AWARD NUMBER: W81XWH-15-1-0054

TITLE: Neurogenic Tremors Training (TRE) for Stress and PTSD: A Controlled Clinical Trial

PRINCIPAL INVESTIGATOR: Martha Kent

CONTRACTING ORGANIZATION:
CARL T. HAYDEN MEDICAL RESEARCH FOUNDATION

PHOENIX, AZ 85012-1839

REPORT DATE: July 2018

TYPE OF REPORT: Final Report

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
JULY 2018	FINAL	1 May 2015 - 30 APR 2018

4. TITLE AND SUBTITLE

Neurogenic Tremors Training (TRE) for Stress and PTSD: A Controlled Clinical Trial

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-15-1-0054

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Martha Kent

EMAIL: martha.kent@va.gov

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

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

Carl T. Hayden Medical Research Foundation
650 E. Indian School Road
Phoenix, AZ 85012-1839

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

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

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

This controlled clinical trial tests the efficacy of a tension and trauma release exercise (TRE) for reducing symptoms of posttraumatic stress disorder (PTSD). Three treatment conditions compared TRE, Placebo, and Wait list control, with 40 participants in each group for a total of 120 subjects. Included are pre-testing followed by randomization to treatment conditions, intervention training, and post-testing. Sustainability is evaluated with follow-up tests at 3 and 6 months. Participants meet twice weekly for four weeks. Study goals and study achievements to date include: (1) establishing and implementing main procedures to do this study, (2) staffing of study, (3) training of staff (4) creating and maintaining data base for consenting, outcome measures, and monitoring measures, and follow-up testing at 3 and 6 months (5) recruiting subjects, (6) intervention training of subjects (7) pre- and post-testing; follow-up testing. Modifications have included screening for physical fitness of subjects as an inclusion criterion, sustained motivation and effort monitoring at all test phases to assure uniform motivation and effort. Recruitment and retention are under fragile control, as recruitment is rather restirctive .

15. SUBJECT TERMS

NONE LISTED

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
Unclassified	Unclassified	Unclassified	Unclassified	26	19b. TELEPHONE NUMBER *(include area code)*

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

Table of Contents

Page

1.INTRODUCTION:
This is a controlled clinical trial that set out to test the efficacy of a tension and trauma release exercise (TRE) approach as an adjunctive treatment for reducing symptoms of Posttraumatic Stress Disorder (PTSD). The study was conducted over a period of three years. Three treatment conditions were compared: TRE with tremors, Placebo or TRE without tremors, and Wait-List Control. Forty (40) participants were recruited for each group, of which 30 were required for significance and 10 to allow for drop out. Thus, a total of 90 participants were required for significance, 30 for drop out, for a total of 120 participants. All participants were pre-tested and then randomly assigned to the three treatment conditions. Then participants underwent four weeks of training, meeting twice weekly in small exercise groups of 10 for 60 minutes. Pre- and post-test self-report measures assessed symptoms of PTSD and depression, emotional well-being, and neurocognitive functions. Sustainability of gains over time were evaluated with follow-up testing at 3 and at 6 months. Order of treatment (TRE or Placebo) and Control were randomly determined during the implementation.

2. KEY WORDS:
Posttraumatic Stress Disorder (PTSD), intervention, randomized clinical trial, adjunctive therapy, tension release exercise (TRE), neuropsychological functions, sustainability over time.

3. ACCOMPLISHMENTS:

What Were the Major Goals of the Project?
The major goals under SOW were: (1) establishing main procedures to implement this study, (2) staffing of study, (3) training of staff (4) creating a data base for consenting, screening tests, monitoring measures, pre- post-test outcome measures, (5) recruiting subjects, (6) implementing intervention for TRE, Placebo, and Wait-List condition, (7) pre- and post-testing; follow-up testing, (8) data analysis, (9) write-ups for presentations and papers.

1. Procedures
   a. Screening of participants according to IRB approved procedures including modifications in informed consent, control documents, and protocol.
   b. Reporting of adverse events according to IRB approved procedures.

2. Staffing
Recruitment of Staff
   a. Without Compensation (WOC) appointment according to procedures.
   b. Human Resources (HR) appointment according to procedures.

3. Training of Staff
   a. Training of trainers/therapists according to approved training manuals for TRE condition and for Placebo condition.
   b. Training of new research assistants in study procedures, pre- post- and follow-up testing, and data collection.

4. Data Base
Designing and setting up data base to be used for recording data from three domains:
   a. Consenting data
   b. Outcome measures of pre- and post-tests and of follow-up tests
   c. Monitoring measures for subjects and for trainers.

5. Recruitment of Subjects

Recruitment of subjects followed IRB approved approaches: (1) announcements at regularly scheduled meetings of main and relevant services, (2) posting of approved fliers in designated areas, (3) mailing of letters to pre-approved list and observing relevant procedures. Standardized recruitment instructions and screens were prepared and used with each patient contact.

