Chapter 1

INTRODUCTION

The aim of this thesis is to elucidate the neural basis of alexithymia, and to shed light onto the nature of disordered emotion processing symptomatic of alexithymia. The term ‘alexithymia’ derives from the Greek (α – lack, lexis – word, thymos – emotion) and means, when literally translated, “no words for feelings”. It was coined by Peter Emanuel Sifneos in 1973 to describe patients with psychosomatic illnesses who exhibited marked difficulties identifying and verbalizing their feelings, and distinguishing them from bodily sensations of arousal. Constricted imagery, as evidenced by a paucity of fantasies, and a stimulus-bound, externally oriented cognitive style with avoidance of a focus on inner experiences were further defined as characteristic features of this personality construct.

Additional ideosyncrasies of the multifaceted alexithymia construct include an exaggerated tendency toward social conformity, an infrequent recollection of dreams, a somewhat stiff wooden posture, and a paucity of facial expressions of emotion (e.g., Krystal, 1979), giving rise to alexithymic individuals sometimes being labeled as emotional illiterates or, with some exaggeration, “human robots”. As Taylor and colleagues put it: “At the extreme, alexithymic individuals are virtually organismic automatons functioning in a one- to two-dimensional world, one that is deprived of the fullness of feelings” (Taylor et al., 1997, p. xii).

With a prevalence rate of approximately ten percent (e.g., Salminen et al., 1999), alexithymia has been recognized as a major risk factor for a variety of psychiatric and medical disorders, such as somatization, hypertension, chronic pain, anxiety, panic disorder, and depression (Taylor et al., 1997). Moreover, alexithymia shows high comorbidity with disorders of the Autism spectrum (e.g., Bird et al., 2010).

Two dimensions of alexithymia

The most widely used measure to assess alexithymia is the 20-item Toronto Alexithymia Scale (TAS-20), a self-report questionnaire with a demonstrated validity, reliability, and stability. The TAS-20 comprises three subscales: (1) difficulty identifying feelings (e.g., “I
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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”). This questionnaire assesses the cognitive dimension of alexithymia.

However, the original definition of the alexithymia concept (Sifneos & Nemiah, 1970; Sifneos, 1972) 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 take into account both alexithymia dimensions, the Bermond-Vorst Alexithymia Questionnaire (BVAQ, Vorst & Bermond, 2001) has recently been developed. This self-report questionnaire comprises five subscales, three of which assess the cognitive alexithymia dimension: (1) difficulty verbalizing feelings, (2) difficulty identifying feelings, and (3) difficulty analyzing feelings. The sum score of these three cognitive subscales correlates highly with the total score of the TAS-20 (r = .80, Vorst & Bermond, 2001; see also Berthoz et al., 2000), indicating that the cognitive BVAQ subscales and the TAS-20 questionnaire measure the same features. In addition, the BVAQ contains two subscales assessing also the affective alexithymia dimension: (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). This two-factor structure of a cognitive and an affective alexithymia dimension has been validated in six languages and seven populations (Bermond et al., 2007).

The criterion validity of the BVAQ in clinical samples has been confirmed in several studies, e.g. for eating disorders (Deborde et al., 2008), alcoholics (Sauvage & Loas, 2006), autism spectrum disorders (Berthoz & Hill, 2005a, b), schizophrenia (Van’t Wout et al., 2007) and high-risk for schizophrenia (Van Rijn et al., 2011). Like the TAS-20, the BVAQ includes self-assessment, which may be compromised in certain clinical samples, although its feasibility in schizophrenia and autism spectrum disorders has been confirmed. In our studies with nonclinical participants this is not a confounding factor.
Alexithymia subtypes

Despite four decades of research on alexithymia, there is a conspicuous equivocality as to whether alexithymia is associated with a primary dysfunction of the perception and experience of emotions, or with deficient processing of emotional information at the cognitive level. The inconsistencies characterizing the alexithymia literature may have been in part caused by a tendency to conceive alexithymia as a unitary phenomenon, without further differentiation between the cognitive level of emotional processing and the level of actual emotional experience, the affective level. Recently, this conception of alexithymia as a unitary construct has been scrutinized, and two related, but distinct subtypes of alexithymia have been proposed instead, which are based on the cognitive and affective two-factor structure of the BVAQ (Vorst & Bermond, 2001; see also Moormann et al., 2008).

