulation) (Urry et al., 2009). Lower gray matter volume in this area has been suggested to result in less efficient emotion regulation (Giuliani et al., 2011b) and difficulties in emotion recognition (Baggio et al., 2012). The underlying cellular basis of volumetric reductions remains poorly understood. Reduced volume can indicate a loss of neurons, which will probably impact the direct function of the area. However, it can also reflect a reduction of dendritic arborization (Kanai and Rees, 2011), which will have an impact on the integrity of the circuit in which this area is involved. This latter would support the theory of Lane et al. (2008), that alexithymia results from a loss of fibers between the ACC and affect-generating brain regions (Lane, 2008). Both ACC activation as well as functional connectivity between the ACC and limbic regions has been reported in emotion evaluation and regulation tasks (Banks et al., 2007; Nomura et al., 2003). Together with the finding of lower dorsal ACC volume in association with cognitive alexithymia reported in previous studies (Borsci et al., 2009; Ihme et al., 2013), this suggests that lower volume in this area may underlie the difficulties in evaluating and regulating emotions that individuals with high cognitive alexithymia experience. It was previously suggested that dysfunctioning of the ACC would result in type-I alexithymia because of its

| Table 3.3 Post-hoc backward elimination results of BVAQ subscales contributing to significant gray matter and white matter clusters |

<table>
<thead>
<tr>
<th>Step</th>
<th>Variable</th>
<th>Beta</th>
<th>t-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Anterior cingulate gyrus</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. removal</td>
<td>Identifying</td>
<td>-.01</td>
<td>-.04</td>
<td>.97</td>
</tr>
<tr>
<td>2. removal</td>
<td>Verbalizing</td>
<td>-.05</td>
<td>-.34</td>
<td>.74</td>
</tr>
<tr>
<td>3. Final model</td>
<td>Analyzing</td>
<td>-.57</td>
<td>-5.17</td>
<td>p&lt;.001</td>
</tr>
<tr>
<td><em>Medial Orbitofrontal cortex</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Final model</td>
<td>Fantasizing</td>
<td>-.29</td>
<td>-2.37</td>
<td>.02</td>
</tr>
<tr>
<td></td>
<td>Emotionalizing</td>
<td>-.32</td>
<td>-2.57</td>
<td>.01</td>
</tr>
<tr>
<td><em>Superior longitudinal fasciculus</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. removal</td>
<td>Emotionalizing</td>
<td>-.16</td>
<td>-1.34</td>
<td>.18</td>
</tr>
<tr>
<td>2. Final model</td>
<td>Fantasizing</td>
<td>-.52</td>
<td>-4.50</td>
<td>p&lt;.001</td>
</tr>
</tbody>
</table>
involvement in both emotional experience and emotional cognition (Bermond et al., 2006; Wingbermühle et al., 2012). Indeed, besides the number of functional imaging studies showing altered dorsal ACC activation in cognitive alexithymia (van der Velde et al., 2013), one study, examining both alexithymia dimensions, showed an association between the affective dimension and dorsal ACC activation (Pouga et al., 2010). However, in the current study no GMV reductions in the ACC associated with the affective dimension were found. Furthermore, a recent VBM study revealed that affective alexithymia was associated with larger volume in the cingulate gyrus (Goerlich-Dobre et al., 2013) and previous structural MRI studies have suggested that lower dorsal ACC volume is associated with schizophrenia (Bora et al., 2011; Glahn et al., 2008), which is related to a pattern of alexithymia scores associated with type-II alexithymia (van der Meer et al., 2009). These results indicate that lower ACC volume underlies cognitive alexithymia and might be particularly related to a profile of high cognitive alexithymia combined with normal or even low affective alexithymia scores (subclinical type-II alexithymia). However, further research on dorsal ACC function and volume is necessary to elucidate the role of this area in type-I and type-II alexithymia.

In association with the affective alexithymia dimension, the results revealed a marginal significant reduction in gray matter volume in the medial OFC. This result is in agreement with the theory of Bermond et al. (2006), whom hypothesized that the medial OFC would be associated with the affective dimension since removal of this area led to flattness of affect without changing emotional cognitions (Trigg, 1970). The OFC has strong connections with the amygdala and other limbic areas and this circuit plays a significant role in the experience of emotions (Price and Drevets, 2012). Furthermore, the medial part of the OFC is responsive to highly salient stimuli and activation in this area reflects emotional arousal (Rothkirch et al., 2012) and emotion induction (Rudrauf et al., 2009). Therefore, disruption of this area or the circuit in which it is involved, might contribute to a reduction of emotional experience associated with emotionalizing. Moreover, the medial OFC is involved in reward imagery (Bray et al., 2010) which might explain the relation between the lack of fantasizing and lower medial OFC volume. Taken together, this makes the medial OFC a likely candidate to underlie the problems with emotionalizing and fantasizing associated with the affective dimension.

