Adapted Cognitive Behavioral Treatment for Depression in Patients With Moderate to Severe Traumatic Brain Injury

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Statistical Analysis Plan

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Preliminary analyses will describe the participants' sociodemographic and clinical characteristics. Comparisons will be made using Mann-Whitney or chi-square tests to determine if the randomization provided a balanced sample and if patients who dropped out differ from those who did not. All analyses will be conducted using the SPSS and/or Stata statistical packages.

Aim 1: (Acceptability, Tolerability, and Adherence in Randomized Trial): We will use descriptive statistics to report the number of intervention sessions attended (we expect > 80%), number of participants recruited per month (we expect 3/mo), randomization rate (number randomized/number consented; we expect about 67% of those consented will be randomized), number of assessment sessions attended (we expect > 80%), retention (number of study completers/number randomized; we expect >80%), and rate of satisfaction with treatment (total STTS-R score).

EXPLORATORY AIM

Aim 2 (To evaluate the potential efficacy of CBTx-TBI for depression in the randomized pilot trial (N=40) and possible moderators and mediators of outcome):

Hypothesis 2a: CBTx-TBI will result in a greater decrease in IDS-C scores after 12 weeks (primary outcome) compared to waitlist control. Response over 12 weeks defined by 50% or greater decrease on IDS-C total; remission ≤6 on IDS-C total. Continuous variables will be analyzed by generalized mixed effect modeling, which impute missing values based on maximum likelihood estimates of missing parameters, allowing analysis of all participants. A time-by-condition interaction will be analyzed to test the intervention's efficacy. Relevant potential covariates (e.g., caregiver presence) will also be examined. The percent of responders and remitters in each group will be computed in order to estimate an effect size for the R01. Although I will test for statistical significance, the primary aim of this pilot RCT is to estimate the intervention's effect size to conduct a larger, more adequately powered R01 study, as is outlined in NIH guidelines for developing behavioral interventions[i]. Given that some prior studies utilizing CBT in patients with TBI suggest large effect sizes for reducing emotional distress and depressive symptoms,[32,34] we expect similar findings.

Hypothesis 2b: CBTx-TBI will produce an increase in coping skills, adaptive thinking, positive self-appraisal, social functioning and activity level compared to waitlist control, and these factors will mediate depressive outcomes. To evaluate the indirect effect of CBTx-TBI to depression (IDS-C) through coping skills, adaptive thinking, positive self-appraisal, social functioning, and activity level, we will employ an SPSS macro (PROCESS) to test the significance of the indirect effect with a bootstrapping approach to obtain confidence intervals.[ii] The constructed conditional process model proposes that CBTx-TBI will lead to increased coping skills, adaptive thinking, positive self-appraisal, social functioning and activity level, and that increase in these mediators will result in reduced depression. Bootstrapping is superior to other methods for determining the significance of indirect effects, as the assumption of normality for the sampling distribution is not required and power is improved.[iii]

Hypothesis 2c: Degree of cognitive impairment at baseline will moderate response to treatment. We will run a hierarchical regression model. The main predictor variables (CBTx-TBI, cognitive

impairment) will be mean centered based on previous research.[iv] Their interaction will then be entered to examine the moderating effect of cognitive impairment on the relationship between CBTx-TBI and depression after entering the covariates (i.e., caregiver presence). To examine the moderation hypotheses, we will employ an SPSS macro (MODPROBE) to test whether there is a significant interaction.[v]

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