Type I alexithymia is characterized by a low level of emotional experience and a poor fantasy life in combination with poorly developed cognitions accompanying the emotions. Individuals of this alexithymia type are emotional cold and distant, which can be advantageous in professions requiring rational thinking devoid of emotional interference, but may lead to problems in personal and intimate relations. In contrast, individuals with type II alexithymia experience emotions to a normal or even heightened degree, but have a poorly developed ability to cognitively regulate and verbalize their feelings. Individuals of type II alexithymia are emotionally unstable and prone to develop anxiety, depression, and dissociative tendencies. The type II alexithymia profile may also be characteristic for individuals with Borderline Personality disorder (Moormann et al., 2008) and schizophrenia (Van’t Wout et al. 2007).

As most previous studies used the TAS-20 scale that assesses cognitive alexithymia only, previously found variance in findings such as increased versus decreased physiological responses to emotional stimuli and differences in the structural correlates of alexithymia as outlined below may be due to varying levels on the affective alexithymia dimension not controlled for in these studies.
Neuroimaging alexithymia

Since the definition of alexithymia, early clinical observations of impaired emotional processing have been corroborated by experimental research. Studies using behavioral paradigms confirmed that alexithymic individuals have difficulty identifying facial expressions of emotion (Prkachin et al., 2009; Swart et al., 2009), matching verbal with nonverbal emotional stimuli (Lane et al., 1996), and remembering words with emotional connotations (Luminet et al., 2006).

The past decades have witnessed a rapid increase of scientific interest in the processing and regulation of emotions and the impact of affective dysregulation on mental and physical health. Within this framework, a growing body of research has been dedicated to investigations of the neurobiological substrates underlying disordered emotional processing in alexithymia. Identification of the neural basis of alexithymia could not only aid the diagnostic process but could also benefit the treatment of affective disorders associated with alexithymia.

Electrophysiology

Autonomic reactivity

Overt impairments during the processing of emotional stimuli such as those mentioned above seem to be preceded by altered affective processing at pre-attentive, automatic processing stages, as the results of electrophysiological studies suggest. Based on preliminary findings in the mid-1980s, a hyperarousal model of alexithymia was put forward, stating that alexithymia is related to somatic illness because it produces prolonged physiological hyperarousal to situational stressors (Papckiak et al., 1985; Martin & Pihl, 1986).

In contrast, later investigations on autonomic physiological reactivity indicated that alexithymic individuals produce lower specific skin conductance, an index of sympathetic nervous response, during the processing of emotional pictures and film clips (Franz et al., 1999; Linden et al., 1996; Pollatos et al., 2008; Newton & Contrada, 1994; Roedema & Simons, 1999; Wehmer et al., 1995), accompanied by lower self-reported arousal. These
findings support a hypoarousal model of alexithymia, which posits that alexithymia is associated with lower sympathetic nervous system activation and limited affective reactivity (Neumann et al., 2004). However, other studies failed to find different levels of self-reported arousal as a function of alexithymia (Franz et al., 1999; Linden et al., 1996).

Taken together, results on autonomic reactivity and self-reported arousal in response to emotional stimuli in alexithymia remain ambiguous, which led some researchers to favor a decoupling hypothesis of alexithymia, which states that individuals with this personality trait are characterized by a decoupling of physiological and subjectively perceived arousal (Franz et al., 1999; Stone & Nielson, 2001). It should be kept in mind that the majority of these studies used the TAS-20 scale that assesses alexithymia only at a cognitive level. Therefore, scores on the affective alexithymia dimension, assessing the extent to which the alexithymic individuals participating in those studies experienced emotions, were not controlled for in those studies, though the degree to which individuals feel aroused by emotional events appears likely to be associated with physiological reactivity to emotion-inducing stimuli.

