Title: TREATING HEARING LOSS TO IMPROVE MOOD AND COGNITION IN OLDER ADULTS

IRB: #7540

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# Statistical Analysis Plan

MRI Data Preprocessing and Analysis

T1 images were processed using previously published automated segmentation processes identifying cortical and subcortical regions using FreeSurfer, followed by visual inspection of segmentation. Regions within the auditory cortex constituted T1 regions-of-interest (ROIs): cortical thickness of anterior transverse temporal gyrus and superior temporal gyrus (lateral, planum polare, and planum temporale). These were selected due to previous evidence that HL is associated with deafferentation-induced atrophy of primary and secondary auditory cortices in older adults.

DTI ROIs included the inferior fronto-occipital fasciculus, inferior longitudinal fasciculus, superior longitudinal fasciculus (SLF), and uncinate fasciculus. These tracts are important for processing of auditory information and also have been shown to underlie constituent executive functions in older adults. DTI data were processed using FMRIB Software Library (FSL) version 6.0.1 (Oxford, UK). After movement and distortion correction using FSL Eddy , extraction of a brain mask using the Brain Extraction Tool, a diffusion tensor model was fitted using FSL DTIFIT for each voxel and used to generate fractional anisotropy (FA) images. TBSS were applied to the FA images by aligning the images to a 1x1x1mm standard space, creating a mean FA image, and projecting all particpants' FA images onto the mean FA skeleton which was then used for statistical analyses. The Johns Hopkins University (JHU) white matter tractography atlas was used to quantify mean FA for the selected ROIs. Nonlinear warps and skeleton projection were also applied to radial diffusivity (RD) images for statistical analyses.

Data Analysis

Participants were randomized to receive hearing aid treatment vs. sham, and analysis of covariance (ANCOVA) was used to analyze the between-group differences (i.e., active-sham effect) on hearing, psychiatric, functional, and cognitive outcomes. For each measure (i.e., HHIE), the outcome modeled was the change from baseline (Week 0) to the end of study (Week 12) with predictors including baseline HHIE, group (active vs. sham), and covariates of age and education. Encompassing all participants (including those randomized to sham), this model provides baseline adjusted estimates of change within group, i.e. the difference from pre- to post-randomization for the active group, the difference from pre- to post-randomization for the Sham group, and the randomization effect between groups (active-sham effect). Differences in the number of hours of hearing aid usage between groups (active vs. sham) by time (Week 2, 6, 12) was analyzed using an analysis of variance (ANOVA) by including the predictors of group, time, and group by time interaction.

Lastly, association analyses were performed between audiometric measures (PTA and SDS) and mean FA and RD of the specified DTI ROIs using partial correlations and adjusting for age and gender as covariates. The same association analyses were performed between audiometric measures and cortical thickness of our T1 ROIs, adjusting for age, gender, and intracranial volume. Given the small sample size, the exploratory analyses did not control for multiple comparisons.