6. Intervention Training

The schedule of treatment delivery is depicted in the tables below. The training for all groups lasts 4 weeks (meeting twice per week). It was preceded by 2 weeks of pre-testing and followed by 2 weeks of post-testing. We implemented one training condition of n=10 participants (TRE or Placebo) and a Control condition group of n=5 participants at a time. Thus, each training condition group was paired with a group of control participants. The final sample would include n=40 in each of the three conditions. Importantly, the planned order of the presentation of TRE versus Placebo was randomized within each Wave across the study period through use of a random numbers table (random.org). Thus, the randomization of both treatment assignment and treatment order assures that no systematic influences (e.g. participants' characteristics, time of year) affected one condition more than another.

For **Year 1**: The implementation schedule of TRE, Placebo, Control, and follow-up testing at 3 and 6 months is outlined in Table 1 below. The groups that could not be completed in Year 1 were carried over into Year 2.

Table 1: Implementation Schedule of Intervention and Follow-up Testing for **Year 1**

Months Years I-II	**Treatment Conditions** **4 Weeks (2 visits/week)** **Pre-testing at weeks 1-2** **Post-testing at weeks 7-8**	**Follow-up – 3rd Month**	**Follow-up – 6th Month**	**Wait-List Training-7th Month**
1-I	Staff recruitment & training, training of trainers by Dr. Berceli	3 month	6 month	7month Wait-List Control
2	TRE 1 (n=10); Control 1a (n=5)	TRE 1; Control 1a	TRE 1; Control 1a	
3				
4				
5	TRE 2 (n=10); Control 1b (n=5)	TRE 2; Control 1b	TRE 2; Control 1b	
6				
7	Placebo 1 (n=10); Control 2a (n=5)	Placebo 1; Control 2a	Placebo 1; Control 2a	
8				
9				Control 3
10	Placebo 2 (n=10); Control 2b (n=5)	Placebo 2; Control 2b	Placebo 2; Control 2b	
11	TRE 3 (n=10); Control 3a (n=5)	TRE 3; Control 3a	TRE 3; Control 3a	
12				Control 1

For **Year 2:** The implementation schedule of TRE, Placebo, control, and follow-up testing at 3 and 6 months for **Year 2** is outlined in Table 2 below. Again, the groups that could not be completed in Year 2 were carried over into Year 3.

Table 2: Implementation Schedule of Intervention and Follow-up Testing for **Year 2**

1-II	TRE 3 (n=10); Control 3a (n=5)	TRE 3; Control 3a	TRE 3; Control 3a	
2				
3				
4	Placebo 3 (n=10); Control 3b (n=5)	Placebo 3; Control 3b	Placebo 3; Control 3b	
5				
6				

7	TRE 4 (n=10); Control 4a (n=5)	TRE 4; Control 4a	TRE 4; Control 4a	
8				
9				Control 3
10	Placebo 4 (n=10); Control 4b (n=5)	Placebo 4; Control 4b	Placebo 4; Control 4b	
11				
12				Control 4

For **Year 3:** The implementation schedule for TRE, Placebo, Control, and follow-up testing at 3 and 6 months for **Year 3** covered the groups that were not completed in Year 2, as outlined in Tables1 and 2 above.

7. Pre- and Post-Testing; Follow-up Testing
Packets for pre- and post-testing and follow-up testing were administered according to the schedules of Tables 1 and 2 above.

8. Data Analysis
Data analysis was conducted toward the end of the study of Year 3 at two times: (1) after all subjects had completed post-testing for preliminary results and (2) after 3-month and 6-month follow-up testing for complete results.

9. Presentations and Papers and Write-ups
Abstracts were submitted to the 2018 annual conference of the International Society for Traumatic Stress Studies (ISTSS) for: (a) a symposium which was not accepted, as it had a cross-cultural rather than community based emphasis (b) a poster presentation which was accepted. Papers are planned to be developed and submitted to leading relevant conferences and journals.

What Was Accomplished Under these Goals?
1. Procedures
Procedures for **Year 1** were devoted to the startup of the study and concerned: modifications of the informed consent, the development of the training manuals for trainers/therapists for the TRE and Placebo condition (**Appendix 2**); monitor questionnaires development (**Appendix 3**); source documents development (**Appendix 4**); and diaries were designed (**Appendix 5**). IRB approval for all of these steps was obtained. The planned treatment and control groups were pre-tested, randomly assigned to conditions, intervention conditions were implemented, and post-testing was begun.
Procedures for **Year 2** continued and maintained the procedures developed during Year 1. A main change concerned the modification of the suicidality screen; the Columbia Suicide Severity Rating Scale (C-SSRS) replaced the Suicide Behavior Questionnaire Revised (SBQ-R). The C-SSRS and the screening algorithm are attached in **Appendix 6**. A stop notice that changed the suicidality screen delayed the study by 6 months. The following ripple effect in this tightly scheduled study caused the study to be delayed by one year.
Procedures for **Year 3** continued the same schedule in the implementation of the intervention and testing of the rest of the study.
The procedures for reporting adverse events continued to be implemented throughout all of the 3 years.

