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14. ABSTRACT

Impairments in new learning and memory (NLM) are common deficits in individuals with Traumatic Brain Injury (TBI) and exert significant negative impact on everyday life. There is thus a need for effective interventions for learning and memory dysfunction in TBI, particularly group-based interventions for which 3rd party payment may be more forthcoming, The current study addresses this need through a double blind, placebo-controlled, randomized clinical trial (RCT) of a group administration of the modified Story Memory Technique (mSMT). Over a decade of research and development at our center has demonstrated the mSMT to be effective for improving NLM in individuals with Multiple Sclerosis (MS) and TBI across three realms of functioning, objective behavior, brain functioning and everyday life. This convincing data provides Class I evidence supporting the efficacy of the mSMT for improving NLM in these populations. Given the strong efficacy data on the mSMT, coupled with the current trends in insurance reimbursement, clinicians worldwide have highlighted the need to provide the mSMT via an effective group format. We have thus modified the treatment protocol for group administration. This pilot

15. SUBJECT TERMS

Memory, TBI, cognition, cognitive rehabilitation, cognitive retraining, new learning, treatment

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1. **INTRODUCTION:**

Impairments in new learning and memory are among the most common deficits in individuals with Traumatic Brain Injury (TBI) and have been shown to exert significant negative impact on everyday life. There is thus a tremendous need for the development of effective interventions for learning and memory dysfunction in TBI, particularly group-based interventions for which 3rd party payment may be more forthcoming. The current study addresses this critical need through the conduct of a double blind, placebo-controlled, randomized clinical trial (RCT) of a group administration of the modified Story Memory Technique (mSMT). Over a decade of research and development conducted at our center has demonstrated the mSMT to be effective for improving new learning and memory in individuals with Multiple Sclerosis (MS) and TBI across three realms of functioning, objective behavior, brain functioning and everyday life. This convincing data provides Class I evidence supporting the efficacy of the mSMT for improving new learning and memory in these populations. Given the strong efficacy data on the mSMT, coupled with the current trends in insurance reimbursement, clinicians worldwide have highlighted the need to provide the mSMT via an effective group format. We have thus modified the treatment protocol for group administration. This pilot RCT tests the efficacy of a group administration of the mSMT for persons with moderate to severe TBI.

2. **KEYWORDS:** *Provide a brief list of keywords (limit to 20 words).*

Memory, TBI, cognition, cognitive rehabilitation, cognitive retraining, new learning, treatment

3. **ACCOMPLISHMENTS:**

What were the major goals of the project?

The current study addresses the following specific aims.

Aim 1. Objectively evaluate the efficacy of the group mSMT to improve new learning/memory in individuals with TBI with documented deficits in this area.
Aim 2. Increase the generalizability and real life application of the group mSMT by assessing outcome following group mSMT with global measures of everyday life, including one objective measure and multiple subjective measures.
Aim 3. Examine the neurofunctional changes resulting from the group-based mSMT in TBI subjects with impairments in new learning and memory. We will examine if neurofunctional changes in the brain are associated with behavioral improvements following the mSMT and if these changes are maintained over time.
Aim 4: Evaluate the long-term efficacy of the group mSMT through a 3-month follow-up.

To accomplish these aims, the following major tasks were identified:

- *Major Task 1: Administratively Prepare for Clinical Trial*
  - *Target completion date: 1/1/17*
  - *Actual completion date: 1/1/17*
  - *Percent of completion: 100%*

- *Major Task 2: Coordinate Study Staff for Clinical Trial*
  - *Target completion date: 4/1/17*
  - *Actual completion date: 4/1/17*
  - *Percent of completion: 100%*
- *Major Task 3: Prepare Research Protocol*
  - *Target completion date: 2/1/17*
  - *Actual completion date: 2/1/17*
  - *Percent of completion: 100%*
- *Major Task 4: Participant Recruitment, Treatment, Participant Evaluation*
  - *Target completion date: 9/30/20*
  - *Actual completion date: n/a*
  - *Percent of completion: 35.5% (16 participants of 45 targeted) or 26.6% (16 of 60 targeted)*
- *Major Task 5: Data Analysis*
  - *Target completion date: 9/30/20*
  - *Actual completion date: n/a*
  - *Percent of completion: n/a*

What was accomplished under these goals?

