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Manipulating Sleep in Young Adults with ACEs Study

Statistical Power and Analysis Plan

Statistical Design and Power

Expected Enrollment: 70 participants (n = 35/group), allowing for a 20% dropout rate

Expected Effect Size for vascular endothelial function (flow mediated dilation (FMD%)): True-mediated effect of 0.2 and post-intervention between-group mean difference (adjusted for baseline scores) of *d* = 0.49.

The *d* was determined using the effect size of interest for FMD which we defined as 0.5x the difference in FMD% between young adults with versus without ACEs (e.g., 1.7%) using a pooled standard deviation of 3.5% based on our data. This effect size was also equivalent to or lower than the reported average effect size of CBT-I on SE% and WASO, and will allow us to detect a true-mediated effect of 0.20 at 0.80 power using ANCOVA with latent change score modeling.

Statistical Power for Primary Outcome: ≥0.8

Approach to Results Analyses: We will utilize a modified intent-to-treat analysis approach, where randomized intervention 'completers' and 'non-completers' are included, but randomized non-attenders are excluded from analyses.

Statistical Analyses: Our primary intent is to estimate the mediated effect of improved sleep on vascular endothelial function (FMD%) in the context of a pretest-posttest randomized control group design. T do so, we will utilize ANCOVA with latent change score modeling, which provides an unbiased effect estimate, best reduces Type I error rates, and generally affords the greatest statistical power. The primary model will include SE% as the mediator (M), with vascular endothelial function (FMD%) as the primary outcome (Y). In these models, the experimental manipulation acts as the independent variable (X). Models will be fit using M*plus*. Secondarily, we will perform separate models where other sleep quality and duration indicators are considered the mediator (M), and vascular endothelial function, inflammation, or oxidative stress as the dependent variable (Y). For all models, we will consider inclusion of a second mediator (e.g., perceived stress, psychological distress) to further improve statistical power. In secondary analysis, we will also explore whether sleep-induced improvements in trauma, depression, and anxiety symptoms, stress, or psychological coping mediate improvements in vascular function if these are responsive to improved sleep.

The cytokine and chemokine data will be analyzed using a repeated measures analyses of variance with simultaneous component analyses – a novel statistical method to separate and visualize multivariate effects from different sources of variation in the data in the context of randomized interventions. As we will measure multiple circulating anti- and pro-inflammatory and oxidative stress biomarkers, this approach is well suited to the task of comparing changes in components between treatment groups across time to better understand the effect of improved sleep on inflammation and oxidative in individuals with ACEs. This approach also is robust to missing outcome data. Secondary analyses methods will include repeated measures ANCOVAs with baseline scores as covariate for FMD%, vascular inflammation, vascular oxidative stress, and PBMC anti-oxidant enzyme expression and activity, as well as regression analyses between changes in dependent variables (FMD%) and changes in secondary outcomes (endothelial NFκB p65, NADPH-oxidase $p47^{phox}$, nitrotyrosine expression) or mediating (WASO, SWS) variables.

Finally, all analyses will be completed with sex included as a covariate, and sex-stratified analyses will be used to explore whether effects are sex-dependent.