2. Recruitment of Staff
Sufficient staff levels were maintained for the conduct of the study.
a. When adding new staff, we continued to observe Without Compensation (WOC) appointments.
b. Human Resources (HR) appointment procedures were observed for all staff actions.

c. The staff members associated with the study at various times during the three years included:

Personnel	Role	Percent Effort
Martha Kent	PI	36%
Brigitte Adamsen	Coordinator	100%
Lisa Orozco	Coordinator	100%
Travis Webb	TRE Trainer	5%
Beth Dietrich	TRE Trainer	5%
Taylor Barnwell	Psychology Technician	50%
Jinah Kim	Psychology Technician	8%
Danielle Ruberto	Psychology Technician	8%
Ashley Knobloch	Psychology Technician	8%
Dominique Gandy	Psychology Technician	50%
Morgan Regalado Hustead	Psychology Technician	20-50%
Gabriela Avila	Psychology Technician	20%
Amer Marji	Psychology Technician	20%
Mary Davis	Statistician, Study Design	Consultant
David Berceli	Expert TRE Trainer of Trainers/Therapists	Consultant
Charles Hoge	Design of Placebo Condition	Consultant

3. Training of Staff

a. Training of Psychology Technicians by PI continued throughout the three years as new persons were added to the study. Training covered: consenting and screening of study participants for eligibility that covered eligibility screens of suicidality, alcohol use, and psychosis (see Appendix 6 for eligibility screens), outcome scales and measures for pre-post-testing, and follow-up testing at 3 and 6 months with a subset of Outcome Measures. Staff were also trained in the Physical Fitness Screening Tool created for screening of physical fitness for participation in the exercises. Staff was also trained in evaluating consistency of motivation and effort at pre- and post-testing (see Appendix 3). Training included spread sheet setup and data entry.

b. Training of Trainers/Therapists was performed by Dr. David Berceli who is the expert developer of TRE. Dr. Charles Hoge consulted on the design of the Placebo Condition

c. Training of study coordinator by PI in consenting, screening, follow-up testing, setting up of chart and data documents, and preparation of reports.

b. The manuals used for training the trainers/therapists were successfully used in the training of therapist staff members.

4. Recruitment of Subjects

The recruitment methods established during the first year were continued during **Year 2** and **Year 3**.

a.Implementing authorized methods for recruitment:
Study announcements in meetings with VA Mental Health and VA Psychology Service. Meeting with VA Primary Care Providers (PCP) for the requirement of PCP approval for subjects' participation in this study.

b. Use of several recruitment approaches to recruit adequate numbers of subjects:
(1). Distribution of fliers at designated areas of the hospital

(2). Staffing a recruitment table at designated area of the hospital
(3). Mailing and making IRB methods of contacting participants with PTSD diagnoses at this VAMC.

c. Use study-specific standardized recruitment instructions and screens (see Appendix 4 for Source Documents).

Data on the recruitment of subjects for **Year 1**:

Process	**Year 2** 5/1/2016-5/23/2017	**Total** 9/15/15-5/23/2017
Consenting	30	72
Screen Failures	5	14
Enrollment	25 (2 on hold)	58 (6 on hold)
Dropouts	1	9
Original Target Number	15	45
Number of Subjects Contacted	200	About 1000

Data on the recruitment of subjects for **Year 2**:

Process	**Year 2** 5/1/2016-5/23/2017	**Total** 9/15/15-5/23/2017
Consenting	64	132
Screen Failures	4	21
Enrollment	49	85
Dropouts	11	23
Original Target Number	60	90
Number of Subjects Contacted	300	About 2000

Data on the recruitment of subjects for **Year 3**:

Process	**Year 3** 1/31/2017-9/14/2017	**Total** 9/15/15-5/23/2017
Consenting	28	140
Screen Failures	0	19
Enrollment	20	92
Dropouts	8	29
Original Target Number	30	90
Number of Subjects Contacted	500	About 3000

(1).A total of 92 Subjects have completed all pre-testing, intervention, and post-testing.
A total of 83 Subjects have fully completed all phases of the study: (1) consenting and screening; (2) pre-testing (3) TRE, Placebo, Wait-List conditions; (4) post-testing (5) follow-up testing at 3 months (6) follow-up testing at 6 months.
(2). Amendments submitted to the IRB and USAMRMC HRPO for review:
During **Year 1**: 7 ICF amendments and 10 Protocol amendments were submitted and approved.
During **Year 2:** 0 ICF amendments and 3 Protocol amendments were submitted and approved.
During **Year 3**: No amendments were submitted to the IRB.
(3). Adverse events:
During **Year 1**: There were thirteen (13) adverse events.
During **Year 2:** There were eleven (11) adverse events.
During **Year 3**: There were four (4) adverse events.

5. Data Base

For Years 1, 2, 3:

The data base was continuously developed and updated. One interruption was the Stop Notice issued in June, 2016. This will be addressed and brought up to date. The data base covered the following areas:

a. Consenting data. Data base was set up for consenting and screening of subjects. The screening tests were: CAPS-5 for presence of PTSD, and exclusion of suicidality as determined by algorithm of C-SSTS screen, active alcohol or substance dependence (AUDIT-C > 3), and active psychosis (Psychosis Screener).
b. Outcome measures of pre- and post-tests and of follow-up tests.
c. Monitoring measures for subjects and for trainers.

