Digital Cognition in Multiple Sclerosis (DigCog)

NCT03569618

August 1st, 2018

SAP: MS BandTogether Phase II RCT

Data Cleaning / Testing of Assumptions: Prior to proceeding with the following data analysis plan, we will examine variable distributions for outliers and evaluate whether the necessary assumptions are met for the planned analyses (e.g., normality and homogeneity of variances, as applicable). If outliers are detected or assumptions are violated, I will consult with CTSI statistics regarding appropriate analytic methods and will consider distribution transformations, non-parametric analyses, and/or analyses methods more robust to such violations. All analyses will be performed according to the intention-to-treat principle (primary) then the per-protocol principle.

- V1 = baseline
- V2 = 6 wks, for efficacy
- V3 = 14 wks after BL, for persistence

Defining adherence

1. Complete >50% sessions - completers
2. Complete <50% sessions but return for V2 +/- V3 – non-adherent
3. Withdraw (technical, MS factors, other) - withdraw

OUTCOMES

1. **Compare effect of BT vs. Words for 6 weeks on:**
   a. Primary outcome: SDMT
   b. Secondary outcomes: Match, CogState DET
   c. Exploratory outcomes: PASAT, CVLT, BVMT, ACE variables, EVO metrics

   - **ITT Superiority analysis – one tailed t-test**
   - ANCOVAs and linear regressions adjusting for age, gender, MS duration, baseline SDMT (subs: baseline SDMT z score), education, fatigue, depression, anxiety, vision, EDSS, dexterity -> stepwise, remove anything that is not significant effect modifier
   - % patients who improve in each
   - % patients who reach 4pt SDMT improvement

   If assumptions are violated and another distribution provides a better fit to the data, then we will proceed with that distribution.

2. **Evaluate persistence of effects at 8 weeks after intervention.**
   Compare groups for changes in SDMT between Visits 2 and 3.
   - Absolute change in SDMT (primary outcome) and in secondary/exploratory outcomes
   - % change in SDMT
   - % who don't decline in SDMT

We will calculate the final regression coefficients for the intervention effects at Post-Test and Follow-Up. Results will be presented as the change in the mean performance score at each time point in the intervention group relative to the control group.

3. **Evaluate adherence and other indicators of intervention acceptability**

- We will use descriptive analyses to calculate how well participants followed the intervention schedule (i.e., using BT's timestamped output files) and summarize participant ratings of BT and Words on the acceptability questionnaire. We will consider BT to show strong ***acceptability*** if ≥75% of participants adhere to the study (i.e. complete ≥50% of the sessions) and rate BT favorably in terms of its ease of use, its enjoyability, and their satisfaction with the training received.
- To identify potential treatment moderators to inform the design of a future RCT, we will explore whether demographics (i.e., age, gender, and education), MS characteristics (disease duration, EDSS, vision, walking, dexterity), comorbidities (depression, anxiety, fatigue), cognition (composite BiCAMS z scores) *or participant adherence (high vs. low based on a median split)* influence treatment effects. We will evaluate these factors as both continuous and categorical [age group (2 groups; quartiles), gender (male vs. female), education (high school vs. greater than high school), baseline SDMT z score (-2 to -1, -1 to 0, 0-1), etc] variables.
- We will evaluate the effect of the BT intervention within these subgroups, examining differences in treatment effects according to subgroup by tests of interaction.
- These analyses will be conducted to assess change in outcomes, comparing the intervention group to the active control group, by subgroups at Visit 2 and Visit 3.