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Brain structure associated with automatic thoughts predicted depression symptoms in healthy individuals

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ABSTRACT

Previous behavioral studies have examined the correlation between personality and depression, and between negative automatic thoughts and depression. Little is known, however, about the relationships among these three factors. Even less is known about how variations in brain structure are related to negative automatic thoughts, which are thought to mediate the association between personality traits and depressive symptoms. A total of 298 healthy participants underwent magnetic resonance imaging and completed the following questionnaires: a Neuroticism scale, the Automatic Thoughts Questionnaire (ATQ), and the Self-Rating Depression Scale (SDS).

We first investigated the relationships among the three questionnaires and found that the ATQ was a mediator between the Neuroticism scale and the SDS. Then, we investigated the neuroanatomical correlates of the ATQ in the participants using voxel-based morphometry. We found that the ATQ was significantly positively correlated with the gray matter volume of the parahippocampal gyrus (PHG). Structural Equation Modeling revealed that negative automatic thoughts mediated the relationship between the GMV of the parahippocampal gyrus and depression. Moreover, the interaction between parahippocampal gyrus volume and neuroticism predicted automatic thoughts.

These findings highlight that negative automatic thoughts might be a good predictor of depression outcome.

1. Introduction

Virtually, all individuals will experience feeling blue or sad at some time in their lives, and some people will undergo a clinical or biobehavioral syndrome called major depressive disorder (MDD) (Fava and Kendler, 2000). Both the transient mood disturbance and the clinical disorder are described as depression. As we know, depression is a heterogeneous disorder with a highly variable course and no established etiological mechanism (Belmaker and Agam, 2008). In the United States, 2–5% of the general population is affected by severe forms of depression, and up to 20% suffer from milder forms (Nestler et al., 2002). Therefore, much research attention has been focused on identifying the risk factors for depression in otherwise healthy individuals.

Cognitive processes play a pivotal role in the phenomenology, treatment, maintenance, and remission of depression, Cognitive dysfunction arises, at least in part, as a consequence of maladaptive thinking styles and negative self-statements (Beck, 1987; Alloy, 1988; Abramson et al., 1989). For example, according to Beck's cognitive theory of depression, both cognitive content and processes involving pervasive, systematically negative distortions lead to various components of the clinical syndrome of depression (Beck, 1963, 1964, 1967). Negative automatic thoughts occur following a stressful event as the consequence of one's information-processing bias; meanwhile, thoughts about failure in response to stress, in turn, contribute to depressive symptoms (Beck, 1983). Thus, based on a general overview of Beck's cognitive theory of depression, Allen (2003) proposed that negative thoughts are central to depression. The “hopelessness theory” also proposes that negative inferences about the self (particularly ideas about

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failure and worthlessness) are associated with increased depression (Abramson et al., 1989). In summary, persons with depression believe they are worthless, the world is unfair, and the future is hopeless, which Beck identifies as the "negative cognitive triad" (Beck, 1976).

It is also well established that personality is related to depression (Klein et al., 1993; Clark et al., 1994; Watson and Clark, 1995). Personality traits can predict the onset of depressive symptoms (Block et al., 1991) and depressive episodes (Kendler et al., 1993a). Neuroticism is a highly heritable (40–50%) and stable personality trait that reflects stress sensitivity and emotional instability, and it shares up to 50% of the genetic risk for major depression (Kendler et al., 1993b; Joffe et al., 2009). Interestingly, previous research has found that a high degree of neuroticism may facilitate the emergence of negative cognition (Leucht et al., 1997). That is, higher levels of neuroticism have been found to be strongly associated with depression and are powerful predictors of the onset of depression (Hayward et al., 2013; Yoon et al., 2013). In fact, neuroticism in early adolescence serves as a distal indicator of vulnerability for depression, conferring a risk of negative automatic thoughts (Kercher et al., 2009). That is to say, negative automatic thoughts may play such an important role in this model that they fully mediate the effect of neuroticism on later depression. The above-reviewed findings, however, are based on behavioral studies of adolescents, and little is known about possible structural brain correlates of this important mediator in adults or the contribution of the brain to behavioral performance.

The development of neuroimaging techniques during the past two decades has promoted a focus on alterations of the limbic system in mood disorders. Subtle changes in the hippocampus are associated with the pathophysiology of depression (Bremner et al., 2000; Videbech and Ravnkilde, 2004; Cole et al., 2011). The parahippocampal gyrus and the hippocampus, structures that are strongly connected, constitute a considerable portion of the limbic system. The hippocampus traditionally has been associated with learning and memory processes (Bunsey and Eichenbaum, 1993; Aguirre et al., 1996), especially emotionally salient memories (Engelien et al., 2000; Burgess et al., 2001). Moreover, a growing body of evidence suggests that inter-individual variability in a wide range of human behaviors can be predicted from the structure of gray matter volume (GMV) measured with magnetic resonance imaging (MRI) (Kanai and Rees, 2011). Until now, however, the relationship between individual differences in negative automatic thoughts as mediators in this behavioral model and brain structure has been little studied.