6. Intervention Training

The intervention training schedule for all three years followed the same schedule as illustrated in the Implementation Schedule on p. 2 above: for TRE, Placebo, Control, and follow-up testing at 3 and 6 months.

7. Pre- and Post-Testing; Follow-up Testing

For all three years the administration of scales and neuropsychological tests at pre- and post-test times for TRE, Placebo, and Control subjects and follow-up testing at 3 and 6 months followed the same schedule as the Implementation Schedule on p. 2 above.

8. Methods Summary. The accomplishments for the three years include: Startup of the study, maintaining the staffing of the study and training of new staff, recruitment of subjects with the use of several methods, intervention training of TRE group, Placebo group training, and Wait-List Control group. All three conditions were preceded by pre-testing, followed by random assignment to the three conditions, and ended with post-testing and follow-up testing at 3 and 6 months.

Succinct description of the methodology:

The methodology of the intervention tested in this study did not change during the three years. The program consists of two basic types of exercises: Phase I: a preparatory set of common stretch and strength exercises, such as are found in yoga. These were to be repeated at each of eight sessions in two weekly meetings for a total of four weeks. This phase induces tension in preparation for Phase II tension release trembling:

Phase I: Stretch and Strength Exercises engaged the subject in a number of stretch positions for the lower leg muscles that involved standing on balls of feet, knee bends, forward bends with touching of floor and raising one leg, bends to stretch back of legs. These positions were held for several breaths. Next, lower leg strength was developed with back against the wall. Upper leg muscles were fatigued from weight bearing positions. Quivering/trembling of muscle fatigue was allowed to continue for several minutes with slow deep breaths. Phase II: Neurogenic Trembling Phase. After completing Phase I, the participant immediately lay down on the mat, back flat on the floor, with knees bent and soles of feet touching each other. This position put some tension on the psoas muscles to hold the knees up off the floor. Typically the trembling continued with the participant lying on a mat, his knees relaxed and in an open position allowing trembling and tension release in legs, pelvis, and lower back. The trembling often spreads to other muscle groups that could be holding tension. It was allowed to continue for 15-30 minutes, or as long as the person was comfortable doing it. The trembling was experienced as relaxing and did not take additional tension to continue. The tremors could be terminated at any time by stretching the legs out flat on the floor.

Treatment conditions included TRE standard condition with trembling, Placebo condition (TRE without Phase II Trembling), and Control condition (Wait-List Control)
Participants in the Control condition waited for the four weeks duration of the intervention treatment condition. They underwent pre- and post-testing identical to that of the treatment condition, but prior to and following the four-week waiting/no treatment period. Treatment was offered to them following completion of follow-up testing.

Participants and Procedures:

The participants in this study were Veterans with a PTSD diagnosis receiving standard psychiatric care at the VA.
Inclusion criteria for eligibility to participate in this study:
1. be 18-69 years of age (to span the conflicts of OEF/OIF. Gulf War and Vietnam)
2. meet criteria for PTSD as confirmed by the screen of CAPS-5*
3. be United States Veterans receive standard mental health care that may include psychotropic medication, medication monitoring, supportive therapy, couples counseling, family counseling. Medical clearance from PVAHCS primary care providers for TRE exercises was requested for inclusion in this study.
Exclusionary criteria were:
1. active suicidality or plans requiring a greater than outpatient level of care (C-SSRS screen)*
2. active alcohol or substance dependence (AUDIT-C > 3)*
3. Active psychosis (Psychosis Screener)*
4. current severe disabling illness (e.g. recent or imminent surgeries, acute illness, conditions precluding physical exercises (primary care provider input, or physical fitness screen)
5. inability to do the physical exercises due to physical limitations such as paralysis (patient self-report, primary care provider input)
6. inability to participate in a small group exercise setting (self-reported)
7. inability to meet attendance requirements: two missed session out of 8.
8. excluded are Veterans receiving concurrent prolonged exposure therapy (PE), cognitive behavior therapy (CBT), cognitive processing therapy (CPT), and dialectical behavior therapy (DBT) for posttraumatic stress disorder (PTSD).
* These screens are located in Appendix 6.
The training sessions each lasted 60 minutes and were delivered biweekly over four weeks. The intervention was implemented in four waves in which one wave consisted of a TRE group (n=10), a Placebo group (n=10), and a Wait-List Control group (n=10). A consort flow diagram in **Appendix 7** illustrates the flow of consenting, screening, randomization, intervention, pre-post testing, and follow-up testing at 3 and 6 months for the four Waves of the study. All treatments were delivered by the same trainer/therapist. Fidelity of treatment was sampled randomly and evaluated by Dr. Berceli himself. A second fidelity expert rater was not available to the study.