Besides lower medial OFC volume, the affective alexithymia dimension was associated with lower white matter volume in the right SLF near the angular gyrus, specifically associated with the fantasizing factor. Via connections to the prefrontal and temporal cortex and the hippocampal complex, the angular gyrus integrates information from different modalities and is involved in a wide range of tasks, such as autobiographical memory and social cognition (Seghier, 2013). Activation in the angular gyrus has shown to reflect both imagery and retrieval success (Huijbers et al., 2011). These imagery processes are generated through the connections between the angular gyrus, medial prefrontal cortex and hippocampal formation via the SLF and the inferior longitudinal fasciculus (Andrews Hanna et al., 2010; Makris et al., 2005). Disruption of these connections, because of lower white matter volume, might therefore impair the function of this network and lead to poor imagination and a restricted fantasy life as reported by individuals with high scores on the affective alexithymia dimension. One previous study examining white matter integrity through diffusion tensor imaging (DTI) in association with the cognitive alexithymia dimension (Kubota et al., 2012) also reported reductions in the SLF near the angular gyrus. However, these reductions were reported on the left side of the brain whereas in the current study, white matter volume reductions on the right side were found. One possible explanation for this difference might be that the left angular gyrus and the regions connected to this area through the left SLF are more involved in language processing (Seghier, 2013). Disruption of this left network might therefore be related to the problems in verbalizing
emotions, which is part of the cognitive dimension. In contrast, the right angular gyrus connected with frontal and temporal regions through the right SLF, is part of the salience network (Seghier, 2013), which might be more related to the affective dimension.

Besides structural differences in the ACC and medial OFC, we were expecting to find differences in the corpus callosum, amygdala and insula. Previous studies on alexithymia showed lower white matter volume (Habib et al., 2003) and lower white matter integrity (Kubota et al., 2012) in the corpus callosum in relation to alexithymia. However, both results were only found in patient groups (multiple sclerosis and schizophrenia), while no differences were reported in the healthy control group (Kubota et al., 2012). This, together with our negative finding, may suggest that volumetric differences in the corpus callosum might be specific to comorbid alexithymia in patient populations. Future studies should further examine this difference between patients and healthy controls. The structural alterations in the amygdala and insula also remain equivocal. Two studies reported larger insula volume (Goerlich-Dobre et al., 2013; Zhang et al., 2011), while others reported smaller insula volume in alexithymia (Borsci et al., 2009; Ihme et al., 2013). Furthermore, one study reported lower gray matter volume in the amygdala in association with alexithymia (Ihme et al., 2013). However, the current study and several previous reports (Borsci et al., 2009; Heinzel et al., 2012; Kubota et al., 2011) failed to link insula or amygdala volume to alexithymia. The negative finding regarding amygdala volume in the current study cannot be explained by smoothing, since applying a smaller smoothing kernel (4 mm) did not reveal any alexithymia-related volume changes in this area. Furthermore, it is unlikely that the above mentioned differences in results between studies can be directly explained by large differences in sample size or applied methods. Thus results regarding structural alterations in the insula and amygdala remain inconclusive. However, our results in line with the negative findings of previous studies (Heinzel et al., 2012; Kubota et al., 2011) do not seem to support the idea that alexithymia is related to morphological differences in these areas which are involved in primary salience detection and interoceptive awareness.

The question remains how the volumetric differences related to alexithymia arise. One possibility is that the volumetric abnormalities are heritable and form the neurobiological basis of alexithymia. Previous research has shown that both brain volume (Batouli et al., 2013) as well as alexithymia (Picardi et al., 2011) are in part heritable. However, the volumetric abnormalities might also be caused by the fact that alexithymic individuals process emotion differently (van der Velde et al., 2013) which may result in a different use of emotional brain regions possibly resulting in volumetric changes. Future research studying brain volume related to alexithymia in a family design or in a longitudinal design is necessary to examine this relationship.

Some limitations of this study should be addressed. First, despite the fact that alexithymia is correlated with depression and anxiety (Berthoz et al., 1999), we did not include depression or anxiety measures in the current study. It should be noted, however, that the participants were selected for not having a psychiatric diagnosis. Second, as far as we know, this is the first imaging study trying to relate structural brain correlates to the different subtypes of alexithymia (e.g. type-I and type-II alexithymia). Unfortunately, this association could only be examined through interaction analyses as the sample was not large enough to compare groups of participants classified as type-I alexithymia versus participants classified as type-II alexithymia. Third, in the current study alexithymia is assessed through a self-report measure. This type of measure relies on reflecting one’s own emotions which is limited in individuals with alexithymia. Therefore, we encourage future studies to combine self-reports with observer-rated alexithymia measurements, such as the structured interview based on the Beth Israel Hospital Psychosomatic Questionnaire for alexithymia (Sriram et al.,
Finally, the current study used a dimensional approach to examine alexithymia. Although some of the participants exceeded the cut-off for clinical alexithymia \([n=13; \geq 53 \text{ (Deborde et al., 2008)}]\), participants were not specifically selected on this criterion and the sample of ‘high’ alexithymics was too small to compare directly to non-alexithymics. Therefore, it remains an open question whether the currently identified morphological correlates also apply to clinical alexithymia.

## CONCLUSION

Our results suggest that there might be different anatomical profiles underlying alexithymia and that alexithymia should not be regarded as a unitary construct. The cognitive emotion processing difficulties might be explained by lower gray matter volume in a region involved in emotion recognition and regulation. Whereas affective alexithymia appears to be associated with lower volume in an emotion induction region and lower white matter in a tract connecting regions of a fantasizing network. These results support the idea that the two alexithymia dimensions, that have been identified psychometrically, are associated with specific brain morphology. However, more research is necessary to further elucidate the morphological correlates of the two alexithymia dimensions, especially focusing on the specific relations in highly alexithymic persons. Future research should directly compare groups of individuals with type-I and type-II alexithymia in order to elucidate the neural systems underlying the different alexithymia subtypes and their specific relation to psychopathology.

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