fMRI and Connectivity Effects of Electro-Convulsive Therapy (ECT) in Depressed Patients

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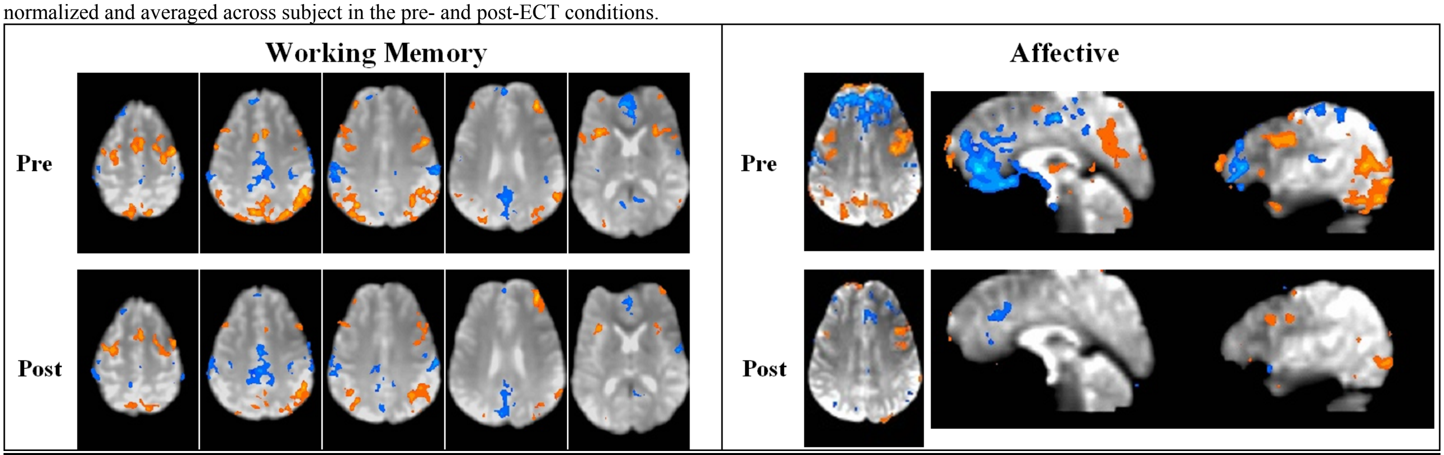
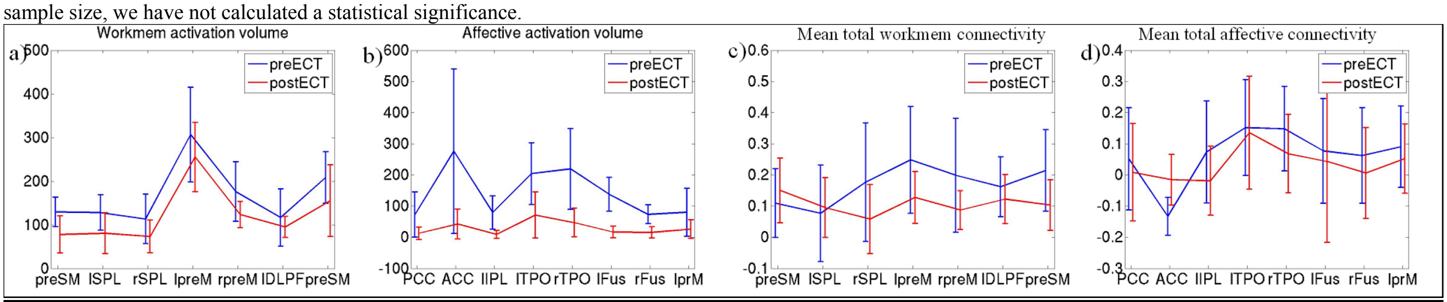
Introduction: Electroconvulsive therapy (ECT) is a safe and effective treatment for major depression often reserved for patients who are either unresponsive to or intolerant of pharmacologic therapies. Controlled trials have consistently found ECT to be equal or superior to antidepressant medication treatment [1]. However, without maintenance ECT, half of treated patients relapse by 6 months [2]. Given the risk for potential side effects and adverse reactions associated with ECT, it would be advantageous to 1) pre-screen patients for likely ECT efficacy and 2) understand the neural mechanisms of successful ECT. Functional Magnetic Resonance Imaging (fMRI) and functional connectivity (fcMRI) have been used to study depression and treatment effect of antidepressant medications [3,4] but have never been applied to the study of ECT. We present pre- and post-ECT fMRI and fcMRI results from an initial sample of 4 ECT-naive patients with treatment-resistant depression. The consensus of past neuroimaging of depression is that increased activation and decreased connectivity in frontal regions in response to tasks are related to cognitive inefficiency. It is our hypothesis that these relationships normalize after successful ECT.

