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Short-term group cognitive behavior therapy contributes to recovery from mild depression: Evidence from functional and structural MRI

Xue Du [a,b,1], Yu Mao [a,b,1], Qian Ran [c], Qinglin Zhang [a,b,*], QingHua Luo [c], Jiang Qiu [a,b,*]

[a] Key Laboratory of Cognition and Personality (SWU), Ministry of Education, Chongqing 400715, China
[b] School of Psychology, Southwest University, Chongqing 400715, China
[c] Department of Psychiatry, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400016, China

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ABSTRACT

We used the functional and structural magnetic resonance imaging to explore the neural correlates of response to group cognitive behavioral therapy (CBT) in mild depression. College students with mild depressive symptoms participated in our 4-week group CBT training. The behavioral results showed that depression symptoms decreased after participation in group CBT. After the training, the gray matter volume (GMV) in the right middle frontal gyrus (MFG) increased and amplitude of low-frequency fluctuations (ALFF) decreased. In addition, GMV in the left postcentral gyrus decreased after the group CBT. Moreover, the increase of percentage change in the right MFG was positively correlated with the decrease of the Beck Depression Inventory (BDI) score, while less decrease in percentage change in the left postcentral gyrus was significantly correlated with greater decrease of BDI score. Finally, after the training, functional connectivity between the right MFG and the insula decreased, while the connectivity between the left postcentral gyrus and the parahippocampal gyrus increased. These findings suggested that short-term participation in group CBT had an effective impact on mild depression. It contributed to decreasing negative bias (salience detection for negative stimuli).

1. Introduction

Depression is a highly prevalent, clinically significant, and disorder (Kessler et al., 2003; Rush et al., 2003; Richards, 2011). Major depression disorder (MDD) is one of the most common psychiatric disorders. Moreover, many individuals experience sub-threshold depressive symptoms that do not meet criteria for full-blown MDD episodes (Furukawa et al., 2009). Previous studies pointed out that persistent depressive symptoms below the threshold for a diagnosis of major depression could cause chronic illness and have a high risk of progression to more serious disorders (Cuijpers and Smit, 2004; Cuijpers et al., 2007). In fact, mild or sub-threshold depression is a state that has been postulated to represent the low end of a continuum of depressive severity. Although sub-threshold depressive states are quantitatively different from MDD, they may not be qualitatively different (Gotlib, 1984).

Mild depression can be considered as a significant indicator of risk for MDD. A more precise understanding of mild depression, which is thought to be prodromal to MDD, might aid in the effort to prevent the onset of clinical depression through early diagnosis and intervention. According to the World Mental Health Survey, mild and sub-threshold cases are prevalent in every country, so the value of treating mild cases should be carefully considered (Demyttenaere et al., 2013). Given the importance of identifying biomarkers of depression, it must be a priority target for society and governments to recognize and treat mild cases of depression to forestall the development of a substantial proportion of future serious cases (Beddington et al., 2008; Sahakian et al., 2010; Collins et al., 2011).

Cognitive behavior therapy (CBT) is a widely investigated and practiced psychotherapeutic approach that can effectively reduce rates of subsequent relapse and recurrence (Beck et al., 1979; Cuijpers et al., 2013). The premise of CBT derives from Beck's Cognitive Theory of Depression, which posits that depression is state in which self-reinforcing dysfunctional negative schemata dominate every aspect of an individual's information processing (Beck, 1967, 1976). Hence, the focus of CBT is on modifying negative cognition, also known as dysfunctional schemata (Beck, 1976). Generally, theoretical models of the action of CBT in depression implicate top-down mechanisms, because the mediation of depression-relevant cognition, affective bias, and maladaptive information processing is emphasized in the intervention (Beck,

* Corresponding authors at: Key Laboratory of Cognition and Personality (SWU), Ministry of Education, Chongqing 400715, China.
E-mail addresses: zhangql@swu.edu.cn (Q. Zhang), doctorlqh@hotmail.com (Q. Luo), qiuj318@swu.edu.cn (J. Qiu).
[1] The authors contributed equally to this work.

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1979; Clak and Beck, 1999). Moreover, group intervention can be used as a therapeutic intervention, as well as a preventative measure (Corey, 2011), due to its cost-effectiveness and potential to facilitate peer support (Edelman et al., 1999; Burlingame et al., 2004).

With the development of functional neuroimaging techniques, many investigators have begun to study the neural mechanisms underlying different forms of CBT. These studies identified showed certain brain regions as being involved in the process, including the anterior cingulate cortex (ACC) and the prefrontal gyrus (Fu et al., 2008; Dichter et al., 2010; Forbes et al., 2010; Ritchey et al., 2011). Although the results are promising, functional imaging studies of CBT are methodologically demanding and have varied dramatically with regard to paradigms and analytic methods (Bennett and Miller, 2010). In fact, structural neuroimaging approaches have more often been performed in clinical practice (Redlich et al., 2014). Until now, there have been few structural neuroimaging studies that examined changes that occurred after group CBT in mild depression. Therefore, we tried to combine the advantage of both functional and structural neuroimaging techniques to explore the neural correlates of response to CBT in mild depression.

