AWARD NUMBER: DM150082

TITLE: **Utility of Repetitive Transcranial Magnetic Stimulation (TMS) in Promoting Rapid Psychiatric Stabilization in Acutely Suicidal Military Service Members**

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CONTRACTING ORGANIZATION: **Dwight David Eisenhower Army Medical Center**
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Fort Detrick, Maryland 21702-5012

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Utility of Repetitive Transcranial Magnetic Stimulation (TMS) in Promoting Rapid Psychiatric Stabilization in Acutely Suicidal Military Service Members

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6. AUTHOR(S)

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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

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11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

- The purpose of this study is to determine if the use of Transcranial Magnetic Stimulation (TMS) provides rapid reduction and sustained attenuation of suicidal crisis. 100% enrollment was completed on 16July2019; 94% completed the 1month assessment, 82% completed the 3month assessment and 68% completed the 6month assessment.

The most common Adverse Events were:

- Headache (74)
- Suicidal Ideations, worsened (37)
- Site Pain (33)
- Nausea (17)
- Anxiety (12)
- Back Pain (11)
- Neck Pain (11)
- Whooziness/Lightheadedness (9)

15. SUBJECT TERMS

Suicide; Suicidal impulses; Suicidal behavior; Suicidal ideation; Suicidal intentions

16. SECURITY CLASSIFICATION OF: U			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON** USAMRMC
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			**19b. TELEPHONE NUMBER** *(include area code)*
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1. INTRODUCTION:

The purpose of this study is to determine if the use of Transcranial Magnetic Stimulation (TMS) provides rapid reduction and sustained attenuation of suicidal crisis. TMS is a treatment for suicidal crisis that is quicker, less invasive, better tolerated, and with fewer side effects than current treatments such as Electroconvulsive Therapy (ECT) and medication therapies. There will be 6 months of follow-up, in order to establish the ongoing and lasting therapeutic effect of TMS.

2. KEYWORDS:

Suicide; Suicidal impulses; Suicidal behavior; Suicidal ideation; Suicidal intentions

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Specific Aim 1: Determine whether active TMS added to standard of care and applied for 9 sessions over 3 days (TMSactive) promotes rapid reduction and sustained attenuation of suicidal crisis more than the control condition of sham TMS added to standard of care (TMSsham).

Specific Aim 2: Determine whether depressive symptoms, post-traumatic anxiety, and quality of life among SMs improve with TMSactive treatment.

Specific Aim 3: Determine whether institutional benefit as defined by pharmacy cost and length of inpatient hospital stay improve with TMSactive treatment.

What was accomplished under these goals?

- Study was initiated with enrollment of first study participant 12 June2017.
- Enrollment was completed July2019, with Target enrollment of 120 met.
- 79% completers (completed full course of 9 TMS sessions)
- Follow-up assessments have been completed, as of December 2019. 94% completed the 1month visit; 82% completed the 3month visit; 68% completed the 6month visit.

Year 2 (Jun2017-Feb2018)	Screened	Enrolled	Completed (9TMS Sessions)
Qtr 2	**56**	**19**	**14**
Qtr 3	**28**	**11**	**8**
Qtr 4	**47**	**8**	**5**
Total Year 2	**131**	**38**	**27**

Year 3 (Mar2018-Feb2019)	Screened	Enrolled	Completed (9TMS Sessions)
Qtr1	44	13	11
Qtr 2	46	10	7
Qtr 3	46	16	13
Qtr 4	56	16	13
Total –Year 3	192	55	44
Year 4 (Mar2019-Feb2020)	Screened	Enrolled	Completed (9TMS Sessions)
Qtr1	37	16	13
Qtr 2	17	11	11
Qtr 3	----	----	---
Qtr 4	----	----	---
Total –Year 4	54	27	24

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

Nothing to report.

How were the results disseminated to communities of interest?

Analysis of Data complete and publication preparation ongoing

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

Publications
Presentations

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?

The data analysis shows positive results for the primary outcome and some of the secondary outcomes, we are encouraged that the results will be actionable regarding the treatment of Suicidal crisis

What was the impact on other disciplines?

Nothing to Report.

What was the impact on technology transfer?

Nothing to Report

What was the impact on society beyond science and technology?

Having a new tool to treat suicidal crisis will benefit society

5. **CHANGES/PROBLEMS:** The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change

Transfer of PI, COVID

Actual or anticipated problems or delays and actions or plans to resolve them

Dr Hines transferred from DDEAMC and is now at WRNMMC, while still actively managing the project and working on the publications Dr Hanson is now the PI for reporting purposes

COVID and health issues with our statistician have delayed our analysis, we have completed data analysis and are preparing first manuscript for submission to the Journal of Psychiatry.

Changes that had a significant impact on expenditures

Nothing to report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

Nothing to report.

Significant changes in use or care of vertebrate animals.

Not applicable.

