Subgenual cingulate cortical activity and connectivity in the antidepressant efficacy of electroconvulsive therapy

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Abstract

Electroconvulsive therapy (ECT) is the most effective treatment for depression, yet its mechanism of action is unknown. Our goal was to investigate the neurobiological underpinnings of ECT response using longitudinally collected resting state fMRI (rs-fMRI) in sixteen patients with treatment-resistant depression and 10 healthy controls. Patients received bifrontal ECT 3 times a week under general anesthesia. We acquired rs-fMRI at 3 time-points: at baseline, after the 1st ECT administration, and after the course of the ECT treatment; depression was assessed with the Hamilton Depression Rating Scale (HAM-D). The primary measure derived from rs-fMRI was fractional amplitude of low frequency fluctuation (fALFF), which provides an unbiased voxel-wise estimation of brain activity. We also conducted seed-based functional connectivity analysis based on our primary findings. We compared treatment-related changes in HAM-D scores to pre- and post-treatment fALFF and connectivity measures. Subcallosal cingulate cortex (SCC) demonstrated higher BOLD signal fluctuations (fALFF) at baseline in depressed patients, and SCC fALFF decreased over the course of treatment. Decrease in SCC fALFF over the course of treatment was strongly associated with HAM-D change. In addition, connectivity of SCC with bilateral hippocampus, bilateral temporal pole, and ventro-medial prefrontal cortex was significantly reduced over the course of treatment. These results suggest that the antidepressant effect of ECT may be mediated by down-regulation of SCC activity and connectivity. SCC function may serve as an important biomarker of target engagement in the development of novel therapies for depression that is resistant to treatment with standard medications.