I know what you’ll feel:

Affective mentalizing in alexithymia, an fMRI study

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ABSTRACT

Background: Alexithymia (‘no words for feelings’) is a subclinical condition characterized by cognitive and affective deficits in the processing of one’s own emotions. Though conceptualized as a deficit in emotional self-awareness, alexithymia may also be associated with deficient awareness of the feelings of others. The aim of this study was to investigate the impact of the cognitive alexithymia dimension (low abilities to interpret, analyze, and verbalize one’s feelings) and of the affective alexithymia dimension (low abilities to emotionalize and fantasize) on the neural correlates of affective mentalizing by means of fMRI.

Methods: Thirty-four (19 female) subjects completed an affective mentalizing task using static scenes of social interactions. During emotion recognition, participants decided what emotion a person was feeling. During emotion inference, participants indicated what a person would feel if they had full knowledge of the situation. Counting the number of persons in the same scenes served as control condition. Scores on the cognitive and the affective alexithymia dimension were correlated with neural activity during emotion recognition and emotion inference while controlling for differences in empathy.

Results: During emotion prediction, affective alexithymia was linked to hyperactivity in middle cingulate cortex, part of the low-level embodied, simulating system of self-referential processing. Cognitive alexithymia was linked to thalamic hyperactivity and to hyperactivity in posterior cingulate cortex and precuneus, part of the higher-level, inference-based system of self-referential processing. No differences in brain activity were found during emotion recognition.

Conclusions: Our results suggest that affective alexithymia is associated with a stronger reliance on low-level embodied, simulating brain regions, whereas cognitive alexithymia seems to be linked to stronger compensatory activity of higher-level, inference-based brain regions of self-referential processing during the prediction of other’s feelings.
INTRODUCTION

Alexithymia (‘no words for feelings’) is a personality construct characterized by deficits in the cognitive processing and the experience of one’s emotions. Difficulty identifying, analyzing, and verbalizing one’s feelings as well as difficulty emotionalizing and fantasizing are the five characteristic features of alexithymia (Sifneos, 1973; Bagby & Taylor, 1997). The first three characteristics refer to the cognitive dimension of alexithymia, the latter two to its affective dimension, the dimension of emotional experience (Vorst & Bermond, 2001). The differentiation of the alexithymia construct into a cognitive versus an affective dimension has been validated by factor analyses in six languages and seven populations (Bermond et al., 2007; see also Bailey et al., 2008; Bekker et al., 2007).

Recently, the two dimensions of alexithymia have been suggested to exert a dissociable impact on emotional processing (Bermond et al., 2010; Moormann et al., 2008). With a prevalence rate of up to 10 percent (Salminen et al., 1999), alexithymia is a major risk factor for a variety of psychiatric and medical disorders, including somatization, anxiety, depression, hypertension, chronic pain, etc (Taylor et al., 1997). Moreover, alexithymia exhibits high comorbidity with disorders of the Autism spectrum (Berthoz & Hill, 2005a, b; Bird et al., 2010; Frith, 2004; Hill et al., 2004).

Alexithymia has been conceptualized as a deficit in emotional self-awareness and referred to as the emotional equivalent of blindsight (‘blindfeel hypothesis’, Lane et al., 1997a). However, previous studies indicate that this personality trait not only affects the processing of one’s own emotions, but is also associated with deficient awareness of other’s feelings. For instance, individuals with alexithymia showed impaired performance on recognizing facial expressions of emotions (Prkachin et al., 2008, Swart et al., 2009), and Bydlowski et al. (2005) observed that patients with eating disorders scoring high on alexithymia were impaired in their ability to describe emotional experiences of others in hypothetical scenarios. At the neural level, alexithymia is associated with aberrant brain activity during the processing of facial and bodily emotional expressions (Berthoz et al.,
Mentalizing (‘Theory of Mind’) is a cognitive skill referring to our ability to understand that others have beliefs, intentions, and desires different from the self (Frith & Frith, 2003). The ability to mentalize has been shown to be impaired in a number of psychiatric disorders alexithymia is associated with, such as Asperger’s syndrome (e.g., Baron-Cohen & Lolliffe, 1997; Lombardo et al., 2007), schizophrenia (van’t Wout et al., 2007; Sprong et al., 2007), and borderline personality disorder (Guttman & Laporte, 2002). All of these disorders have in common an ambiguous boundary between the self and others, including proneness to adopt the feelings of others paired with an inability to decouple one’s own from other’s emotions, leading to poor interpersonal relationships and compromised quality of life (e.g., Baron-Cohen, 1995; Brunet-Gouet & Decety, 2006). Consequently, elucidating the role of alexithymia in the ability to comprehend the mind and emotions of others could significantly contribute to our current understanding of psychopathology associated with this personality trait.