Measures:

Pre- and Post-intervention assessment

Participants completed scales assessing mental health symptoms, well-being and physical health, and neuropsychological tests of attention, memory, and executive functions. After pre-testing, all individuals were randomly assigned to TRE, Placebo, or Wait-List Control conditions. The intervention was implemented in four waves (Wave 1 n=30; Wave 2 n=30; Wave 3 n=30, Wave 4=30). Following completion of a wave, participants and Controls for that wave were scheduled for post-intervention assessments identical to the pre-intervention assessments, and occurred within two weeks of the final treatment session.
Follow-up testing was performed with all participants in the three treatment conditions at 3 and 6 months after they had completed training. Follow-up tests consisted of an efficient subset of pre-tests.
In addition, during the treatment conditions participants indicated in diaries the extent to which they experienced tremors during TRE training and relaxation during Placebo training. They also

indicated whether they had experienced tremors or relaxation for their respective conditions when they were completing post-testing and on follow-up at 3 and 6 months. In homework diaries, participants recorded the frequency with which they exercised (committed to exercise and actually exercised). All testing occurred under blind conditions in which the person administering the tests was blind to the participants' assigned treatment condition.
Because of the repeated testing at pre- and post-test times and at follow-up times at 3 months and 6 months, particular attention was paid to neuropsychological measures that had valid repeatable versions, or to the selection of measures that were rather abstract and devoid of semantic content and, therefore, would be less affected by learning through repeated exposure.
The following outcome measures were used in this study:
Symptom Measures. Pre-to-post change in mental health symptoms were assessed with The PTSD Symptom Scale (PSS, Foa). Depression was assessed with the Patient Health Questionnaire-9-Depression Scale (PHQ-9). Changes in physical symptoms assessed chronic pain with the McGill Pain Questionnaire (MPQ), sleep with the Insomnia Severity Index (ISI), physical symptoms with the Patient Health Questionaire-15 - Somatic Symptom Scale (PHQ-15).
Well-Being Measures. Emotional well-being was assessed with the RAND 36-item Health Survey (SF-36) that covered self-reported Vitality, Social Functioning, Emotional Role functioning, and Mental Health. Well-being was also assessed with three subscales of the Psychological Well-Being Scales (Ryff, 1989): Purpose in Life, Positive Relations with Others, and Personal Growth. The RAND 36-item Health Survey (SF-36) covered self-reported physical health in subscales of Physical Functioning, Physical Role, Bodily Pain, and General Health.
Neurocognitive Functions. Executive functions were assessed with the subtests Verbal Fluency Test and the Color-Word Interference Test of the Delis-Kaplan Executive Function System (D-KEFS). Simple and complex attention as well as verbal memory and visual memory were assessed with repeatable measures of the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). Speed and flexibility of thinking were assessed with the Word Generation test of the Neuropsychological Assessment Battery (NAB).
All outcome tests and measures are listed in the Table of Outcome Measures in **Appendix 8**. References are provided in **Appendix 1**.

9. Data Analysis:

Sample characteristics. Of the 140 participants assessed for eligibility, 92 completed the pre-assessment, the randomly assigned treatment condition, and post-testing. The treatment conditions included TRE (*n*=30), Placebo or Placebo Yoga (*n*=32) and Wait-List Control (*n*=30). The majority of the participants were male (75%), had an average age of 49.8 years (*SD* = 13.4) and had a mean education level of 15.5 years (*SD* = 2.0). The sample was ethnically diverse; participants endorsed being Caucasian (58.7%), African American (20.7%), Hispanic (16.3%), Native American (2.2%), or Pacific Islander (2.2%).

Equivalence of groups at pre-treatment. Comparisons of the treatment groups on demographic characteristics as well as initial levels of all outcome measures were evaluated via chi-squared tests and one-way analysis of variance, with *p*-values ≤ .05 considered statistically significant. Findings indicated that the groups were equivalent prior to beginning the treatment (or Wait-List Control) on all demographic and pre-assessment outcome measures. Thus, random assignment yielded groups that were equivalent at pre-treatment.

Equivalence of timing of assessments. Pre- and post-assessment included completion of standardized questionnaires that assessed mental health symptoms, positive emotional health, and neurocognitive functions. Because this was a small group intervention, randomization occurred in waves. Participants in the three conditions within a treatment wave who completed

questionnaire post-assessments (*N* = 92) did so within two weeks of the final treatment session. The interval between pre- and post-assessment averaged 7.18 weeks (*SD* = 2.94), with no differences between the three groups (*F* (2,89) = 0.18*, ns).*

Evaluation of treatment effects. Initial analyses evaluated whether each group showed change over time, by conducting within-group repeated measures analyses, followed by simple comparisons of post-intervention levels with pre-levels to determine whether changes over time were significantly different from initial levels. Next, between-group comparisons of change from pre- to post-assessment(s) was accomplished via 3 (Group assignment) X 2 (Time: pre-, post) or 4 (Time: pre-, post-, 3-mo f/u; 4-mo f/u) repeated measures analyses of variance (ANOVA). A significant Group X Time interaction indicates that groups varied in magnitude of change over time, and were followed by post hoc between group comparisons of the magnitude of change from pre-intervention levels.

