Mindfulness Intervention to Study the Neurobiology of Depression (MIND)

Statistical Analysis Plan

Date: 07/01/2014

Identifiers: NCT01905267 Unique Protocol ID: 2012-0689

fMRI seed-based connectivity

A 19 voxel sphere left PCC seed (–5, –50, 36, MNI coordinates) will be derived based on previous work examining PCC connectivity [23,37] and previous literature examining resting state connectivity of the PCC to probe the DMN [38-40] . Correlation coefficients will be calculated between mean time course for seed regions and all other voxels of the brain, resulting in 3-dimensional correlation coefficient images (r images), transformed to z scores using a Fisher transformation and compared in SPM8. Whole brain correction will be achieved at $p < .05$ by using AlphaSim with 1000 Monte Carlo simulations to determine a joint threshold of height and extent ($p < .005$, cluster extent of 440 mm^3). A full factorial second-level model including the effects of group and time will be created. Given the current investigation was not adequately powered to detect treatment-by-time interactions; we will examine the main effect of time in the RFCBT group alone. To verify that these differences are related to treatment, we will confirm that all regions of interest (ROIs) that change from baseline to week eight in the RFCBT group do *not* change over time in the AO group. Thus, only ROIs that change in the RFCBT group and do not change in the AO group will be evaluated.

Post-hoc analyses will evaluate relations between clinical symptoms and connectivity. Two-tailed Pearson correlations between change in depression and rumination (baseline to 8 week) and change in extracted connectivity values (scan one to scan two) will be conducted.

Clinical data analyses

Mixed-effects regression models (MRMs) will be conducted on the Intent-to-Treat (ITT) sample using SPSS MIXED. MRMs allow for the dependencies inherent in repeated assessments, are robust to missing data, and can be used to estimate scores using group trajectories. MRMs will be used to assess the effects of treatment, and treatment-by-time (quadratic terms will be included and removed in the case of non-significance), on the RRS, RADS, and CDRS-R across eight weeks. Clinical results based on the sample of treatment completers as well as the fMRI sample will also be examined.

23. Jacobs RH, Jenkins LM, Gabriel LB, Barba A, Ryan KA, et al. (2014) Increased coupling of intrinsic networks in remitted depressed youth predicts rumination and cognitive control. PLoS One 9: e104366.
37. Jacobs RH, Barba A, Gowins JR, Klumpp H, Jenkins LM, et al. (2016) Decoupling of the amygdala to other salience network regions in adolescent-onset recurrent major depressive disorder. Psychol Med 46: 1055-1067.
38. Laird AR, Eickhoff SB, Li K, Robin DA, Glahn DC, et al. (2009) Investigating the functional heterogeneity of the default mode network using coordinate-based meta-analytic modeling. J Neurosci 29: 14496-14505.
39. Di X, Biswal BB (2014) Identifying the default mode network structure using dynamic causal modeling on resting-state functional magnetic resonance imaging. Neuroimage 86: 53-59.
40. Wang Z, Yuan Y, Bai F, You J, Li L, et al. (2012) Abnormal default-mode network in angiotensin converting enzyme D allele carriers with remitted geriatric depression. Behav Brain Res 230: 325-332.