Research on the neural basis of mentalizing has suggested that people use emotion-related neural mechanisms to simulate other’s emotional experiences in order to best understand their thoughts and feelings (simulation theory, Gallese & Goldman, 1998; Gallese et al., 2004). Mentalizing about others thus involves self-referential processing, and studies investigating self- and other-referential processing have shown that the neural circuits subserving these processes are largely identical (for a review, see Lombardo et al., 2010). This circuitry consists of two systems, a low-level embodied, simulative system comprising anterior insula, middle cingulate cortex, frontal operculum/ventral premotor cortex, and somatosensory cortex, which is active during the observation of other’s acting or experiencing emotional or somatosensory states, and a higher-level inference-based system recruited during reflection about oneself and others, comprising the medial prefrontal cortex (mPFC), PCC/precuneus, and temporo-parietal junction (TPJ).

To date, only a few studies have directly investigated the relation between alexithymia and mentalizing skills. High-scorers on alexithymia showed no impairment
on the False Belief’s task (Wastell & Taylor, 2002), suggesting an intact ability to understand other’s beliefs. Similarly, no impairment to recognize other’s beliefs in relation to alexithymia was found by Swart and coworkers (Swart et al., 2009). The only neuroimaging study on mentalizing in alexithymia to date (Moriguchi et al., 2006) presented high- and low-scorers on alexithymia with triangles that either acted like humans or moved randomly. The authors reported lower performance on recognizing intentionality and appropriateness in high-scorers compared to low-scorers on alexithymia, indicative of impairment in understanding other’s intentions. This impairment was accompanied by hypoactivity of medial prefrontal cortex.

How alexithymia, a deficit in emotional self-awareness, specifically relates to recognizing the emotional states of others (‘affective mentalizing’) has been addressed only by one previous study. Using behavioral measures, this study reported that high-scoring individuals on the verbalizing subscale of the BVAQ alexithymia questionnaire (Vorst & Bermond, 2001) performed significantly worse on recognizing first order emotions on the Conflicting Beliefs and Emotions task (Swart et al., 2009). The neural correlates of affective mentalizing in alexithymia are hitherto unknown.

The current study was therefore designed to investigate the neural basis of affective mentalizing in alexithymia by means of fMRI. Specifically, we aimed to disentangle the impact of the cognitive versus the affective dimension of alexithymia on activity of brain areas belonging to the low-level embodied, simulating system (e.g., middle cingulate cortex) versus those mediating higher-level, inference-based reflection about self and others (e.g., PCC/precuneus) during the recognition and prediction of other’s emotional responses. As empathy has been shown to significantly correlate with activity in the mentalizing network (e.g., Hooker et al., 2008) and to be negatively related to alexithymia (Guttman & Laporte, 2002; Moriguchi et al., 2006; 2007; Swart et al., 2009), empathy scores were additionally assessed and controlled for in order to isolate the specific impact of cognitive and affective alexithymia on brain activity during affective mentalizing.
METHODS

Participants

Subjects were recruited via the community-based subject pool run by the Psychology Department of Harvard University. The 20-item Toronto Alexithymia Scale (TAS-20, Bagby et al., 1994a,b) was used as a brief assessment tool of cognitive alexithymia scores. Only right-handed, fluent English speaking subjects aged above 18 years with no neurological or psychiatric condition in present or past were invited to the scan session as assessed via a phone interview. Further exclusion criteria were: loss of consciousness resulting from head injury, psychological problems such as feelings of depression, anxiety or any other current or past emotional problems, substance abuse or dependence, and significant vision problems. MRI safety screening was further included in the phone interview, and repeated prior to the scan session. Subjects gave informed consent before the scan session. The study protocol was approved by the International Review Board (IRB) of Harvard University. Subjects received compensation for their participation.

The final study sample comprised 34 subjects, with 19 subjects scoring high on the TAS-20 (≥ 61, 8 male, mean age 23.5 years) and 15 subjects scoring low on the TAS-20 (≤ 30, 7 male, mean age 28.5 years). Prior to the scan session, participants filled out the 40-item Bermond-Vorst Alexithymia questionnaire (BVAQ, Vorst & Bermond, 2001). The resulting scores on the cognitive alexithymia dimension ranged from 20 to 100 (mean: 61.76 SD: 20.53), scores on the affective alexithymia scores ranged from 20 to 70 (mean: 46.82 SD: 10.72). Cognitive and affective alexithymia scores were used for behavioral and MR data analyses in order to test the hypothesized differential impact of the two alexithymia dimensions on brain activity during affective mentalizing.

