Journal of Affective Disorders 193 (2016) 362–372

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

Neural connectivity of alexithymia: Specific association with major depressive disorder

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ARTICLE INFO

Article history:
Received 6 September 2015
Received in revised form
19 December 2015
Accepted 26 December 2015
Available online 1 January 2016

Keywords:
Alexithymia
Depression
White-matter
Resting-state
Corpus callosum
Superior longitudinal fasciculus

ABSTRACT

Background: Alexithymia has been frequently associated with major depression disorders (MDD). Yet little is known about the exact relationship of alexithymia and MDD. In order to explore this subject matter, the neural connectivity associated with alexithymia in people with MDD and matched nonclinical controls were compared.
Methods: Twenty-two females diagnosed with first-episode MDD and twenty-one matched nonclinical controls were MRI brain-scanned with diffusion-tensor-imaging and resting-state-functional-imaging methods, and self-reported the Chinese 20-item Toronto Alexithymia Scale.
Results: Voxel-wise multiple regression analysis showed a group interaction effect regarding the correlation between white-matter-connectivity and alexithymia. Significant correlations were observed at the corpus-callosum in MDDs and at the right superior-longitudinal-fasciculus in the controls. These findings were then used to derive seeds for analyzing resting-state-functional-connectivity in each group separately. The results further revealed that alexithymia in MDDs were associated with reduced functional-connectivity in the right precentral-gyrus and several regions of the brain on the right which are associated with cognitive regulation in the default-mode-network. In contrast, among the control subjects, alexithymia was correlated with increased functional-connectivity between the right inferior-frontal-gyrus-triangularis and the right superior-occipital-lobe, which is associated with emotional response to external stimuli.
Limitations: Better participant selection, especially recruitment of medication-free samples, and the engagement of additional alexithymia assessments, should be considered in future investigations.
Conclusions: These findings supported our a priori hypothesis that MDDs and controls have distinct white-matter correlates of alexithymia, and these corresponded to the existing proposed neural correlates for the cognitive and affective characteristics of alexithymia respectively. Extended impacts of these microstructural changes on remote functional networks might help explain the distinct behavioral characteristics of alexithymia for these groups, as well as implications for therapeutic intervention of MDD.

1. Introduction

Alexithymia (literally meaning “no words for feelings”) was first introduced by Sifneos (1973) to describe psychosomatic patients characterized by difficulties in identifying and communicating personal feelings, constriction of emotional expressions and fantasies, and a thinking style preoccupied by external events and limited introspections (Bankier et al., 2001; Nemiah et al., 1976; Sifneos, 1973). Contemporary studies have identified alexithymia as a personality trait (Salminen et al., 2006), with prevalence estimated at ~10% amongst the general population (Franz et al., 2008; Mattila et al., 2006), and a predisposing factor for psychopathologies (Bankier et al., 2001; Taylor and Bagby, 2004).

1.1. Relationship between alexithymia and Major Depressive Disorder (MDD)

In particular, alexithymia and MDD are strongly related. Not only is there a much higher prevalence of alexithymia reported amongst the MDD population (~23–46%) (Honkalampi et al.,

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http://dx.doi.org/10.1016/j.jad.2015.12.057
0165-0327/

2000; Saarijärvi et al., 2001), but also people with alexithymia were found to have aggravated depressive symptoms, especially the somatic/affective symptoms of MDD (Guidi et al., 2011; Honkalampi et al., 1999). Such correlations allow alexithymia to be proposed as a potential candidate for subtyping MDD (Vanheule et al., 2007). Nevertheless, inconsistent findings have also been reported. A recent prospective study had found that alexithymia cannot be used to predict MDD, as based on the general population in Finland (Honkalampi et al., 2010). Factor analyses had also found that although alexithymia and depression were separate constructs (Marchesi et al., 2000; Parker et al., 1991), there were frequent overlaps during the measures conducted for both conditions (Hintikka et al., 2001). Hence, the relationship between alexithymia and MDD is relatively unclear.

