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Research Report

Alexithymia is related to differences in gray matter volume: A voxel-based morphometry study

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ABSTRACT

Objective: Alexithymia has been characterized as the inability to identify and describe feelings. Functional imaging studies have revealed that alexithymia is linked to reactivity changes in emotion- and face-processing-relevant brain areas. In this respect, anterior cingulate cortex (ACC), amygdala, anterior insula and fusiform gyrus (FFG) have been consistently reported. However, it remains to be clarified whether alexithymia is also associated with structural differences. **Methods**: Voxel-based morphometry on T1-weighted magnetic resonance images was used to investigate gray matter volume in 17 high alexithymics (HA) and 17 gender-matched low alexithymics (LA), which were selected from a sample of 161 healthy volunteers on basis of the 20-item Toronto Alexithymia Scale. Data were analyzed as statistic parametric maps for the comparisons LA>HA and HA>LA in a priori determined regions of interests (ROIs), i.e., ACC, amygdala, anterior insula and FFG. Moreover, an exploratory whole brain analysis was accomplished. **Results**: For the contrast LA>HA, significant clusters were detected in the ACC, left amygdala and left anterior insula. Additionally, the whole brain analysis revealed volume differences in the left middle temporal gyrus. No significant differences were found for the comparison HA>LA. **Conclusion**: Our findings suggest that high compared to low alexithymics show less gray matter volume in several emotion-relevant brain areas. These structural differences might contribute to the functional alterations found in previous imaging studies in alexithymia.

1. Introduction

The construct of alexithymia, which literally means "no words for emotion", has been characterized as the inability to identify and describe feelings. Moreover, alexithymics show an externally oriented cognitive style and mundane fantasies (Sifneos, 1973). In order to assess alexithymia, most studies use a convenient self-report instrument, the

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20-item Toronto Alexithymia Scale (TAS-20, Bagby et al., 1994).

Despite extensive research on the neural basis of emotion processing deficits in alexithymia, no distinct neural circuit causing these deficits could be identified. Some researchers argue in favor of a reduced automatic processing of emotional information in alexithymia. This is reflected in diminished activity in structures involved in these automatic processes such as amygdala, insula or sensory areas (Duan et al., 2010; Eichmann et al., 2008; Kugel et al., 2008; Pollatos and Gramann, 2011; Reker et al., 2010). For example, the study of Kugel et al. (2008) reports a negative correlation between individual TAS-20 score and amygdala reactivity to masked emotional faces. This finding was confirmed by Reker et al. (2010) using the same paradigm. Moreover, the work of Reker et al. (2010) revealed reduced automatic insula activation and reactivity of the fusiform gyrus (FFG) as a function of alexithymia. FFG is seen as a sensory area most relevant in face processing (Kanwisher et al., 1997; McCarthy, et al., 1997) whose early activity can be modulated by emotions (Pizzagalli et al., 2002; see also Adolphs, 2002). Smaller FFG reactivity in high alexithymia has been frequently reported (Duan et al., 2010; Eichmann et al., 2008) and might play a role in alexithymics' deficits in reading emotions from faces (Parker et al., 2005). Therefore, this diminished early activity in amygdala, insula and fusiform gyrus may lead to reduced development of emotions in alexithymics.

However, other theories suspect that alexithymics automatically generate emotional reactions, but rather direct too little attention to these. This causes a diminished conscious experience of emotions (Lane et al., 1997; Lane, 2008). Therefore, Lane (2008) has argued that altered functioning of the dorsal ACC would be crucial for the development of alexithymic features. Still, the role of the ACC is not clear, yet: whereas a recent study (Heinzel et al., 2010) reports an increase in ACC activation to different emotional stimuli in a group of high alexithymics compared to low ones, other studies (Kano et al., 2003; Lane et al., 1998; McRae et al., 2008) report diminished activity in the ACC with increasing alexithymia.

As the insula is thought to play an eminent role in the development of conscious feelings and empathy (Singer et al., 2009), alexithymia might also be related to its altered functioning. Recently, insula activity was found to be reduced in an empathy-for-pain experiment in high alexithymics compared to low ones (Bird et al., 2010). Similarly, Silani et al. (2008) reported that reduced anterior insula activity is associated with less emotional awareness in interoception. From these findings, it can be concluded that alexithymic traits might be linked to difficulties to engage (anterior) insula when focusing on emotions and a failure to simulate forward representations of bodily states within the insula (Silani et al., 2008; Singer et al., 2009).

In summary, it seems that altered processing of emotional stimuli as found in alexithymia is primarily accompanied by reduced brain reactivity in ACC, amygdala, anterior insula as well as in the fusiform gyrus. From this, the question arises if there are differences in gray matter volume that might promote the functional and behavioral differences.

This question was first examined by Gündel et al. (2004) using a region-of-interest-(ROI)-based approach with manual tracing of sagittal magnetic resonance images (MRI). Their study revealed that gray matter volume in the ACC is larger in high alexithymics than in low ones. However, the administered manual procedure is susceptible to variance induced by human perception of tissue boundaries. With the emergence of voxel-based morphometry (VBM), an automated approach to investigate brain morphology based on T1-weighted images was developed. In this process, gray and white matter are automatically segmented, so that their volume can be compared voxel-wise in different brains (Ashburner and Friston, 2000). In contradiction to Gündel et al. (2004), Borsci et al. (2009) used VBM and found that high female alexithymics compared to low ones show smaller ACC gray matter volume. Yet, these results could not be confirmed by a recent VBM study examining gray and white matter volume in a whole brain approach and in the ACC depending on alexithymia in healthy young men (Heinzel et al., 2011): the authors could not reject the null hypothesis of no differences between high and low alexithymics.

Taken together, studies on structural differences in alexithymia so far yielded inconsistent findings. This could result from the different volumetric procedures (manual vs. automatic) but also from different thresholds for statistical significance. While Borsci et al. (2009) used a very liberal uncorrected threshold revealing a difference, Heinzel et al. (2011) administered a conservative false-discovery-rate-(FDR)-correction, which tends to reduce the significance threshold in smoothed data (Nichols and Hayasaka, 2003). The current study aims at examining size of brain structures of high compared to low alexithymics using the method of clustering (Forman et al., 1995) to correct for multiple testing. This approach uses Monte Carlo simulation to generate a null distribution of voxel activations based on the noise for a particular model in the current search volume. From this distribution, the probability of occurrence of a certain cluster size (i.e., the number of contiguous voxels k) in a data set solely consisting of noise can be determined at a particular preset t-threshold (e.g. $t=3.39$ or $p=0.001$). From that, one can empirically identify which cluster extent k can be seen as significantly different from noise, e.g. its occurrence by chance is less probable than 0.05. With this procedure, the assumption is taken into account that, in comparison to noise, structural properties like gray matter volume in specific brain areas or interesting areas of neural activity tend to extend more than individual voxels (Forman et al., 1995).

As functional neuroimaging studies have revealed differences in reactivity of several brain regions in high alexithymics compared to low, we conducted a ROI-based analysis examining gray matter volume in the ACC, amygdala, anterior insula and fusiform gyrus. Moreover, an exploratory whole brain analysis was calculated. In our model, we included age and gender as covariate of nuisance to control for age- and gender-related influences on gray matter volume.

2. Results

2.1. *ROI-based analysis*

For the contrast low alexithymia versus high alexithymia (LA > HA) a significant cluster in the ACC (bilateral, cluster size: 3565 voxels, [$x=2$, $y=44$, $z=-3$]) was revealed. The peak of this cluster was in the area of the subgenual ACC