Toronto Alexithymia Scale (TAS-20)

The TAS-20 is the most widely used measure of alexithymia with a demonstrated validity, reliability, and stability. The scale consists of 20 self-report items rated on a 5-point Likert scale (1: strongly disagree, 5: strongly agree).
The TAS-20 comprises three subscales assessing alexithymia at a cognitive level: (1) difficulty identifying feelings (e.g., “I often don’t know why I’m angry”), (2) difficulty describing feelings (e.g., “I find it hard to describe how I feel about people”), and (3) externally oriented thinking (e.g., “I prefer talking to people about their daily activities rather than their feelings”). 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. The clinical threshold for alexithymia is a score of 61.

The TAS-20 assesses only the cognitive dimension of alexithymia. However, the original definition of the alexithymia concept (Nemiah & Sifneos, 1970; Sifneos, 1973) included not only deficits at the cognitive level (i.e., reduced capacities in identifying, verbalizing, and analyzing emotions), but also at the level of emotional experience (i.e., reduced capacities in emotionalizing and fantasizing), the affective dimension of alexithymia. With the aim to differentiate between these two alexithymia dimensions, the Bermond-Vorst Alexithymia Questionnaire (BVAQ, Vorst & Bermond, 2001) has recently been developed.

**Bermond-Vorst Alexithymia Questionnaire (BVAQ)**

The BVAQ is a 40-item self-report scale, which consists of five subscales with eight items per scale. The five subscales of the BVAQ are: 1) (Difficulty) Verbalizing one’s own emotional states, (2) (Difficulty) Identifying the nature of one’s own emotions, (3) (Difficulty) Analyzing one’s own emotional states, (4) (Difficulty) Fantasizing: the degree to which someone is inclined to imagine, day-dream, etc., and (5) (Difficulty) Emotionalizing: the degree to which someone is emotionally aroused by emotion-inducing events (Bermond et al., 2001). Answers are scored on a 5-point Likert scale (1 = certainly does not apply to me, 5 = certainly applies to me). Higher scores indicate higher levels of alexithymia.
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The three subscales identifying, analyzing, and verbalizing feelings assess the cognitive alexithymia dimension. Substantial overlap between the cognitive subscales of the BVAQ and the TAS-20, reflected in a high correlation between the sum scores on these three BVAQ subscales and the TAS-20 sum score (r = .80, Vorst & Bermond, 2001; see also Berthoz et al., 2000), indicating that these scales measure the same features (Vorst & Bermond, 2001). The two BVAQ subscales emotionalizing and fantasizing assess the affective dimension of alexithymia. The validity of the two-factor structure of the BVAQ with an affective dimension versus a cognitive dimension of alexithymia has been demonstrated by factor-analyses in six languages and seven populations (Bermond et al., 2007; see also Bailey et al., 2008; Bekker et al., 2007). A validated English version of the BVAQ was used for the present study.

Task and stimuli

Forty static scenes of social interactions between multiple characters served as stimuli for the affective mentalizing task. In these scenes, each character's emotional state depends on their belief concerning the social situation: one character has full knowledge about the situation, that is, a True Belief, whereas the other character has partial knowledge or a misperception, that is, a False Belief. These scenes of social interaction were presented in two conditions: Emotion Recognition (“What is X feeling?”) and Emotion Inference (“What would X feel if they had full knowledge about the situation?”), with X referring to either the False Belief Character or the True Belief Character in the scene marked with an X (see figure 1 for an example scene). Subjects made an emotion judgement by choosing one out of four given emotions by pressing a button. Emotion choices for each scene were identical across conditions. Eight emotions were used in total for the task: happy, angry, sad, surprised, afraid, annoyed, confused, and embarrassed (see Hooker et al., 2008, for further details on task creation and characteristics).

Subjects completed a pre-scan comprehension task to familiarize them with the scenes of social interactions and to ensure that they understood their contents. Subjects could inspect each scene for as long as necessary to comprehend its content and then answered
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three factual multiple choice questions for each scene (e.g., ‘Where is the scene taking place? i) outside, ii) in someone's house, iii) in a supermarket). Subjects were then shown an example trial for each condition as it would occur in the scanner. For the Emotion Recognition condition, subjects were instructed to respond to the question “What is X feeling?” by choosing one out of four emotions presented together with the scene. For the Emotion Inference condition, subjects were instructed to respond to the question “What would X feel if they had full knowledge about the scene?” For the Control condition, subjects were asked to count the number of characters in the scene and to press the respective key on the keyboard during the practice session (/the respective button on the button box during the scan session). Subjects could repeat the practice trials as many times as needed until they felt sufficiently prepared for the scan session.