*Event-related potentials*

Event-related potentials (ERPs) are small changes in electrical potentials (in the range of microvolts) occurring in response to a stimulus (e.g., an emotional image) that are measured with the electroencephalogram (EEG). Due to their excellent temporal resolution, ERPs make it possible to characterize the time course of, for instance, emotional processing in the range of milliseconds.

Studies measuring ERPs in response to visual emotional stimuli in alexithymia have reported differences during early as well as late processing stages as a function of this personality construct. A recent ERP study on the processing of emotional pictures in alexithymia, for instance, found that the early P1 component (occurring 100 ms after stimulus onset) was reduced for positive pictures in alexithymia, while the N2 component (occurring 200 ms after stimulus onset) was larger in response to negative pictures in alexithymia (Pollatos & Gramann, 2011). The later occurring P3 (a longer-lasting positive
component starting 300 ms after picture onset), indicative of conscious stimulus evaluation and classification, was reduced for negative pictures, confirming findings of a previous study that likewise presented alexithymics with emotional pictures (Bermond et al., 2008).

Generally, ERP studies have provided evidence for an association of alexithymia with altered responses to visual emotional information both during early (presumably automatic) and late (conscious) processing. Auditory information was only investigated by one previous ERP study (Schaefer et al., 2007). This study identified significantly larger amplitudes of the P1-N1 complex (40 – 200 ms post stimulus onset) in alexithymics compared to non-alexithymics in response to aversive white noise, whereas intensity and pleasantness of the aversive stimuli were rated equally by the two groups. These results were interpreted as indicative of a hypersensitivity to unpleasant external stimulation.

**Functional Magnetic Resonance Imaging**

Magnetic Resonance Imaging (MRI) has an excellent spatial resolution and is therefore used for attempts to localize behavior (function) to brain structure, that is, to identify brain areas that are active during, for instance, the processing of emotions. MRI measures the Blood Oxygenation Level Dependency (BOLD) effect (i.e., changes in the ratio of oxygen bound to hemoglobin molecules in venous blood), which is thought to reflect neuronal activity (Logothetis, 2002).

Starting in the year 2002, studies using functional MRI have begun to shed light onto the neural basis of abnormalities in the processing of emotions associated with alexithymia. Lane and colleagues (Lane et al., 1997a) had conceptualized alexithymia as the emotion equivalent of blindsight (‘blindfeel’) and suggested that the core deficit of this personality trait lies in an impairment of conscious awareness and experience of emotion, mediated by the anterior cingulate cortex (ACC). Indeed, altered activation of the ACC was observed in several subsequent studies using functional MRI or Positron Emission Tomography (PET) to investigate emotional processing in alexithymia (Kano et
al., 2003; Berthoz et al., 2002; Mantani et al., 2005; Moriguchi et al., 2006, 2007; Karlsson et al., 2008).

In addition to the ACC, several other emotion-related regions have been suggested to contribute to the emotion processing deficit in alexithymia, such as the posterior cingulate cortex (Mantani et al., 2005), medio-frontal gyrus (Berthoz et al., 2002; Mantani et al., 2005; Mériau et al., 2006; Moriguchi et al., 2006), parietal and premotor cortex (Karlsson et al., 2008; Moriguchi et al., 2008; Reker et al., 2009), amygdala (Kugel et al., 2008; Reker et al., 2010), insula (Bird et al., 2010; Kano et al., 2003; Karlsson et al., 2008; Moriguchi et al., 2007; Reker et al., 2010), and a deficient interaction between amygdala and hippocampus (Aleman, 2005).

Structural Magnetic Resonance Imaging

While a number of neuroimaging studies has been devoted to the identification of brain regions that show aberrant functioning during emotion processing in alexithymia, only a few studies have attempted to determine how alexithymia manifests at the structural brain level. To date, studies investigating volume and density of emotion-related brain regions as a function of alexithymia have provided equivocal results.

