Functional and Structural Alterations Induced by Cognitive Behavioral Therapy in Social Anxiety Disorder

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Introduction: Recently, cognitive behavioral therapy (CBT) has been one of the first-line treatments for psychiatric disorders, and especially for social anxiety disorders (SAD). So far, many functional magnetic resonance imaging (fMRI) studies for SAD have focused on activities in the fear-related neural circuits including the amygdala for facial expression pictures [1]. However, studies concerning how CBT modifies neural circuits involved in the regulation of negative emotions were limited [2]. On the other hand, selective changes of resting state networks (RSNs) were observed in patients with SAD [3], and also white matter neuroplasticity was changed in short-term (4 weeks) meditation [4]. Here, to assess the effect of CBT on neural networks, we investigated the alterations in intrinsic connectivity networks at rest and white matter integrity induced by CBT using resting state fMRI (rsfMRI) and diffusion tensor imaging (DTI) in addition to the evaluation of BOLD responses in the fear-related neural network to social anxiety provocation tasks in patients with selective serotonin reuptake inhibitor (SSRI)-resistant SAD.

Materials and Methods: Twenty-three patients with SSRI-resistant social anxiety disorder (33.3 ± 8.5 years) and 18 healthy subjects (HC, 32.3 ± 9.5 years) were recruited for this study. Patients were randomly assigned to treatment as usual (TAU) or 16-week CBT with TAU (CBT) groups and fMRI and DTI were performed both pre- and post-treatment. Social anxiety and depression levels were measured with the Liebowitz Social Anxiety Scale (LSAS), Social Phobia and Anxiety Inventory (SPAI), and Beck Depression Inventory (BDI) prior to and following the CBT sessions. fMRI and DTI were acquired with 3T MRI (Siemens MAGNETOM Verio) equipped with a 32-channel array coil with the following parameters: TE = 25 ms, TR = 2000 ms, flip angle = 75°, matrix size = 64×64, imaging resolution = 3.44 × 3.44 × 3.70 mm^3, acquisition bandwidth = 2,232 Hz/Px as fMRI, TE = 85 ms, TR = 8300 ms, matrix size = 128×128, imaging resolution = 2 × 2 × 2 mm, number of MPG directions = 30, b-value = 1000 sec/mm^2, repetitions = 2 as DTI. rsfMRI was analyzed by conn toolbox with seed regions of affective network consisting of the amygdala, orbitofrontal cortex, anterior cingulate cortex, insula, and striatum. Fractional anisotropy (FA) maps were generated using FSL, and statistical analysis was conducted using TBSS. Random effect was performed using SPM8 to assess activated brain regions during the social anxiety tasks consisting of facial expression pictures. Thereafter, region-of-interest (ROI) analysis was performed in amygdala regions.

Results and Discussions: LSAS scores in patients with SAD were stable in TAU, while they were significantly decreased after 16-week CBT and were at a level similar to that of HC (Fig. 1). SPAI scores also showed a similar trend. BOLD response to facial expression pictures in the amygdala was decreased more in the CBT group after treatment compared with the TAU group (Fig. 2). Neuronal connectivity at rest between the dorsal anterior cingulate cortex and the striatum was increased after CBT compared with HC ($p < 0.001$, uncorrected; Fig. 3). This suggested that suppressed emotional regulation in patients with SAD was recovered after CBT [5]. FA values were decreased in the right anterior limb of the internal capsule after CBT compared with HC ($p < 0.01$, uncorrected; Fig. 4). This is considered to be the main path between the striatum and prefrontal and orbitofrontal cortex interactively, and therefore decreased white matter integrity after CBT suggested compensatory decrease by relief from sustained contextual anxiety [6]. Our results suggested that alterations in neuronal circuit-related emotion induced by CBT resulted in functional and structural alterations in the short term.

References: [1] Freitas-Ferrari MC et al., Prog Neuropsychopharmacol Biol Psychiatry, 2010, [2] Porto PR et al., J Neuropsychiatry Clin Neurosci, 2009, [3] Liao W et al., Neuroimage, 2010, [4] Tang YY et al., PNAS, 2010, [5] Blair KS et al., Biol Psychiatry, 2012, [6] Hasler G et al., J Neurosci, 2007

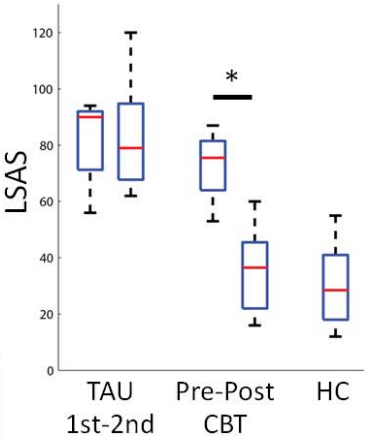

Fig. 1. Decreased Liebowitz Social Anxiety Scale (LSAS) scores after 16 weeks CBT (*$p < 0.05$).

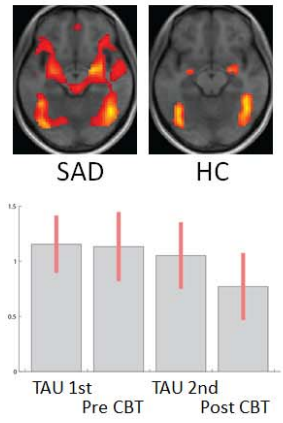

Fig. 2. BOLD response for facial expression image in amygdala was decreased after CBT.

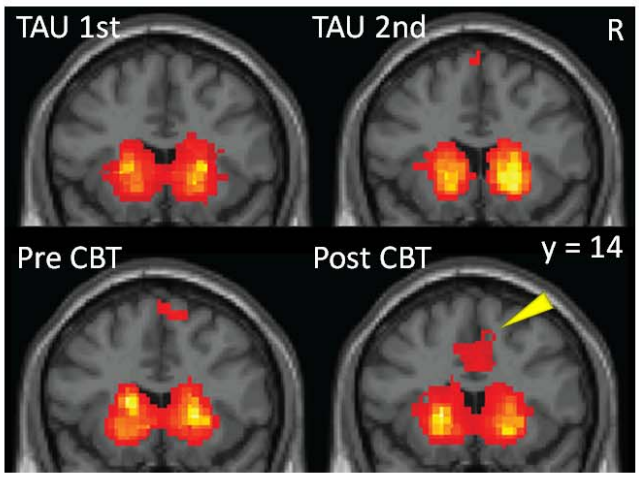

Fig. 3. Increased neuronal connectivity at rest between the dorsal anterior cingulate cortex and the striatum after CBT compared with healthy control (arrowhead, $p < 0.001$).

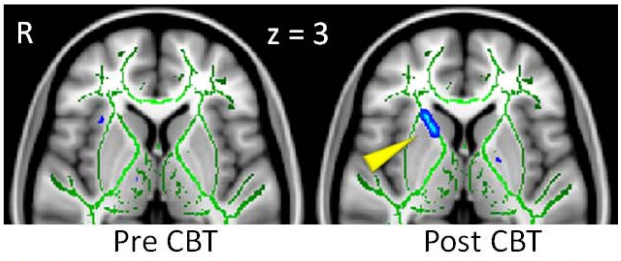

Fig. 4. Decreased FA values in the right anterior limb of internal capsule after CBT compared with healthy control (arrowhead, $p < 0.01$). No significant voxels were found in TAU.