Emotion judgements were made on either the False Belief or the True Belief character in either the Emotion Recognition or the Emotion Inference condition. This design resulted in a $2 \times 2$ design with the following four experimental conditions: 1) Emotion Recognition: False Belief (ERFB), 2) Emotion Recognition: True Belief (ERTB), 3) Emotion Inference: False Belief (EFIB), 4) Emotion Inference: True Belief (EITB). In the Control condition, subjects were presented with the same 40 scenes of social interactions, but were asked to indicate how many characters the scene contained (varying from two to five). The control condition was designed to exclude emotional processing while keeping stimulus characteristics constant between experimental and control conditions.
The task was presented in a mixed event-related/block design. Each subject completed four runs of 9.54 minutes, resulting in a total task duration of 39.16 minutes. Each run consisted of 50 trials blocked into two Emotion Recognition blocks (20 trials), two Emotion Inference blocks (20 trials), and one Control block (10 trials). In total, this resulted in 80 trials for each of the experimental conditions (ERFB, ERTB, EIFB, EITB) and 40 control trials. Within each block, trials were presented in a fixed random sequence. The sequence of each run was as follows: a task instruction slide presented for 3 s indicated an Emotion Recognition (ER), Emotion Inference (EI), or Control (C) block, followed by 10 task trials presented for 6 s (including the four emotion answer choices) with a jittered inter-trial interval of 2, 4, or 6 s. To prevent order effects, five versions of each run were created (version 1: ER 1 – EI 2 – Control – ER 2 – EI 1; version 2: EI 1 – Control – ER 2 – EI 2 – ER 1, etc.) which were randomized across subjects.

![Figure 1](image.png)

*Figure 1:* Example scene of the four experimental trial types with the correct response underlined. The subject is directed either to the True Belief character (woman on the right) or the False Belief character (woman in the middle) by the fixation cross. In the Emotion Recognition condition, the subject is asked to answer the question ‘What is (+) feeling?’; in the Emotion Inference condition, the subject is asked to answer the question ‘What would (+) feel if they had more information?’.
Image acquisition

MR data were acquired with a 3-Tesla Siemens Magnetom Trio Trim scanner at the Center for Brain Science (CBS) of Harvard University using a 32-channel RF head coil. Foam pillows were used to restrict head motion during MR data acquisition. Stimulus display and recording of subject's responses was controlled using E-Prime software (PST, Pittsburgh, PA, USA). Stimuli were projected onto a backlit projection screen within the magnet bore. Subjects viewed the stimuli via a mirror mounted in the head coil.

Functional images were acquired during four fMRI runs which began with four dummy scans (with no data acquisition) to ensure steady state magnetization for all data used for analysis. During each of the four experimental runs 228 whole brain scans were acquired, resulting in a total of 912 whole brain volumes for each subject. Images were acquired with parameters used to optimize signal in regions susceptible to drop-out due to inhomogeneities of the magnetic field. A high-resolution 3D T1-weighted structural scan and an in-plane low-resolution T2-weighted structural scan were acquired for anatomical localization. Whole brain functional images were acquired interleaved with a fast-gradient echo in 40 3 mm thick slices with a 0.5 mm inter-slice gap and with an anterior – posterior slice encoding direction. A one-shot T2*-weighted echo-planar image (EPI) sequence (TR = 2.56 s, TE = 30 ms, FoV = 216 mm, contrast flip angle = 85º) was used to acquire blood-oxygenation level dependent (BOLD) signal. EPI voxel size at acquisition was $3 \times 3 \times 3$ mm$^3$.

fMRI data analysis

Imaging data were processed and analyzed in SPM8 (www.fil.ion.ucl.ac.uk/spm). EPI volumes were realigned in space to the mean of the 228 volumes of each run using a rigid-body transformation algorithm. After realignment, volumes were normalized into the standard space defined by the Montreal Neurological Institute (MNI) template with a voxel size of $3 \times 3 \times 3$ mm$^3$, and smoothed with a Gaussian filter of 8 mm full width at half maximum (FWHM).
For each subject, a general linear model (GLM) was created modeling the hemodynamic response for each event from the onset of the trial. In order to measure the hemodynamic response only during the actual task but to exclude potential additional processing occurring after the subject’s responses, mean response times for each condition were calculated per subject and defined as trial offset. The canonical hemodynamic response function (HRF) was then convolved with brain activity starting at the onset of the trial type (ERFB/ERTB/EIFB/EITB/Control) up to the offset (mean response time) for the respective condition. Brain activity was high-pass filtered at 128 s, scaled by the global mean, and corrected for serial autocorrelation. Residual motion effects were corrected for by including the six estimated motion parameters for each subject as regressors of no interest. First-level contrast images for the four conditions of interest subtracted by the control condition were created in each subject. The resulting first-level contrast images (ERFB > C, ERTB > C, EIFB > C, EITB > C) were then taken to the second-level analyses.