Significant changes in use of biohazards and/or select agents

Not applicable.

6. PRODUCTS: List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications.

Preparing first manuscript for submission to the Journal of Psychiatry

  Books or other non-periodical, one-time publications.

Nothing to Report.

  Other publications, conference papers, and presentations.

Nothing to Report.

- **Website(s) or other Internet site(s)**

Nothing to Report

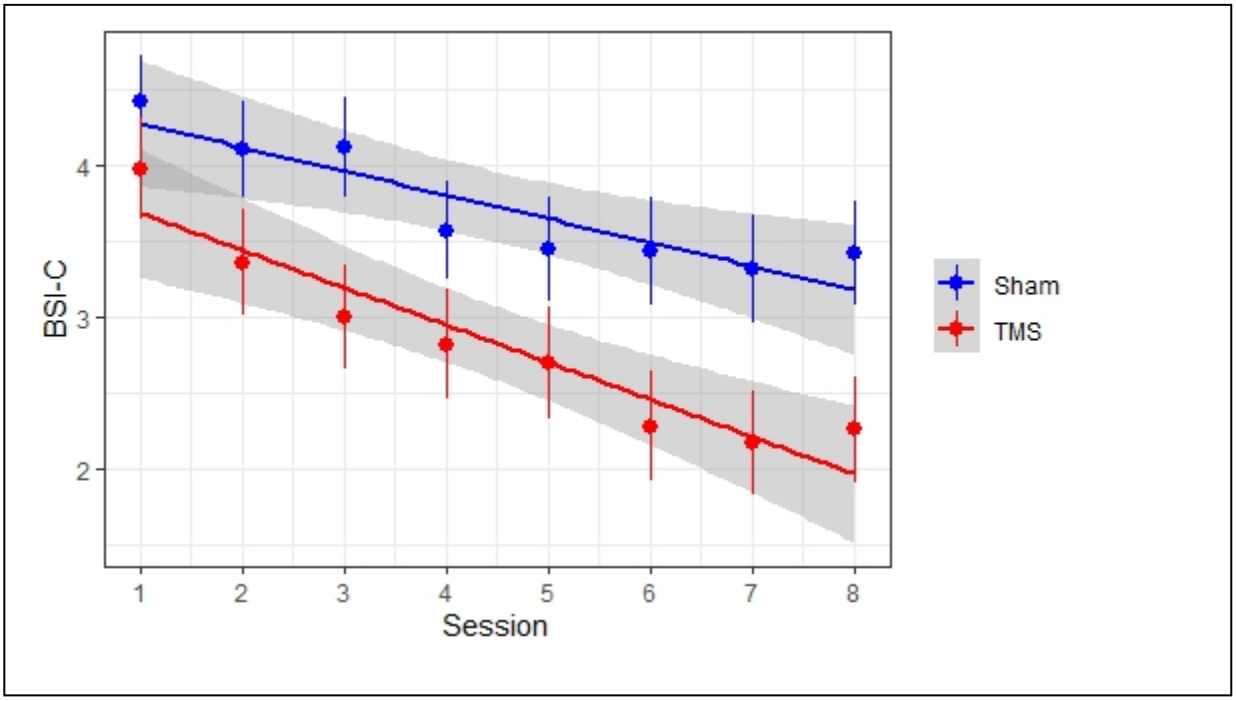
- **Technologies or techniques**

Nothing to Report

- **Inventions, patent applications, and/or licenses**

Nothing to Report

- **Other Products**



*Continuous variable with range 0 (first post-baseline session) to 7 (final treatment session).

	Estimate	SE	t	df	p
Intercept	3.66	0.39	9.43	103	<0.001
Baseline BSI-C minus 5.2 (group mean)	0.73	0.07	10.23	103	<0.001
Age minus 27.4 (group mean)	-0.01	0.03	-0.35	103	0.73
Sex: male (1) vs female (0)	-0.02	0.36	-0.06	103	0.96
Diagnosed depression: yes (1) vs no (0)	0.48	0.33	1.48	102	0.14
Treatment group: TMS (1) vs sham (0)	-0.07	0.31	-0.22	103	0.83
Time (treatment session)*	-0.16	0.04	-4.01	98	<0.001
Interaction of TMS group with time	-0.12	0.06	-2.03	99	0.04

Table 2. Linear mixed effects model of BSI-C score changes over post-baseline treatment sessions.

Primary analysis

The primary analysis compared rates of change in current suicide ideation (BSI-C) score over the intervention phase in the TMS versus sham group. A linear mixed effects model was used to analyze as the dependent variable the BSI-score at each of the 8 post-baseline sessions. The model included fixed effects for treatment group, time (treatment session (continuous)), treatment-by-time interaction; a random intercept for subject and random slope with time; and BSI-C score at baseline, gender, age at baseline and diagnosis of depression as covariates. Restricted maximum likelihood estimation was used with an unstructured covariance structure for the random effects. The Kenward-Roger approximation was used to estimate degrees of freedom. Analyses were performed separately among the intent-to-treat (ITT) population of all subjects who were randomized, and the per-protocol population of "completers", defined as subjects who completed all sessions of treatment with the scheduled number of pulses per session.