1) Major Activities:

	Deadline	Status
Major Task 1: Administratively Prepare for Clinical Trial	1/1/17	complete
Major Task 2: Coordinate Study Staff for Clinical Trials	4/1/17	complete
Major Task 3: Prepare Research Protocol	2/1/17	complete
Major Task 4: Participant Recruitment, Treatment, Participant Assessment	9/30/20	ongoing

2) Specific Objectives:

	Deadline	Status
Major Task 1: Administratively Prepare for Clinical Trial		
Subtask 1: Prepare Regulatory Documents and Research Protocol		
Finalize consent form & human subjects protocol	1/1/17	complete
Submit protocol to IRB	1/1/17	complete
Submit protocol for Military IRB Review (ORP/HRPO)	4/1/17	complete
Submit amendments, adverse events and protocol deviations as needed	As needed	
Coordinate with Sites for annual IRB report for continuing review	Annually	

Milestone Achieved: Local IRB approval at KF	1/1/17	complete
Milestone Achieved: HRPO		
Major Task 2: Coordinate Study Staff for Clinical Trials		
Subtask1: Hiring and Training of Study Staff		
Prepare job description design	11/1/16	complete
Advertise and interview for project related staff	1/1/17	complete
Coordinate for space allocation for new staff	1/1/17	complete
Train staff for treatment and assessment activities	3/1/17	complete
Milestone Achieved: Research staff trained	4/1/17	complete
Subtask 2: Facilitate hiring, training, supervision and fidelity checks as needed for attrition and treatment fidelity	ongoing	
Milestone Achieved: Maintained trained and available staff throughout duration of clinical trial	ongoing	
Major Task 3: Prepare Research Protocol		
Finalize administration procedures for group mSMT	2/1/17	complete
Finalize assessment procedures; assemble testing binders and testing files for NPE and AGF	2/1/17	complete
Ensure appropriate programming of ePrime stimulus delivery of neuroimaging stimuli	2/1/17	complete
Finalize timing and parameters for the collection of optimal imaging data	2/1/17	complete
Milestone Achieved: both outcome assessments and treatment protocol finalized and running smoothly	ongoing	
Major Task 4: Participant Recruitment, Treatment, Participant Evaluation		
Subtask 1: Participant recruitment & enrollment		
Begin recruitment and screening of appropriate potential participants for study participation	4/1/17	complete
Milestone Achieved: 1st 3-5 participants consented, screened and enrolled	5/1/17	complete
Milestone Achieved: First group treatment period completed successfully	7/1/17	complete
Recruitment and screening continues	ongoing	ongoing
Participants complete assigned condition group treatment to reach target n of 90	ongoing	ongoing
Complete follow-up assessments 3 months after completion of treatment	ongoing	ongoing
Milestone Achieved: Data collection complete; data analysis begins	9/30/20	ongoing

3) Significant results or key outcomes:

Data collection is ongoing and has been progressing well. We have encountered slowed enrollment and we have tried several means of addressing this. This is a very difficult study to recruit for because individuals have to come to Kessler for treatment and because it is a group treatment, their schedules need to coincide. We have begun to recruit off-site at day treatment programs (clubhouse). This has increased enrollment somewhat and we will thus continue. We are currently exploring the possibility of expanding recruitment to a 3rd location – another

outpatient day treatment program in NJ. There are no other results to report as data collection is ongoing.

4) other achievements.

As summarized above, given that this is a randomized clinical trial (RCT), there are several aspects to the protocol that required attention. The initial grant year tackled these tasks, including preparing regulatory documents and the research protocol, coordinating the study staff for the clinical trial (hiring, training, advertising for the study, compiling all assessment and training protocols, coordinating space allocation, and identifying technological needs and capabilities), and preparation of the research protocol. Finally, participant recruitment, testing and enrollment could be initiated. The 2nd year of the grant focused on participant recruitment, screening and enrollment. Recruitment has been increasingly difficult, detailed below. We have added a 2nd performance site, a clubhouse in Milburn, NJ, which has helped recruitment. We are additionally currently exploring 3rd potential performance site, an outpatient day program in the area, to further enhance participant recruitment.