Whole brain images were analyzed in a flexible factorial design including the factors gender (female vs. male) and condition (ERFB vs. ERTB vs. EIFB vs. EITB), and interactions of cognitive and affective alexithymia scores with each condition as regressors. To control for the impact of empathy on brain activity during affective mentalizing, the Empathic Concern (EC) and Personal Distress (PD) subscales of the IRI, which were found to significantly correlate with alexithymia scores in our sample (see behavioral data), were additionally included as covariates of no interest. Because of the strong association between EC and PD scores with the cognitive alexithymia dimension, scores on the EC and PD subscales were orthogonalized to cognitive alexithymia scores in order to maintain orthogonality between columns in this design.

An initial significance threshold of $p_{uncorr} < 0.001$ and an extent threshold of cluster $k > 40$ voxels was used. Results will be reported with respect to whether or not they survived family-wise error correction for multiple comparisons at the cluster threshold $p_{FWE} < 0.05$. Comparisons of interest are the interactions between the cognitive and affective alexithymia dimensions and the four affective mentalizing conditions.
RESULTS

Behavioral data

Cognitive alexithymia scores ranged from 20 to 100 (mean: 61.76 SD: 20.53), affective alexithymia scores ranged from 20 to 70 (mean: 46.82 SD: 10.72). Scores on the two alexithymia dimensions were not significantly correlated (r = -0.108, p = 0.544). Further, alexithymia scores did not significantly differ between female and male participants (cognitive: t(32) = 0.489, p = 0.629; affective: t(32) = -0.434, p = 0.677), and were unrelated to the age of the participants (cognitive: r = -0.114, p = 0.521, affective: r = 0.275, p = 0.115).

Behavioral data analysis identified two outliers performing > 2 SD below the mean, who were thus excluded from the analysis. Repeated-measures ANOVA of the remaining 32 subjects with the factors Emotion (ER vs. EI) and Belief (FB vs. TB) and sex as between-subjects factor revealed significant main effects of Emotion and Belief (p < 0.001), indicating significantly higher performance accuracy during Emotion Recognition than during Emotion Inference (76% vs. 63%), and significantly higher accuracy in True Belief as compared to False Belief conditions (72% vs. 67%). A significant main effect of gender further showed that female subjects performed significantly better during all mentalizing conditions than male subjects (mean difference 10%, p = 0.028 Bonferroni-corrected).

To test for the impact of alexithymia dimensions on behavioral performance during affective mentalizing, Pearson’s correlations were performed between cognitive and affective alexithymia scores and accuracy on the four conditions. Results showed that neither cognitive nor affective alexithymia correlated with affective mentalizing performance (all correlations p > 0.05).

To further test for the relation between alexithymia dimensions and empathy and a possible impact of empathy scores on behavioral affective mentalizing performance, additional Pearson’s correlations were performed between the cognitive and affective alexithymia dimension and the four IRI subscales Perspective Taking (PT), Empathic Concern (EC), Fantasy (FS), and Personal Distress (PD) on 30 participants whose IRI
scores were additionally available. Cognitive alexithymia showed a significant negative correlation with the EC subscale of the IRI ($r = -.509, p = 0.004$), and a significant positive correlation with the PD subscale ($r = .416, p = 0.022$), suggesting reduced empathic concern and increased personal distress in cognitive alexithymia. Scores on the PT and FS subscales were unrelated to the cognitive alexithymia dimension ($p > 0.05$). Affective alexithymia showed a significant negative correlation with the PD subscale ($r = -.532, p = 0.002$) and was unrelated to the other three IRI subscales ($p > 0.05$), indicating an association of affective alexithymia with reduced personal distress. When correlated with behavioral performance on affective mentalizing, however, neither the EC nor the PD subscale was significantly associated with task performance ($p > 0.05$).