1.2. Behavioral characteristics of alexithymia in MDD and nonclinical samples

Furthermore, alexithymia is a multi-dimensional construct with both cognitive and affective characteristics (Bermond et al., 2007; Taylor and Bagby, 2004). In fact, by reviewing past behavioral studies of alexithymia, distinct characteristics of alexithymia had been reported, depending on whether MDD or nonclinical samples were recruited. Studies taken from nonclinical samples had found that people with alexithymia have reduced sensitivity regarding response to emotional stimuli (Lane et al., 1996; Parker et al., 1993), attenuated interoceptive awareness and physiological reactivity that reflect diminished emotional experience (Herbert et al., 2011). This group has also had tendencies to focus on somatic sensations rather than symbolic representations of words and images upon emotional arousal (Karlsson et al., 2008). In contrast, studies of MDD patients had reported that alexithymia was associated with heightened emotional and physiological arousals, which were interpreted as displacement behaviors for compensating their difficulties in cognitive regulation of emotional experiences (Troisi et al., 2000). Another postulation also suggested that symptoms of helplessness and hopelessness among MDD patients with alexithymia were associated with their attribution of emotional experiences to situational, dispositional or psychological causes due to difficulties in identifying and expressing bodily sensations and feelings (Duddu et al., 2003). As explained by a recent review-study: when capacities regarding both the experiencing and cognitive processing of emotional information are reduced (affective characteristics of alexithymia), the need for emotional regulation was relatively low (drawn from nonclinical samples); whereas for the case where the capacities regarding experiencing emotional information were high but capacities regarding cognitive processing of the information were low (cognitive characteristics of alexithymia), reduced cognitive regulation would lead to experiences of emotions being intensified (especially negative ones, as in MDD patients) (van der Velde et al., 2013). Nevertheless, empirical evidence is required to corroborate such postulations.

1.3. Major hypotheses on the neural correlates for the cognitive characteristics of alexithymia

There is not yet a universally accepted theory on the neural correlates of alexithymia and various brain regions have been hypothesized for their roles in shaping the cognitive and affective characteristics of alexithymia.

One prominent view holds that damages at the corpus-callosum (CC) would lead to the cognitive characteristics of alexithymia due to the compromised interhemispheric transferral of information, which would interfere the coordinations of the two cerebral hemispheres in due course of cognitive processing of emotional information (Larsen et al., 2003). The CC hypothesis was originally proposed in study of split-brain patients (Hoppe and Bogen, 1977) and more recent studies also found supporting evidence (Lumley and Sielky, 2000; Parker et al., 1999; Romei et al., 2008). Nevertheless, direct neuroimaging evidence is lacking, while questions have been raised on the nature and directionality of the proposed impairments during cognitive transferral of information (Tabibnia and Zaidel, 2005).

1.4. Major hypotheses on the neural correlates for the affective characteristics of alexithymia

Hypotheses on the neural correlates for the affective characteristics of alexithymia are more diverse. A longstanding view proposed deficits at the right hemisphere (or preference of the left hemisphere) (Bermond et al., 2005; Paradiso et al., 2011) would lead to dysfunctional perception and regulation of emotional behaviors (Borod et al., 1998). More recent evidence have focused on the role of the anterior cingulate cortex (ACC), although findings were mixed. Some studies found activities at ACC correlated negatively with alexithymia and suggested reductions in attention and response selection (Chester et al., 2015; Kano et al., 2003; Lane et al., 1998). Other studies claimed that alexithymia was correlated with increased activity at the dorsal ACC and implied this as the defense for increasing emotional inhibition (Pouga et al., 2010). Mixed findings were similarly reported regarding correlations between alexithymia and gray-matter measures of ACC in structural studies, with positive (Gündel et al., 2004), negative (Borsci et al., 2009; Ihme et al., 2013) and non-significant (Heinzel et al., 2012) results all being reported. To explain these controversial findings, an inverted U-shaped activation pattern has been proposed for the dorsal ACC, meaning that when tasks are low in cognitive load, ACC activities would increase with alexithymia, while when cognitive load in the tasks becomes strenuous, ACC activities associated with alexithymia would decrease (McRae et al., 2008; van der Velde et al., 2013). Another possible explanation for the differences in these findings might be the still debating functions of the dorsal ACC (which may be related with cognitive regulation, or appraisal and expression of emotions) (Etkin et al., 2011). Nevertheless, neuroimaging studies consistently found that dorsal ACC is coupled with activities in the right anterior insular (Paulus et al., 2003; Paulus and Stein, 2006), a brain region proposed for somatotopic representation of integrated sympathetic (versus left for parasympathetic) information from posterior-to-anterior progression (Craig, 2009). Hence, we speculate that the ACC and right hemisphere hypotheses for the affective characteristics of alexithymia may be linked with this strong coupling between ACC and the right-lateralized insular for processing of afferent information. Corroborating evidence can be found in the observation that reduced ability in labeling and identifying emotional faces in healthy subjects with alexithymia, particularly when they were under perceptual or temporal constraints, was accompanied by the reduced activations of the limbic and paralimbic brain regions (including the insular) (Ihme et al., 2014; Reker et al., 2010). In sum, a large body of research has suggested that dorsal ACC and right-lateralized deficits are related to alexithymia, particularly the affective characteristics associated with perception and experience of emotions, yet the exact underpinning mechanisms are still largely unknown.

A possible limitation in the existing body of literature is that most of the studies are based on gray-matters, while the role of white-matter fibers for providing connections of ACC with insular and other related brain regions might have been overlooked. To fill this gap, it would be important to identify the white-matter correlates for the affective characteristics of alexithymia. We hypothesized that disruptions at the right superior longitudinal