

# **Vagus Nerve Stimulation and Stress Reduction Training for Migraine**

NCT03592329

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## **Statistical Analysis Plan**

### **Project 1:**

Longitudinal analyses will use post-treatment fMRI response to forehead somatosensory stimulation contrasted between the four treatment arms using a generalized linear model. An omnibus ANCOVA F-test will assess overall group differences, followed by main effects analyses (NEC vs. MBSR and active vs. inactive RAVANS), with planned post hoc pairwise comparisons between each treatment arm. This model will evaluate post-treatment fMRI response in the insula as the dependent variable, treatment group main effect as the predictor, and baseline fMRI response as a covariate (i.e., an ANCOVA). A statistically significant main effect will be interpreted as evidence that treatment assignment induces a differential change in fMRI response. These changes will be further evaluated using planned contrasts designed to evaluate the impact of group assignment in False Discovery Rate (FDR) adjusted pairwise contrasts.

### **Project 2:**

Longitudinal analyses will use post-treatment HF-HRV response to an emotional reactivity task contrasted between the four treatment arms using a generalized linear model. This model will evaluate post-treatment HF-HRV response as the dependent variable, treatment group main effect as the predictor, and baseline HF-HRV response as a covariate (i.e., an ANCOVA). A statistically significant main effect will be interpreted as evidence that treatment assignment induces a differential change in HF-HRV response. These changes will be further evaluated using planned contrasts designed to evaluate the impact of group assignment in FDR-adjusted pairwise contrasts.

### **Project 3:**

Longitudinal analyses will use post-treatment PET [11C]PBR28 SUVR signal contrasted between the four treatment arms using a generalized linear model. An omnibus ANCOVA F-test will assess overall group differences, followed by main effects analyses (NEC vs. MBSR and active vs. inactive RAVANS), with planned post hoc pairwise comparisons between each treatment arm. This model will evaluate post-treatment [11C]PBR28 SUVR signal in the insula as the dependent variable, treatment group main effect as the predictor, and baseline Insula SUVR as a covariate (i.e., an ANCOVA). A statistically significant main effect will be interpreted as evidence that treatment assignment induces a differential change in PET signal. These changes will be further evaluated using planned contrasts designed to evaluate the impact of group assignment in FDR-adjusted pairwise contrasts.