Table 1 depicts the means (*SD*) of pre- and post-intervention, and 3-month and 6-month followups, for primary and secondary outcome measures separately by group assignment, as well as F values for time and time X group effects. Primary outcomes include psychological symptoms (PTSD and depressive symptoms). Secondary outcomes include physical health and symptoms (pain, sleep, physical functioning), well-being, and neurocognitive function (attention, working memory, and executive function).

Primary Outcome: Psychological Symptoms.

PTSD symptoms (assessed via the PTSD Symptom Scale). Within-group analyses indicated that both the TRE group [Time effect *F* (3,51) = 4.15, *p* < .02] and the Yoga-sham group[(Time effect *F* (3,75) = 3.35, *p* < .03] showed significant change in PTSD symptoms over time, with no significant change in the control group [Time *F* (3, 45) = 1.38, *ns*]. Follow-up within-group simple contrasts revealed that both the TRE and Yoga-sham groups showed sustained change from pre-levels through the 6-month follow-up. Comparisons across groups in the magnitude of change showed that the sample as a whole showed change over time [Time effect *F*(3,240) = 4.64, *p*=.006], but the magnitude did not vary by group [Group X Time *F* (6,240) = 1.30, *p* = *ns*].

Depressive symptoms (assessed via the PHQ-9). Within-group analyses indicated that neither the TRE group [Time effect *F* (3,84) = 2.04, *ns*] nor the Control group *[*Time effect *F* (3,78) = 0.15, *ns*] showed significant change in depressive symptoms over time. However, the Yoga-sham group did improve [Time effect *F* (3,78) = 2.79, *p* < .05]. Follow-up within-group simple contrasts revealed that neither the TRE nor the control groups showed any improvement from pre-levels at any point over the course of the 6-month follow-up, whereas the Sham-yoga group showed significant improvement from the pre- to the post-assessment (*p* < .03). Comparisons across groups in the magnitude of change showed that the sample as a whole showed change over time [Time effect *F*(3,240) = 2.85, *p*=.04], but the magnitude did not vary by group [Group X Time *F* (6,240) = 1.40, *ns*].

Secondary Outcome: Physical symptoms and functioning

Physical Health (assessed via the SF36 Physical Health Composite). Within-group analyses indicated that none of the groups showed a change over time in physical health (all *F* < 1.73, *ns*). Comparisons across groups in the magnitude of change showed that the sample as a whole showed no change over time [Time effect *F*(3,240) = 0.15, *ns*], and the magnitude did not vary by group [Group X Time *F* (6,240) = 0.81, *ns*].

Affective pain symptoms (assessed via the McGill Pain Inventory-Affective component). Within-group analyses indicated that none of the groups showed improvement in the affective component of pain from pre-to-post over time, although both the TRE and the Yoga-sham groups showed marginal improvement (*ps* < .10). Evaluations comparing all groups showed that the sample as a whole showed improvement over time [Time effect $F(1,89) = 6.86$, $p=.01$]), but the magnitude of change did not vary by group [Group X Time $F(6,240) = 1.40$, *ns*].

Sleep symptoms (assessed via the Insomnia Severity Index). Within-group analyses indicated that none of the groups showed significant improvement insomnia symptoms from pre-to-post over time, although both the TRE and the Yoga-sham groups showed marginal improvement (*ps* < .10). Evaluations comparing all groups showed that the sample as a whole showed improvement over time [Time effect $F(1,89) = 6.96$, $p=.01$], but the magnitude of change did not vary significantly by group [Group X Time $F(2,89) = 2.54$, $p < .09$)].

Secondary Outcome: Positive Mental Health

Well-being (assessed via the Ryff Psychological Well-being Scale). Within-group analyses indicated that none of the groups showed improvement in well-being over time (all *F*s < 1.45, all *ps* > .25). Evaluations comparing all groups showed that the sample as a whole also did not show improvement over time in well-being [Time effect $F(3,240) = 2.06$, *ns*], nor did the magnitude of change vary significantly by group [Group X Time $F(2,89) = 0.54$, *ns*].

Secondary Outcome: Neurocognitive function.

Attention (assessed via List Learning the RBANS battery). Within-group analyses indicated that the TRE group showed significant improvement [$F(1,29) = 12.57$, $p < .001$] and the Yoga-sham group marginal improvement [$F(1,29) = 2.75$, $p < .11$] from pre to post. In contrast, the control ground showed no change [$F(1,31) = 0.30$, *ns*] . Evaluations comparing all groups showed that the sample as a whole showed improvement over time [Time effect $F(1,89) = 12.90$, $p=.001$] and that the magnitude of change varied by group [Group X Time $F(2,89) = 3.46$, $p=.04$]. Simple comparisons indicated that the TRE group improved more than did the control group, with no other group differences achieving significance.