Recruitment details:

- ***407** people with moderate to severe TBI were contacted for potential participation in the study.*
    - ***68 of the 407** were background screened*
        - *Thirty-three (33) didn't qualify based on background screen.*
        - *Thirty-five (35) qualified based on the background screen*
        - *Twenty-six (26) were willing to complete the in-person screen*
            - *Three (3) failed in-person screen*
            - *Two (2) chose not to participate after passing the in-person screen*
            - *Twenty (20) people passed the screenings and were enrolled*
            - *One (1) person is scheduled to be screened*

          Sixteen (16) participants completed the study
            - *Two of the 16 also completed the imaging assessments at baseline and one of the two also complete the follow-up scans.*
        - *One (1) participant is enrolled but treatment initiation is pending location availability*
        - *Three (3) participants are currently in treatment*
        - *Six (6) additional participants dropped out after completing the baseline assessment*
    - ***78 of the 407** were not interested due to time commitment or couldn't travel to us*
    - ***194 of the 407** could not be reached after multiple attempts and did not return our calls*
    - ***22 of the 407** moved out of state or could not travel to appointments*
    - ***5 of the 407** asked to be called back in a few weeks or months*
    - ***40 of the 407** did not qualify based on information garnered during a casual conversation (e.g. had a stroke rather than TBI)*

What opportunities for training and professional development has the project provided?

This project was not intended to provide training and professional development. However, staff recruited for the study include bachelor's level research assistants that received substantial on-the-job training in neuropsychological assessment, working with persons with TBI and the cognitive rehabilitation protocol being studied. This is done through one-on-one

work with a mentor and results in increased knowledge or skill in neuropsychological assessment and functioning. All study staff additionally participate in the semi-annual TBI Consumer Conference held (9/27/2019) and have many opportunities to attend lectures and workshops at Kessler or Rutgers University.

How were the results disseminated to communities of interest?

Nothing to Report. Data collection is ongoing.

What do you plan to do during the next reporting period to accomplish the goals?

Goals for the next reporting period continue to focus on participant recruitment, enrollment and treatment. We have met with a 2nd local day treatment TBI program and have been able to hold a group at their center. We will also be continuing to run groups at Kessler Foundation and we are working with our patient recruitment specialist to increase awareness of the study in the TBI Community and hopefully referrals for participation.

4. **IMPACT:**

What was the impact on the development of the principal discipline(s) of the project?
Nothing to Report. Data collection is ongoing.

What was the impact on other disciplines?
Nothing to Report. Data collection is ongoing.

What was the impact on technology transfer?
Nothing to Report. Data collection is ongoing.

What was the impact on society beyond science and technology?
Nothing to Report. Data collection is ongoing.

5. **CHANGES / PROBLEMS:**

While we are exploring different options for recruiting participants, this will not involve any changes to the study protocol. All methodology will remain as proposed.

Changes in approach and reasons for change
none

Actual or anticipated problems or delays and actions or plans to resolve them
The only anticipated delay is the delay in recruitment that we have already encountered and is being addressed

Changes that had a significant impact on expenditures
none

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
none

Significant changes in use or care of human subjects
none

Significant changes in use or care of vertebrate animals.
none

Significant changes in use of biohazards and/or select agents
none

6. PRODUCTS:

Nothing to Report. Data collection is ongoing.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Nancy Chiaravalloti, PhD; PI; no change

Glenn Wylie, D.Phil.; co-I; no change

John DeLuca, PhD; co-I; no change

Ekaterina Dobryakova, PhD; co-I; no change

Nancy Moore, MA; Research Manager; no change

Name:	*Alec DeGraaf*
Project Role:	*Research Assistant*
Nearest person month worked:	*4*
Contribution to Project:	*Mr. DeGraaf has been involved with participant recruitment and conducting the treatment sessions*
Funding Support:	*NIDILRR Field Initiated grant*

Name:	*Suzanne Zuckerman*
Project Role:	*Research Assistant*
Nearest person month worked:	*5*
Contribution to Project:	*Ms. Zuckerman has been involved with participant recruitment and conducting the Assessment sessions.*
Funding Support:	*NIDILIRR Field Initiated grant*
Name:	*Eric Stone*
Project Role:	*Research Assistant*
Nearest person month worked:	*1*
Contribution to Project:	*Mr. Stone has been involved with participant recruitment.*
Funding Support:	National MS Society and NJ Commission on TBI Research
Name:	*Tiffany Chang*
Project Role:	*Research Assistant*
Nearest person month worked:	*2*
Contribution to Project:	*Ms. Chang had been involved with participant recruitment and conducting the Assessment sessions. She has now left the organization.*
Funding Support:	*NIDILIRR Field Initiated grant*

Name:	*Michael Pellicane*
Project Role:	*Research Assistant*
Nearest person month worked:	*2*
Contribution to Project:	*Mr. Pellicane had been involved with participant recruitment and conducting the treatment sessions. He has now left the organization.*
Funding Support:	*NIDILIRR Field Initiated grant*

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to Report.