Results

Patient characteristics

Of the 120 enrolled patients, 59 were randomized to TMS and 61 to sham (Figure 1). Seventy-two percent of the study population was male and 66% had diagnosed depression. Demographic and clinical characteristics were similar across treatment groups (Table 1).

Primary outcome

In the ITT analysis of BSI-C changes over treatment sessions, the TMS group had accelerated decline in suicidal ideation versus sham: Beta for interaction = 0.12 points greater BSI-C decline per session (SE = 0.06) in TMS versus sham; p = 0.04 (Table 2). Significant main effects were found for baseline BSI-C score (mean-centered) (Beta = 0.73 (SE = 0.07)) and session (Beta for rate of BSI-C decline in the sham group = -0.16 (SE = 0.04)).

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	CPT Brett Hansen
Project Role:	PI
Nearest Person month worked	1
Contributions to project:	No Change. Assumed PI role in the absence of Dr. Hines, providing regulatory oversite through study closeout.
Name:	Christopher Hines, MD
Project Role:	PI
Nearest Person month worked	1
Contributions to project:	Regulatory and budget management. Publication of paper and presentations.
Name:	Scott R. Mooney, PhD
Project Role:	AI
Nearest Person month worked	1
Contributions to project:	No change
Name:	Joanne Huff
Project Role:	Research Coordinator
Nearest Person month worked	1
Contributions to project:	Complete follow-up assessments; manage regulatory aspects of study.

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?

The Geneva Foundation
Tacoma, WA
– provides Personnel and Fund Management

Augusta University – Dr. Stephen Looney, BioStatistician conducting data analysis.

Walter Reed National Military Medical Center
– Dr. Christopher Hines relocated, however, will complete study analysis and publications.
- Nora Watson, PhD; Biostatistician; WRNMMC Department of Research Programs conducting data analysis

8. **SPECIAL REPORTING REQUIREMENTS; N/A**
   COLLABORATIVE AWARDS: N/A
   QUAD CHARTS:

9. **APPENDICES:** N/A

Utility of repetitive transcranial magnetic stimulation (TMS) in promoting rapid psychiatric stabilization in acutely suicidal military Service Members

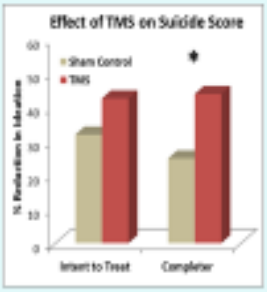
Log No. DM150082 Final Report
Award No. 11142141
PI: CPT Brett Hansen **Org:** Dwight David Eisenhower Army Medical Center **Award Amount:** $956,204.00

Study/Product Aim(s)

- Determine whether active TMS added to standard of care (SOC) and applied for (9) 60-min sessions over 3 days (TMSactive) promotes rapid reduction and sustained attenuation of suicidal crisis more than control condition of sham TMS added to SOC(TMSsham).
- Determine whether depressive symptoms, post-traumatic anxiety, and quality of life among SMs improve with TMSactive treatment.
- Determine whether institutional benefit as defined by pharmacy cost and length of inpatient hospital stay improve with TMSactive treatment.

Approach

Patients enrolled during suicidal crisis will be assigned to a single-blinded TMSactive or TMSsham group. At various intervals during treatment, selected psychometric tests will be administered, with most tests repeated at follow-up time points of 1, 3, and 6 months. Primary outcome relies on Beck Scale for Suicide Ideation (SSI), with several related psychometric scales and health care costs analyzed for secondary outcome.



In the only previous study to examine the effect of high-dose TMS on suicidality, George, et al. (2014) found a significant reduction in score immediately following 3 days of treatment, when controlling for non-completers. Current study will determine these effects on younger, Active Duty Service Members over long-term follow-up.

Timeline and Cost

Activities	CY 17	18	19	20
Screening, Enrollment				
Tx, Post-Tx Data Collection				
Healthcare Data Collection				
Analysis, Interpretation				
Reporting				
Estimated Budget ($K)	**$258**	**$265**	**$197**	

Updated: 25aug2020

Goals/Milestones

- **CY19 Goal – Completed enrollment & Data Collection**
- **CY 20 Goal – Analysis & Dissemination**
  - Complete data analysis
  - Complete reporting, presentation, publication

Comments/Challenges/Issues/Concerns

-Dr. Hines remains the lead for publication and presentations
-Extended budget contract with NATICK from 19 June 2020, to 19 March 2021to allow for publication expenses

Budget Expenditure to Date

Projected Expenditure:$962,173.35
Actual Expenditure: $719,731.19