**Imaging data**

Two-sample t-tests ($N = 34$) controlling for gender showed that each of the four affective mentalizing conditions, contrasted to the control condition, elicited activity in a primarily right-hemispheric network comprising the superior temporal gyrus (STG) and middle temporal gyrus (MTG), temporal pole (TP), the inferior frontal gyrus (IFG), the rolandic operculum, pre- and postcentral gyrus, inferior parietal lobule, insula, putamen, and hippocampus at a threshold of $p_{uncorr} < 0.001$, with the True Belief conditions during Emotion Inference additionally activating the left STG, the left TP, and the left insula. These regions have been previously associated with affective aspects of mentalizing (e.g., Adolphs, 2003, 2006; Hooker et al., 2008). Figure 2 gives an overview of the brain regions active during the four affective mentalizing conditions.
Direct contrasts between the four conditions (subtracted by the control condition) showed that during Emotion Inference, True Belief conditions compared to False Belief conditions elicited significantly more activity in the left middle and superior temporal gyrus (left MTG and STG) at a cluster threshold of pFWE < 0.05. In addition, True Belief conditions during Emotion Recognition as compared to Emotion Inference were associated with significantly more activity in the right rolandic operculum at the same threshold (see figure 3). No significantly different activity was found for True versus False
Belief conditions during Emotion Recognition, and for False Belief conditions in Emotion Recognition versus Emotion Inference at $p_{uncorr} < 0.001$.

The flexible factorial design testing the impact of cognitive and affective alexithymia on brain activity during affective mentalizing showed no main effect of gender for Emotion Recognition and Emotion Inference conditions (no significantly activated voxels at $p_{uncorr}$).
< 0.001). Correlations between alexithymia dimensions and brain activity were therefore conducted across the entire sample of participants.

| Table 1. Positive correlations between alexithymia dimensions and brain activity during emotion inference. |
|---|---|---|---|---|
| **Alexithymia Dimension** | **Contrast** | **Brain Region** | **BA** | **MNI Coordinates (x, y, z)** | **T** | **Volume (voxels)** | **Significance Threshold** |
|  |  |  |  | **x** | **y** | **z** | **Peak Level** | **Cluster Level** |
| Cognitive Alexithymia | Emotion Inference: True Belief > Control | L. Thalamus | -3 | 0 | -4 | 16 | 264 | ✓ | ✓ |
|  |  | L. Lateral Posterior Nucleus | -15 | -19 | 16 | 4.83 | | |
|  |  | L. Posterior Cingulate | 23 | 12 | -31 | 25 | 355 | ✓ | ✓ |
|  |  | L. Precuneus | 31 | 18 | -58 | 34 | | |
| Affective Alexithymia | Emotion Inference: True Belief > Control | L. Middle Cingulate | 0 | -31 | 49 | 4.58 | 64 | ✓ | - |

Cognitive and affective alexithymia were found to have a differential impact on brain activity during the prediction of other’s emotional responses (Emotion Inference) but not during the recognition of other’s emotional states (Emotion Recognition). Table 1 summarizes the brain regions correlating with cognitive and affective alexithymia during Emotion Inference. During Emotion Inference (True Belief), cognitive alexithymia was associated with significantly increased activity in the left posterior cingulate cortex (PCC) extending into the right cerebrum and the middle cingulate gyrus (BA 23 and 31), the bilateral precuneus, the thalamus including the left ventral anterior and lateral posterior nucleus, and with increased activity in a left-hemispheric cluster in the superior parietal and occipital lobe including the cuneus and precuneus (BA 7 and 31) at a family-wise error corrected threshold of \( p_{FWE} < 0.05 \) (cluster level). Affective alexithymia correlated positively with activity in the left middle cingulate cortex during Emotion Inference (True Belief) at a threshold of \( p_{uncorr} < 0.001 \), however this result did not survive correction for multiple comparisons. Figure 4 depicts the brain regions correlating with cognitive...
alexithymia, figure 5 the brain regions correlating with affective alexithymia during the prediction of other's emotional responses.

**Figure 4**: Positive correlations between cognitive alexithymia and brain activity during emotion inference controlling for empathy. EITB > C: Emotion Inference True Belief > Control. Depicted are sagittal (upper row), coronal (middle row) and axial (lower row) multislices. Significance threshold $p_{FWE} < 0.05$ (cluster level).
DISCUSSION

The aim of this study was to elucidate the relation between alexithymia and affective mentalizing, and to disentangle the impact of the cognitive versus the affective dimension of alexithymia on neural activity of brain areas part of the low-level embodied, simulating system versus those belonging to the higher-level, inference-based mentalizing system. We found that despite unimpaired task performance, alexithymia was associated with increased neural activity during the prediction of other’s emotional responses, whereas neural activity during emotion recognition did not differ as a function of alexithymia. Interestingly, the pattern of neural hyperactivity during emotion prediction indicated a dissociation between the two alexithymia dimensions: whereas affective alexithymia was
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associated with hyperactivity of middle cingulate cortex, part of the low-level simulating system, cognitive alexithymia correlated positively with activity of the PCC and precuneus, part of the higher-level inference-based mentalizing system, and with thalamic activity, an area generally involved in emotion perception, experience, and recall (e.g., Lane et al., 1997b; Damasio, et al., 2000). To the best of our knowledge, this is the first neuroimaging study on the neural correlates of affective mentalizing in alexithymia.

