MBSR During AI Therapy for Breast Cancer
NCT03253627

Statistical Analysis Plan

08-08-2017

Statistical Analysis Plan (SAP) for R00NR015473
August 8, 2017

Data analysis. Data analysis will be performed using SPSS Statistics 24 (IBM Corp., Armonk, NY). Using exploratory and descriptive analyses, we will first evaluate whether any data anomalies (e.g., nonrandom missing data, erroneous outliers, multicollinearity, possible confounding) may invalidate planned analyses and then summarize data in terms of location and variability using appropriate descriptive statistics, given the variable's level of measurement and observed data distribution. As needed, appropriate remedial approaches (e.g., data transformations, imputation, nonparametric analysis methods) will be applied.

Aim 1: Evaluate the preliminary efficacy of MBSR to improve neural markers of cognitive changes during AI therapy. fMRI: Data will be preprocessed using Statistical Parametric Mapping-12 (SPM-12; www.fil.ion.ucl.ac.uk/spm) to normalize images into standard space so that all brains can be compared. Talairach PickAtlas will be used to define regions of interest (ROIs) for cognitive and emotion processing. Neural activation will be evaluated using the blood-oxygen-level-dependent (BOLD) signal. SPM-12 will extract BOLD activation in these ROIs. Brain activation maps will describe (1) between-group differences in brain activation in ROIs for the MBSR versus active control group pre- and post-intervention and (2) within-group change scores in brain activation for each group pre- to post-intervention. fcMRI: BOLD signal time series will be extracted from ROIs of the default mode network. Physiological noise and motion artifact regressors will be removed. Residual time series from each ROI will be filtered between 0.01-0.08 Hz. Analyses will be performed with and without a global signal regressor to assess impact on connectivity. Parameter estimates representing connectivity between neural regions will be extracted. Functional connectivity maps will describe between-group differences in connectivity in ROIs pre- and post-intervention and within-group change scores in connectivity pre- to post-intervention. dMRI: Data will be analyzed using ExploreDTI (www.exploredti.com), FreeSurfer (surfer.nmr.mgh.harvard.edu), and the diffusion toolbox of the Functional MRI tool of Brain Software Library (www.fmrib.ox.ac.uk/fsl) to perform quality assurance for images, process them for characterization of the integrity of white matter tracts, and match white matter tracts to structural MRI data. White matter tracts between cortical and subcortical ROIs will be evaluated to describe how white matter integrity is affected. Fractional anisotropy (FA) values for white matter tracts will be extracted. FA maps will describe (1) between-group differences in FA in ROIs for the MBSR versus active control group pre- and post-intervention and (2) within-group change scores in FA pre- to post-intervention.

Exploratory Aim 2a: Describe relationships between neural markers and changes in cognitive function. Change scores for neuroimaging parameters obtained in Aim 1 will be correlated with change scores on measures of cognitive function to describe how neural markers are associated with cognitive changes. If no changes in neural markers are found, relationships between baseline neural markers and changes in cognitive function will be described. ***Exploratory Aim 2b: Describe relationships between neural markers and changes in affect.*** The methods in 2a will be used to describe relationships between neural markers and changes in affect. ***Exploratory Aim 3: Explore the moderating effect of inter-individual differences in the expression of genes involved in stress responses on the relationship between AI therapy and neural markers during MBSR.*** Differential expression (DE) of genes in relation to fMRI, fcMRI, and dMRI parameter estimates at each time point will be determined using correlational analysis. Expression intensity varies widely over genes and needs to be adjusted between genes to provide a reliable measure of DE. We will adjust the standard errors and estimate the correlation of genes with each outcome. We will adjust for multiple hypothesis testing through estimation of the FDR using the Benjamini-Hochberg procedure. The FDR q-value will be determined empirically.

Possible Problems and Solutions. The sample size is too small to make inferences about relationships evaluated in the R00 study to the larger population of postmenopausal women with breast cancer. The effect sizes for these relationships will be determined in the R00 study, which will inform the sample size for a well-powered study planned for future R01 applications (see Plan for Research Independence in the Final Progress Report for the K99 Phase). If no relationships are found between gene expression levels for stress response pathways and neural markers, other pathways will be evaluated (e.g., DNA repair).