Methods: Four patients with treatment-resistant depression were recruited by the treating physician after being identified as candidates for an initial series of ECT. Subjects were scanned in an IRB-approved protocol in a Siemens 3T Trio using a bitebar to reduce head motion, in a 12-ch receive head coil. Subjects were scanned within a week before their first ECT session (pre-ECT imaging) and between one and three weeks following their final ECT session (post-ECT imaging). Separate informed consent was obtained for pre and post-ECT scanning sessions. Imaging performed in each session: T1 anatomic scans, three block-paradigm fMRI scans and two resting connectivity scans. fMRI tasks were one 2-back spatial working memory task and two affective picture viewing tasks during which patients passively viewed stimuli from the International Affective Picture System (IAPS) [5] described in [6]. Each of the four total affective fMRI contained unique pictures across pre and post-ECT scan sessions. fMRI and connectivity data analyses as described before [7]. Functionally relevant ROIs identified from the activation maps were chosen and drawn on anatomy. Activation volume inside ROIs were calculated for each ROI, each activation map. Nine-voxel activation-based seeds were created in each ROI for each subject for connectivity analyses. From the working memory activation, ROIs were: left dorsolateral PFC (DLPF), , inferior or superior parietal lobule (IPL or SPL), pre-motor (preM) and preSMA (preSM). From the affective activation, ROIs were: anterior cingulate (ACC), posterior cingulate (PCC), left IPL, left preMotor, temporo-parietal-occipital junction (TPO) and fusiform gyrus (FUS). In each case, activation from the task was used within the ROI to generate the connectivity seed. Averaged, low-pass (0.085Hz) filtered timeseries were created for each seed and these were correlated to assess connectivity between these regions. For an ROI, its connectivity to all other investigated ROIs was averaged to determine mean total correlation. For display purposes, the activation and connectivity maps were spatially normalized and averaged across subject in the pre- and post-ECT conditions.



Results: The mean activation volume in all ROIs, both tasks decreased following ECT. As seen in Fig 1, the activation appears subjectively smaller after ECT. Figure 2a) and b) give the activation volume in 7 working memory ROIs and 8 affective ROIs before and after ECT. The mean total connectivity between ROIs is shown in Fig 2c) and d) and shows that for some but not all ROIs there were decreases in resting connectivity as identified by either task. PCC and preSMA connectivity showed a trend to greater connectivity but within errors, while ACC showed a small increase. The average total connectivity over all ROIs for the affective task was 0.065±0.141 for preECT affective, 0.035±0.146 for post ECT affective, 0.170±0.148 for preECT workmem, 0.106±0.088 for post ECT workmem. Due to the small sample size, we have not calculated a statistical significance.



Discussion: The overall impression is consistent with some past observations of a normalization of activation. We observed a decrease in both activation volume and connectivity following ECT. In particular, connectivity between the ACC and other regions changed from a negative overall connectivity to close to zero connectivity.

References: 1) Pagnin et al, J ECT 2004;20:13–20. 2) Prudic et al., Am J Psychiatry, 1996;153:p985-92. 3) Sheline et al, Biol Psychiatry, 2001;50:p651-8. 4) Fu et al, Arch Gen Psychiatry, 2004;61:p877-89. 5) Lang et al, Technical Report A-6. 2005, University of Florida: Gainesville, FL. 6) Anand et al, Biol Psychiatry 2005;57:p1079-88. 7) Lowe et al, Human Brain Mapp 2008;29:p818-827