Behavioral data

Predicting a future emotional state was found to be significantly more difficult than merely recognizing the emotional state of others, as were false belief conditions as compared to true belief conditions. Further, female subjects performed significantly better on all affective mentalizing conditions than male subjects in the present study, suggesting a generally higher sensitivity to emotions of other’s in women compared to men. The absence of alexithymia-related differences in task performance during affective mentalizing does not confirm the findings of a previous study using behavioral measures to assess affective mentalizing in alexithymia (Swart et al., 2009). This study found that individuals scoring high on the verbalizing subscale of the BVAQ, also used in the present study, showed poorer understanding of first order emotions (i.e., the emotional state of actor A in the Conflicting Beliefs and Emotions task) than low-scorers on the verbalizing scale. However, performance on second order emotions (i.e., the understanding of the emotional state of actor A as perceived by actor B) did not differ between high- and low-scorers. The authors ascribe this lack of difference due to the fact that the second order emotion questions were difficult to interpret, possibly obscuring alexithymia-related differences. Possibly, the same could account for the absence of behavioral alexithymia-related differences in the present study, which used quite complex scenes of social interactions as stimuli.

Empathy was found to be significantly related to alexithymia in the present study. Specifically, empathic concern, a measure of mature empathy, decreased with increasing scores on cognitive alexithymia, whereas personal distress, a measure of more immature
empathy, increased. This indicates that individuals with difficulty identifying, analyzing, and verbalizing their feelings show less empathic concern for others and at the same time experience more personal distress, confirming previous findings of reduced empathic concern and increased personal distress in individuals with high alexithymia scores (Guttman & Laporte, 2002; Moriguchi et al., 2006; 2007; Swart et al., 2009). Affective alexithymia scores, on the other hand, were not significantly related to empathic concern, but showed a negative correlation with personal distress, suggesting that individuals with low abilities to emotionalize and fantasize in turn experience less personal distress when confronted with other’s feelings. This finding is in line with the ‘cold-blooded’ personality of individuals with alexithymia (Taylor et al., 1997). The dissociation in the experience of personal distress between cognitive and affective alexithymia suggests that the two dimensions of alexithymia are differentially related to the way emotions are experienced, which underlines the benefit of differentiating between cognitive and affective alexithymia in future research.

**Imaging data**

Scores on empathic concern and personal distress were included as covariates of no interest in the analysis of imaging data in order to control for empathy-related differences and to isolate the effect of cognitive and affective alexithymia scores on neural activity during affective mentalizing. During emotion recognition, shown to be easier than emotion inference by the behavioral data, we did not observe alexithymia-related differences. During emotion inference, we found that cognitive alexithymia correlated positively with activity in posterior cingulate cortex (PCC), precuneus, and thalamus, whereas affective alexithymia was associated with significantly increased activity in middle cingulate cortex. These differences in neural activity in relation to alexithymia were only found in true belief conditions, but were absent in false belief conditions in the present study. Given that our behavioral results showed that false belief conditions were significantly more
difficult than true belief conditions, it is conceivable that task difficulty in false belief conditions during emotion inference was too high to reveal alexithymia-related differences. This would be in line with the observation of significant alexithymia-related differences during first order emotion questions, but no such differences during second order emotion questions, interpreted to have been due to too high task difficulty of second order emotion questions in the previous study on affective mentalizing in alexithymia (Swart et al., 2009).