Volumes of the anterior cingulate, for instance, were found to correlate positively with levels of alexithymia in a study by Gündel and colleagues (Gündel et al., 2004), whereas smaller volumes of this region were observed in alexithymic versus non-alexithymic women in a study by Borsci and coworkers (Borsci et al., 2009). In contrast, three subsequent studies on the structural correlates of alexithymia failed to observe differences in anterior cingulate structure. Instead, these studies reported volumetric differences in the bilateral ventral striatum, the left ventral premotor cortex, the left supramarginal gyrus (Kubota et al., 2011) and differences in left insula density (Zhang et al., 2011) as a function of alexithymia. On the other hand, Heinzel and coworkers did not observe any differences in gray and white matter volumes in healthy men in relation to alexithymia (Heinzel et al., 2011).
In sum, the existing literature on the structural correlates of alexithymia has produced inconsistent findings. This may in part be due to differences in alexithymia scores between the study samples: in three out of the five previous studies (Gündel et al., 2004; Kubota et al., 2011; Zhang et al., 2011), no participant reached the clinical cut-off score on the TAS-20 indicating actual alexithymia (> 61) as defined by Taylor and colleagues (1994a,b). Further, all of the previous studies used the TAS-20 scale, which assesses cognitive alexithymia only. Consequently, scores on the affective alexithymia dimension were not controlled for, which could contribute to the reported differences in findings.

Outline of the thesis

As described above, the literature on alexithymia is characterized by a conspicuous inconsistency regarding the nature of deficits in emotion processing and their underlying electrophysiological and neural correlates. In addition, there are several aspects of emotion processing fundamental to human experience which have not been addressed by previous studies, including, for instance, the impact of alexithymia on the processing of emotions conveyed by speech, and on the ability to predict the emotional responses of others.

The aim of this thesis is to shed more light onto how alexithymia affects the processing of emotions and how deficits in emotional processing associated with this personality trait manifest at the electrophysiological and neural level. To this end, we employ behavioral measures, event-related potentials (ERPs), and functional as well as structural MRI to test emotional stimuli and paradigms that have not, or barely, studied before in the context of research on alexithymia. This includes the use of auditory emotional material (music and speech prosody) in ERP studies presented in Chapter 2, 3, and 4, the use of an affective mentalizing paradigm in a functional MRI study in Chapter 5 as well as the application of Voxel-Based Morphometry (VBM) in a structural MRI study in Chapter 6.

In Chapter 2, an auditory oddball paradigm is employed using emotional speech prosody, while early and late ERP components are measured. The aim of this study is to
test the impact of the cognitive and the affective dimension of alexithymia on the conscious as well as subconscious processing of emotions conveyed by speech.

In Chapter 3, a cross-modal affective priming paradigm between music, speech prosody, and words with emotional connotations is employed, while the EEG is concurrently measured. The aim of this study is to investigate the impact of alexithymia on affective priming effects at the behavioral level, and on amplitudes of the N400 ERP component, an indicator of the brain’s processing of mismatches in affective meaning.

In Chapter 4, we go on an excursus to a systematic investigation of the underlying mechanisms of affective priming effects and negativities in the N400 time-window in affective categorization tasks such as employed in Chapter 3. The aim of this study is to test the contribution of spreading activation versus response competition mechanisms to affective priming.

In Chapter 5, we investigate affective mentalizing skills in high-scorers and low-scorers on alexithymia in a functional MRI study. The aim of this study is to investigate the impact of alexithymia on the recognition and prediction of other’s emotional responses, and the brain regions associated with differences in affective mentalizing in relation to the cognitive and the affective dimension of alexithymia.

In Chapter 6, voxel-based morphometry (VBM) is applied in a structural MRI study. The aim of this study is to detect regional differences in whole-brain gray matter volume between high-scorers and low-scorers on alexithymia, and to investigate whether the cognitive and the affective alexithymia dimension show a discriminable impact on brain volume.

In Chapter 7, I summarize the results of the present studies and embed them into the previous literature on alexithymia. Further, I illustrate the novelty of the present findings and discuss their relevance for future research as well as their clinical implications.
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