A study by Joffe et al. (2009) found that Val66Met carriers, compared with non-carriers, of brain-derived neurotrophic factor (BDNF) showed higher neuroticism, which, in turn, was associated with lower total GMV of the hippocampus and with depression. Moreover, compared with healthy controls or MDD patients, high-risk individuals who have first-degree family members with depression have been found to have a reduction in parahippocampal/hippocampal volume (de Geus et al., 2007; Baaré et al., 2010; Chen et al., 2010; Amico et al., 2011; Carballedo et al., 2012), or greater GMV in the bilateral hippocampus (Romanczuk-Seiferth et al., 2014). In summary, we hypothesize that premorbid variations in brain structure may be important for the early detection and prevention of the disease in healthy volunteers (Forness et al., 2000). By analogy, individuals at high risk for psychosis can be distinguished from healthy controls, specifically on the basis of working memory performance (Smith et al., 2006; Pflueger et al., 2007). For example, Ladouceur et al. (2008) reported that individuals with increased volume of the parahippocampal/hippocampal region have a high risk of developing bipolar disorder. Moreover, previous studies have shown correlations between depression severity and hippocampal volume (Vakili et al., 2000; Saylam et al., 2006), although other studies have not replicated the correlation (Vythilingam et al., 2002; Frodl et al., 2004, 2006). Meta-analyses of depression research (Videbech and Ravnkilde, 2004; Campbell et al., 2004a, 2004b; Lorenzetti et al., 2009; Cole et al., 2011) have identified reduction in parahippocampal/hippocampal structure as the most replicated finding and a potential diagnostic neuro-biomarker for depression; however, more persistent forms of MDD, medication effects and gender tend to have an impact on hippocampal volume so that it is difficult to draw firm conclusions about the specificity of its relationship to the onset of depression. Therefore, drawing upon findings from neuroimaging studies with psychiatric samples, we proposed that individual differences in negative thoughts about oneself (i.e., the important mediator in this model) would be associated with parahippocampal/hippocampal volume in a healthy sample.

2. Methods

2.1. Participants

Participants were 298 volunteers (140 males, mean age=20.17, S.D.=1.30 years; 158 females, mean age=19.74, S.D.=1.23 years) from an ongoing project at Southwest University examining associations among brain imaging, creativity and mental health. Participants were all Chinese and right-handed. They had normal or corrected-to-normal vision. The study was approved by Southwest University Brain Imaging Center Institutional Review Board. Exclusion criteria were history of past or present psychiatric care, or presence of acute or chronic medical illness. In accordance with the Declaration of Helsinki (2008), written informed consent was obtained from all individuals before engagement in the research tasks.

2.2. Behavioral assessments

All the self-reported questionnaires were scored by trained graduate students with specialization psychology according to the respective criteria of each scale.

Therapeutic approaches designed to alter negative beliefs have been shown to be particularly effective in both symptom reduction and prevention of relapse (Rush et al., 1977; Kovacs et al., 1981). Therefore, a scale assessing irrational beliefs and related cognitive characteristics of depression is important (Clark, 1988). Fortunately, the Automatic Thoughts Questionnaire (ATQ) (Hollon and Kendall, 1980), a 30-item self-report measure that assesses the frequency of occurrence of automatic negative thoughts (negative self-statements) associated with depression, is available (Hollon and Kendall, 1980; Harrell and Ryon, 1983). Subjects are instructed to read each item and indicate on a 5-point scale, from "none" to "all the time", whether the thought is present. Scores range from 30 to 150, with higher scores signifying more negative cognition and thoughts (Hollon and Kendall, 1980). The initial psychometric evaluation of the measure demonstrated adequate split-half reliability in college students ($r=0.97$, $\alpha=0.96$, $p<0.001$; Hollon and Kendall, 1980). A subsequent evaluation reported the association of items and total scores ($r=0.56$–0.91; Harrell and Ryon, 1983). Individual item-total correlations range from $r=0.47$ ("I've let people down") to $r=0.78$ ("My life's not going the way I want it to"). In our study, Cronbach's alpha coefficient for internal consistency in this sample was 0.95. In summary, the ATQ-30, as a measure of the automatic negative thoughts that are posited in cognitive theories to be related to the state of depression, has a good concurrent validity (Hollon and Kendall, 1980).

A large number of rating scales have been developed for the systematic assessment of depression. Among them, the Self-Rating Depression Scale (SDS) (Zung et al., 1965) is a self-evaluating test that was designed to provide a brief quantification of depressive state and that has been frequently used. The self-administered scale has the advantage of having more standardized administration and scoring procedures than interviewer-based assessment instruments. Correlations with the Beck Depression Inventory (BDI), the Hamilton Rating Scale for Depression (HRSD), and the Minnesota Multiphasic Personality Inventory-Depression subscale (MMPI-D) are in the moderate-high range. Zung has used the scale in a normal adult population (Zung, 1971) and documented its effectiveness as a screener (Zung, 1990). To some extent, our studies might be called an "analogue study" because we wanted to document some indicators of the potential to develop clinical depression. The SDS addresses the syndrome of depression and the symptoms that underlie the DSM definition, including 20 items scored from "none" to "all the time". Raw scores range from 20 to 80, with higher scores indicative of more severe depressive symptom. Scores on the SDS are reliable and not influenced by age, gender, economic status and other demographic factors. The initial psychometric evaluation of the measure revealed adequate split-half reliability ($r=0.92$; Zung, 1986). Cronbach's alpha coefficient for internal consistency in our sample was 0.81.