received ketamine, it appears that ketamine may normalize patterns of neural activity to that seen in healthy populations.
Supported By: NIH IRP
Keywords: Ketamine, fMRI Resting State, MEG, fMRI

175. Cognitive Behavioral Therapy for Depression and the Neural Correlates of Emotion Regulation: Prediction of Treatment Outcome and Longitudinal Effects

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Background: Cognitive behavioral therapy (CBT) is effective for a substantial minority of patients with major depressive disorder (MDD), but its mechanism of action is unknown, and predictors of treatment outcome are lacking. As core techniques of CBT seek to enhance emotion regulation, we examined the neural correlates of emotion regulation using functional Magnetic Resonance Imaging (fMRI) before and after a course of CBT for MDD.
Methods: 31 unmedicated MDD participants underwent baseline fMRI scanning during tasks in which they engaged in a voluntary emotion regulation strategy during A) recall of negative autobiographical memories and B) presentation of emotionally aversive photographs. 23 participants completed scanning post-treatment. Treatment outcome was assessed using the Beck Depression Inventory and the Hamilton Depression Rating Scale. Image processing and statistical analyses were performed in FSL.
Results: While regulating responses to negative autobiographical memories, those with better treatment outcome showed post-treatment suppression of BOLD contrast in subgenual anterior cingulate, medial prefrontal cortex, and lingual gyrus clusters (voxel-wise $z>3.1$, FWE-corrected $p<0.05$). From the photographs task, greater pre-treatment BOLD responses to emotionally negative images in a cluster in hippocampus predicted worse treatment outcome (statistical thresholding as above).
Conclusions: CBT response may be mediated by enhanced downregulation of neural activity during emotion regulation; regions identified overlap with those found using a similar task in a normative sample, and are implicated in self-referential/emotion processing. Hippocampal activation during viewing of aversive images may reflect overgeneralization processes predisposing to poor treatment outcome. Future studies should examine the specificity of these effects to CBT.
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Keywords: Cognitive Behavioral Therapy, Major Depression, fMRI, Emotion Regulation

176. Evidence of Differential Changes in Cortical Thickness and Volume Between SSRI and Placebo Treated Patients With Major Depressive Disorder

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Background: To date, clinical translation of biomarkers for major depressive disorder (MDD) treatment response has been limited. Development of noninvasive, MRI based biomarkers could allow for individualized treatment selection, reducing time spent on ineffective treatments and the cost burden of MDD.
Methods: Multisite pre- and early-treatment (1-week) T1-weighted structural MRI scans acquired from 184 MDD patients randomized to an 8-week trial of sertraline or placebo were analyzed. This study is the largest placebo-controlled effort to characterize pre- or early-treatment structural alterations, in an effort to predict antidepressant treatment response in MDD patients. To standardize measures, a novel data harmonization procedure, shown to improve the reproducibility of subsequent statistical analyses, was applied.
Results: Across the a priori regions (rostral and caudal anterior cingulate, lateral orbitofrontal, rostral middle frontal, and hippocampus) a robust region-specific differential treatment effect was found in pre- and early-treatment morphometry between the placebo ($N=97$) and sertraline ($N=87$) treated groups. Region-specific pre-treatment ($p=0.040$) and early-treatment changes in cortical thickness ($p=0.004$) and volume ($p=0.046$), differentially predicted clinical response between the treatment groups. Post-hoc analysis revealed that this effect was significant in the rostral middle frontal cortex in placebo-treated patients and in the rostral anterior cingulate cortex in sertraline-treated patients. Mediation and moderation analyses were further examined.
Conclusions: Overall, we revealed short-term morphometric alterations that differentially associated with antidepressant and placebo treatment response. These findings, obtained with a site harmonization method shown to boost statistical reproducibility, enhance our understanding of the anterior cingulate cortex's role in the SSRI mechanism of action.
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Keywords: Structural MRI, Individualized Treatment, Major Depressive Disorder (MDD), Cortical Thickness, Anterior Cingulate Cortex (ACC)