What other organizations were involved as partners?

None. Nothing to Report.

8. **SPECIAL REPORTING REQUIREMENTS**

none

9. **APPENDICES:**

none

A Randomized Controlled Trial of the Group-Based Modified Story Memory Technique in TBI

PI: Chiaravalloti, Nancy D., PhD **Organization**: Kessler Foundation **Award #:** W81XWH-16-1-0726 **Award Amount:** $753,669

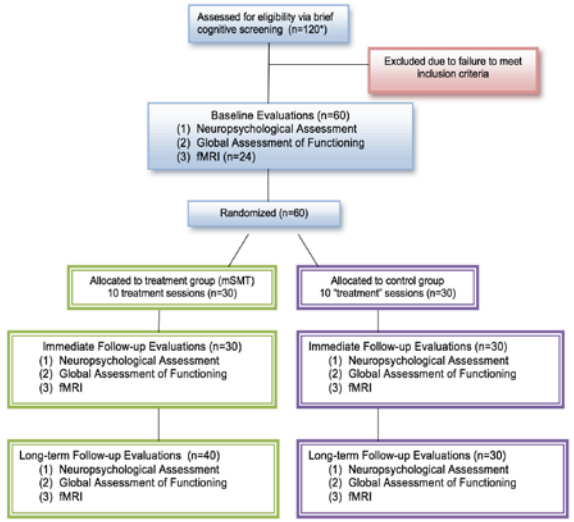
Study Aims

Aim 1. Objectively evaluate the clinical utility of the group mSMT to improve new learning/memory (NLM) in individuals with TBI with documented deficits in this area.
Aim 2. Increase the generalizability and real life application of the group mSMT
Aim 3. Examine the neurofunctional changes resulting from the group-based mSMT in TBI subjects with impairments in NLM.
Aim 4. Evaluate the long-term efficacy of the group mSMT in TBI through a 3-month follow-up.

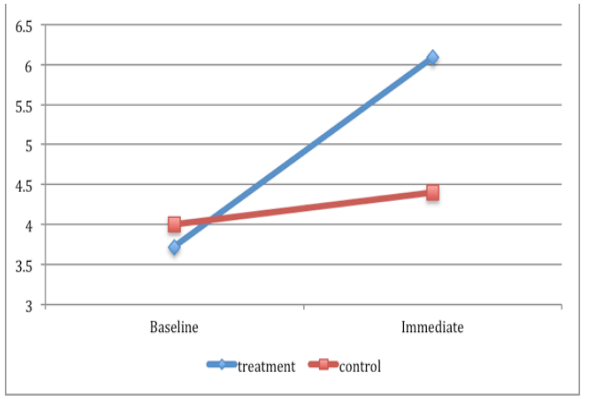
Approach

This double blind placebo control randomized clinical trial (RCT) will include a total of 50 participants with moderate to severe and documented deficits in NLM randomly assigned to a treatment (n=25) or a placebo control group (n=25). Participants will complete a baseline assessment, move through treatment / control treatment, complete an immediate follow-up assessment and then return for a long term follow-up assessment 3 months after completion of the treatment phase.

Experimental Overview



Prose Memory Delayed Recall from before to after mSMT individual treatment by group (p<.05)



Timeline and Cost

Activities	Year 1	Year 2	Year 3
Prepare for Clinical Trial	X		
Study Staff Training	X		
Prepare Research Protocol	X		
Recruitment, Treatment, Evaluation	ongoing	ongoing	ongoing
Data Analysis			
Estimated Budget	$251,000	$251,000	$251,000

Updated: 10-15-2019

Goals / Milestones

Goal 1: Administratively Prepare for Clinical Trial

- ✓ Prepare Regulatory Documents and Research Protocol
- ✓ Submit protocol to Foundation and Military IRB (ORP/HRPO)
- ✓ Hiring and Training of Study Staff
- ✓ Prepare Research Protocol

Goal 2: Recruitment, Treatment, Evaluation : Data Analysis; Data Collection

- ❑ Participants complete assigned condition to reach target n of 60
- ❑ Complete follow-up assessments 3 months after completion of treatment

Goal 3: Data Analysis

- ❑ Perform all analyses according to specifications, share output and finding with all investigators
- ❑ Dissemination of findings (abstracts, presentation, publications, DOD)