Additionally, a large number of reports found that different dependent measures of depression might have different reliabilities and sensitivities to change (Brown et al., 1995; Shafer, 2006). Thus, the choice of different assessment instruments might lead to different conclusions about the efficacy of the various therapies under investigation. In considering of our aim, we chose the Beck Depression Inventory (BDI) as a conservative means of measuring change in depressive symptomatology (Dobson, 1989). In this study, we predicted that (1) behavioral symptoms could be reduced after group CBT, (2) the efficacy of CBT in mild depression might be reflected in associated changes in brain regions, such as the prefrontal gyrus, which has been related to cognitive and affective processing (Bush et al., 2000; De Lange et al., 2008; Kumari et al., 2009; Etkin et al., 2011; Ritchey et al., 2011). To some extent, this study might be the first one to combine functional and structural techniques to explore the neural correlates of response to CBT in mild depression. As such, it should provide potential suggestions for future clinical applications and early intervention in cases of mild depression.

2. Methods

2.1. Participants

Twenty participants (mean age (SD)=19.94 (1.06) years; 10 women, 10 men) were recruited from our ongoing project to examine the associations among brain-imaging findings, creativity and mental health. None of the participants in the present study met DSM-IV criteria for depression (American Psychiatric Association, 1994). Because of our focus on mild depression, the 21-item BDI was used as the assessment instrument in our study. According to the norm in China, the inclusion criteria for minor depression require at least 4 points on the BDI (Beck, 1967; Hongbo and Yanping, 1987). Participants who had a history of psychiatric or neurological disorders were also excluded. In total, four subjects were excluded from the training group: two had dropped out of the training, and two had excessive head motion in the scanner. Therefore, the data that were analyzed derived from 16 participants, including both pre- and post-training scans. Written informed consent was obtained from all participants before study. This study was approved by the Institutional Human Participants Review Board of Southwest University Imaging Center for Brain Research.

2.2. The intervention

The 4-week group CBT program was designed and led by two licensed psychologists. The group met for 90-min sessions for 4 consecutive weeks. Participants received a manual at the start of the training, as well as handouts and homework exercises at every session. The intervention incorporated the use of cognitive and behavioral techniques, including encouragement to express feelings and to provide group support. For example, the training emphasized how to identify and challenge maladaptive thoughts and beliefs. This included elements of basic cognitive skills, regulation of emotion, stress management, relaxation training, and group support. Elements of the group discussion specific to "disputing" of negative perceptions and the use of coping statements were included. The intervention's brevity was determined from research suggesting the efficacy of short-term interventions (Ashton et al., 2009; Grilo et al., 2006).

2.3. Data acquisition

Structural and functional magnetic resonance imaging (MRI) was acquired on a Siemens 3.0 T-Magnetom Sonata scanner (Siemens Medical, Erlangen, Germany). Subjects were equipped with a circularly polarized standard head coil; in addition, foam pads and headphones were used to reduce head motion and scanner noise. High-resolution T1-weighted anatomical images were acquired using a magnetization-prepared rapid gradient echo (MPRAGE) sequence: repetition time (TR)=1900 ms; echo time (TE)=2.52 ms; inversion time (TI)=900 ms; flip angle (FA)=9; field of view (FOV)=256 × 256 mm^2; resolution matrix=256 × 256; slices=176; thickness=1 mm; voxel size=1 × 1 × 1 mm. At the same slice locations as in the structural images, functional images were collected axially by using an echo-planar imaging (EPI) sequence: TR=2000 ms; TE=30 ms; FA=90°; FOV=220 × 220 mm^2; resolution matrix=64 × 64; slices=20, thickness=3 mm; voxel size=3.4 × 3.4 × 4 mm. Before being scanned in a resting state, participants were instructed to keep their eyes closed but not to sleep. Instead, they were asked to relax their minds and remain motionless during the EPI data acquisition. The scan lasted for 488 s including 32 slices which were used to cover the whole brain. Each section contained 242 volumes.

2.4. Voxel-based morphometry (VBM)

The MR images were processed using the SPM8 program (Wellcome Department of Cognitive Neurology, London, UK; www.fil.ion.ucl.ac.uk/spm) implemented in Matlab 7.8 (MathWorks Inc., Natick, MA, USA). Firstly, each MR image was displayed in SPM8 to monitor artifacts or anatomical abnormalities. To enhance registration, the reorientation of the images was manually set to the anterior commissure. Then, the New Segment Toolbox from SPM8 was used on every T1-weighted MR image to extract tissue maps corresponding to the gray matter volume (GMV), white matter volume (WMV), and cerebral spinal fluid in native space. After segmentation, we performed registration, normalization, and modulation by DARTEL in SPM8, which generates a more precise registration than the standard VBM procedure. For each voxel of GMV and WMV, Jacobian determinants were used for normalization to ensure that regional differences in the absolute amount of gray matter were conserved. The images were then resampled to 1.5-mm isotropic voxels in Montreal Neurological Institute (MNI) space. Finally, the warped modulated images of gray and white matter were smoothened through the convolution of an 8-mm full-width at half-maximum isotropic Gaussian kernel to increase their signal-to-noise ratio.

The resulting maps representing the GMV of each participant in