Statistical Analysis Plan

Depression Symptoms

An analysis exploring the effects of ultrasound on depression symptoms will be employed. A multi-level model approach will be used to assess whether there is a significant difference in depression symptoms before and after treatment at post1 and post3 (if applicable), with time as the factor. This analysis will be conducted on our main outcomes of interest, the HDRS, BDI-II, and PTQ, as well as our secondary outcome WHOQOL. It is predicted that there will be significant improvement in respective symptoms and quality of life as a result of the ultrasound protocol. This analysis will be repeated with the addition of session-day assessments for the self-report measures (BDI-II and PTQ).

A secondary analysis exploring the effects of ultrasound on MADRS scores will be employed. A multi-level model approach will be used to assess whether there is a significant difference in MADRS scores before and after treatment at post1 and post3 (if applicable), with time as the factor. It is predicted that there will be significant improvement in respective symptoms as a result of the ultrasound protocol.

DMN Connectivity

A functional connectivity analysis exploring DMN connectivity will be conducted in the Functional Connectivity Toolbox (CONN; Whitfield-Gabrieli & Nieto-Castanon, 2012) in MATLAB (The MathWorks Inc., United States). An ROI-to-ROI approach will be employed wherein a contrast comparing post 1 and post 3 (separately) against baseline will be used to model the effects of transcranial ultrasound before and after treatment [baseline (-1) versus post1 or post3 (1). A full ROI to ROI connection matrix will be calculated using spatial pairwise clustering statistical approach to assess significance of effects. To assess the relationship between

change in DMN connectivity and change in depression symptoms as a result of ultrasound treatment, change in depression symptoms (baseline to end of treatment) will be entered as a covariate with the prediction that there is a significant relationship between change in DMN connectivity and change in symptoms.