Our imaging data suggest on the one hand that alexithymia is related to increased neural activity during the prediction of other's emotional responses. On the other hand, they indicate that the cognitive and affective alexithymia dimensions are differentially related to neural hyperactivity during emotion prediction. Increased middle cingulate cortex activity, as observed here in relation to increasing scores on affective alexithymia, is commonly found in response to one's own social decisions and emotions (Jackson et al., 2006; Lamm et al., 2007; Singer et al., 2004; Tomlin et al., 2006), and is part of the low-level embodied, simulating system during self-referential processing. This system has been shown to respond both to our own actions, emotions, and sensations, and when we observe other’s acting or experiencing similar emotional or somatosensory states (e.g., Keysers et al., 2004; Singer et al., 2004; Gazzola & Keysers, 2009). According to the simulation theory (Goldman, 2006), we reach an understanding of others by accessing our own self-representations. The fact that affective alexithymia significantly correlated with activity in middle cingulate cortex may indicate that individuals with low ability to emotionalize and fantasize (i.e., high scores on affective alexithymia) compensate for this deficit by hyper-engaging the low-level, simulating system when asked to predict other’s emotional responses in order to reach the same behavioral outcome as individuals with higher abilities to emotionalize and fantasize (i.e., low scores on affective alexithymia).

In contrast to affective alexithymia, cognitive alexithymia scores significantly correlated with activity of the PCC and precuneus, areas of the higher-level, inference-based system of self-referential processing, as well as with activity of the thalamus, an area generally involved in emotion perception, experience, and recall (e.g., Lane et al., 1997b; Damasio, et al., 2000), which has been shown to be integral to the experience of monitoring one's
own internal feeling states (George et al., 1995; Kimbrell et al., 1999; Damasio et al., 2000). In a similar line of reasoning as above, these findings may suggest that individuals with low abilities to interpret, analyze, and verbalize their feelings (i.e., high scores on cognitive alexithymia) compensate for these deficits by hyper-activating areas of the higher-level, inference based system (PCC and precuneus), with thalamic hyperactivity reflecting increased efforts to generate an emotional response and to monitor one’s own feeling states in order to reach similar behavioral outcomes during the prediction of other’s feelings, compared to individuals with higher abilities to interpret, analyze, and verbalize their emotions (i.e., low scores on cognitive alexithymia).

Our finding of neural hyperactivity during the prediction of other’s emotional responses is seemingly at odds with the results of the previous fMRI study on intention mentalizing in alexithymia (Moriguchi et al., 2006), in which hypoactivity of medial prefrontal cortex (mPFC) was observed. However, individuals with high alexithymia scores performed significantly worse during intention mentalizing at the behavioral level in this study, a deficit that was reflected in decreased mPFC activity. This does not necessarily contradict the findings of the present study, as the observed increased activity of self-referential processing regions was paired with successful behavioral performance during affective mentalizing, indicative of compensative neural hyperactivity in the subjects of our study. One should keep in mind that no causal inferences can be drawn from these data, as fMRI studies are based on a correlational approach which does not allow for conclusions as to whether it is neural activity that causes behavioral performance, or vice versa. Moreover, the previous neuroimaging literature on alexithymia shows mixed results concerning neural hypo- versus hyperactivity during emotion processing, as some studies reported increased neural activity related to high alexithymia scores (e.g., Berthoz et al., 2002; Kano et al., 2007; Karlsson et al., 2008; Mériaux et al., 2006; Pouga et al., 2010), whereas others reported decreased activity in relation to high alexithymia scores during emotion processing (e.g., Frewen et al., 2008; Huber et al., 2002; Kano et al., 2003; Kugel et al., 2008; Mantani et al., 2005; Reker et al., 2009).
Chapter 5

Limitations

The scenes of social interactions used as stimuli in the present study were created using a computer graphics program. It is possible that the use of real human characters in future research may produce stronger neural responses and could reveal more subtle aspects of the relationship between alexithymia and its neural substrates during affective mentalizing. Moreover, the social scenes contained multiple different emotions and specific emotions could not be analyzed separately. Since it is possible that alexithymia influences the processing of certain emotions more than others, this aspect may be better controlled for in future studies. With respect to our imaging data, the findings of neural hyperactivity associated with cognitive alexithymia scores were statistically robust, whereas our result of middle cingulate hyperactivity correlating with affective alexithymia scores did not survive family-wise error correction for multiple comparisons. This result should thus be considered preliminary and replicated in future studies investigating the affective dimension of alexithymia.

Conclusions

The results of the present study suggest that alexithymia is associated with neural hyperactivity during the prediction of other’s emotional states. This hyperactivity appears to be differentially related to the cognitive and the affective dimension of alexithymia. Affective alexithymia was linked to hyperactivity in middle cingulate cortex, suggesting stronger reliance on low-level embodied, simulating brain regions of self-referential processing during the prediction of other’s feelings. In contrast, cognitive alexithymia was associated with hyperactivity of the PCC and precuneus, indicating stronger compensatory activity of higher-level, inference-based brain regions in addition to thalamic hyperactivity, indicative of higher efforts to monitor one’s own feeling states when predicting the emotional responses of others.
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