Working memory (assessed via the Digit Span). Within-group analyses indicated that the TRE group showed significant improvement in digit span from pre-to-post [$F(1,29) = 5.78$, $p < .03$], whereas neither the Yoga-sham nor the Control group showed improvement [*Fs* < 1.97, *ns*]. Evaluations comparing all groups showed that the sample as a whole showed did not show improvement over time [Time effect $F(1,89) = 12.90$, $p=.001$], but the magnitude of change tended to vary by group [Group X Time $F(2,89) = 3.02$, $p = .06$]. Simple comparisons indicated that the TRE group improved more than did the Yoga-sham group, with no other group differences achieving significance.

Executive function (assessed via Category Inhibition, Category Fluency, List Fluency, and Category Switching).

A. **Category Inhibition**: Within-group analyses indicated that the Yoga-sham group [$F(1,29) = 14.26$, $p < .001$] and the control group [$F(1,31) = 4.31$, $p < .05$] showed significant improvement in category inhibition from pre-to-post, whereas the TRE group showed no change. Evaluations comparing all groups showed that the sample as a whole did not show improvement over time [Time effect $F(1,89) = 0.95$, $p=.ns$], but the magnitude of change did vary by group [Group X Time $F(2,89) = 3.14$, $p=.05$]. Simple

comparisons indicated that the Yoga-sham group improved more than did the TRE group, with no other group differences achieving significance.

B. **Category Fluency**: Within-group analyses indicated that the Control group [$F(1,31) = 4.23$, $p < .05$], TRE group [$F(1,29) = 5.23$, $p < .03$], but not the Yoga-sham group [$F(1,29) = 1.84$, *ns*] showed **declines** in category fluency from pre-to-post treatment. Evaluations comparing all groups showed that the sample as a whole showed declines over time [Time effect $F(1,89) = 4.49$, $p < .001$], but the magnitude of change did vary by group [Group X Time $F(2,89) = 0.01$, *ns*].

C. **List Fluency:** Within-group analyses indicated that none of the groups showed a significant change in list fluency from pre- to post-treatment [all Fs < 1.78, *ns*]. Evaluations comparing all groups showed that the sample as a whole showed improvement over time [Time effect $F(1,89) = 3.79$, $p < .001$], but the magnitude of change did not vary by group [Group X Time $F(2,89) = 0.01$, *ns*].

D. **Category Switching**: Within-group analyses indicated that none of the groups showed a significant change from pre to post in category switching [all Fs < 0.32, *ns].* Evaluations comparing all groups showed that the sample as a whole showed did not show improvement over time [Time effect $F(1,89) = 0$, *ns*], and the magnitude of change did vary by group [Group X Time $F(2,89) = 0.29$, *ns*].

Table 1. *Pre-, Post-, 3-month, and 6-month Scores (SE) for Neurocognitive, Symptom, and Well-being Measures by Treatment Group*

Measure	**Group Means (*SD*)[a]**			**Time effects[a]**	**Group X Time effects[a]**
	Control (n=30)	**TRE (n=30)**	**Yoga-Sham (n=32)**	**Total Sample (*N*=92)**	
Psychological symptoms					
PTSD Symptom Scale				*F*(3,240) = 4.64, *p*=.006	*F* (6,240) = 1.30, *ns*
Pre-	33.94 (6.35)	33.17 (9.00)	31.38 (12.79)	32.60 (10.20)	
Post-	34.81 (7.28)	29.72 (11.43)*	27.42 (11.54)*	30.08 (10.81)**	
3-month F/U	30.94 (9.24)	27.22 (8.75)**	28.08 (10.55)+	28.58 (9.65)**	
6-month F/U	32.69)10.65)	29.94 (8.71)*	27.08 (10.51)*	28.53 (10.19)***	
PHQ-9: Depression				*F*(3,240) = 2.85, *p*=.04	*F* (6,240) = 1.40, *ns*
Pre-	14.30 (6.06)	14.52 (6.47)	14.19 (6.89)	14.34 (6.41)	
Post-	14.33 (5.23)	11.93 (5.63)	11.67 (6.06)	12.63 (5.71) ***	
3-month F/U	14.81 (5.74)	12.86 (5.64)	12.00 (6.43)	13.22 (5.98) +	
6-month F/U	14.48 (5.37)	13.59 (6.33)	11.04 (6.52)*	13.05 (6.20) +	
Physical Health					
SF-36 Physical Health Component				*F*(3,240) = 0.48, *ns*	*F* (6,240) = 0.81, *ns*
Pre-	50.98 (8.34)	48.80 (8.51)	50.72 (8.50)	50.13 (8.38)	
Post-	49.35 (8.22)	49.55 (8.03)	50.55 (7.96)	49.81 (7.99)	
3-month F/U	49.63 (7.38)	49.59 (8.37)	50.96 (9.35)	50.05 (8.33)	
6-month F/U	49.51 (7.38)	49.49 (8.15)	51.04 (9.19)	50.00 (8.03)	

Measure	Group Means (*SD*)[a]			Time effects[a]	Group X Time effects[a]
	Control (*n*=30)	**TRE (*n*=30)**	**Yoga-Sham (*n*=32)**	**Total Sample (*N*=92)**	
McGill Affective Pain Component				*F*(1,89) = 6.86, *p*=.01	*F* (2,89) = 0.15, *ns*
Pre-	2.84 (3.54)	3.60 (3.87)	3.73 (3.90)	3.38 (3.75)	
Post-	2.19 (2.49)	2.50 (3.05)+	2.77 (3.43)+	2.48 (2.98)**	
Insomnia Index				*F*(1,89) = 6.96, *p*=.01	*F* (2,89) = 2.54, *p* < .09
Pre-	20.56 (5.50)	18.13 (7.21)	16.83 (7.26)	18.55 (6.79)	
Post-	20.17 (4.40)	15.93 (6.78)+	15.40 (6.53)+	17.42 (6.38) **	
Positive Mental Health					
Well-being				*F*(3,240) = 2.06, *ns*	*F*(3,240) = 0.54, *ns*
Pre-	105.33 (21.31)	104.90 (21.43)	108.52 (21.54)	106.22 (21.54)	
Post-	108.63 (21.34)	109.48 (20.04)	110.70 (19.88)	109.60 (201.9)	
3-month F/U	104.81 (18.96)	109.28 (21.21)	113.26 (21.95)	109.12 (20.79)	
6-month F/U	107.85 (21.96)	109.37 (18.11)	112.44 (20.38)	109.88 (20.01)	
Neurocognitive Measures					
Attention: List Learning				*F*(1,89) = 12.90, *p*=.001	*F*(2,89) = 3.46, *p*=.04 Pre-post change: TRE > Control*
Pre-	9.88 (3.51)	9.17 (4.00)	9.23 (3.80)	9.43 (3.74)	
Post-	10.13 (3.18)	11.23 (3.93)***	10.03 (3.00)	10.46 (3.40)***	

Measure	Group Means (*SD*)[a]			Time effects[a]	Group X Time effects[a]
	Control (*n*=30)	**TRE (*n*=30)**	**Yoga-Sham (*n*=32)**	**Total Sample (*N*=92)**	
Working Memory: Digit Span				*F*(1,89) = 0.95, *p=.ns*	*F*(2,89) = 3.02, *p* =.06 Pre-post change: TRE > Yoga*
Pre-	10.59 (3.61)	10.53 (3.31)	10.40 (3.85)	10.51 (3.56)	
Post-	10.91 (3.77)	11.83 (2.87)*	9.73 (3.64)	10.83 (3.52)	
Executive Function					
A. **Category Inhibition**				*F*(1,89) = 12.11, *p*=.001	*F*(2,89) = 3.14, *p*=.05 Pre-post change: Yoga > TRE*
Pre-	9.38 (3.41)	10.43 (2.74)	8.97 (3.26)	9.59 (3.18)	
Post-	10.06(2.91)*	10.50 (2.79)	10.23 (3.27)***	10.26 (2.97)***	
B. **Category Fluency**				*F*(1,89) = 4.49, *p*<.001 (Declined)	*F*(2,89) = 0.01, *ns*
Pre-	11.38 (4.26)	11.43 (3.42)	10.77 (3.66)	11.20 (3.77)	
Post-	10.34 (3.82)*	10.00 (3.07)*	10.00 (2.83)	10.12 (3.25)***	
C. **List Fluency**				*F*(1,89) = 3.70, *p*<.001	*F*(2,89) = 0.01, *.ns*
Pre-	10.97 (3.19)	11.20 (3.66)	10.53 (3.35)	10.90 (3.37)	
Post-	11.44 (3.65)	11.77 (3.71)	11.03 (3.16)	11.41 (3.49)***	

Measure	**Group Means (*SD*)[a]**			**Time effects[a]**	**Group X Time effects[a]**
	Control (n=30)	**TRE (*n*=30)**	**Yoga-Sham (*n*=32)**	**Total Sample (*N*=92)**	
D. **Category Switching**				*F*(1,89) = 0.00, *ns*	*F*(2,89) = 0.29, *ns*
Pre-	10.56 (3.71)	9.63 (2.75)	9.70 (2.97)	9.98 (3.18)	
Post-	10.22 (4.64)	9.57 (3.74)	10.13 (3.12)	9.98 (3.87)	

Note: *** $p < .001$; ** $p < .01$; * $p \leq .05$; + $p \leq .10$. Columns with [a] suprascript compare pre-levels of a variable with each subsequent measure of that variable within the column.

Summary of findings

Primary Outcomes: The sample as a whole improved in depression and PTSD symptoms, and the improvements were sustained at 6 month follow-up. However, groups did not vary in the magnitude of change in symptoms, contrary to the study hypotheses that the TRE group would show more substantial improvements relative to the other two groups.

Secondary Outcomes. The sample as a whole improved in reports of the affective component of pain and insomnia symptoms from pre-to-post. However, groups did not vary in the magnitude of change in these health symptoms, contrary to the study hypotheses that the TRE group would show more substantial improvements relative to the other two groups.

Neither the physical health component of the SF-36 nor well-being (Ryff's overall scale) improved from pre across to the 6-month follow-up, contrary to study hypotheses. None of the treatments really targeted these explicitly (with a more specific focus on mental health), so perhaps this is not surprising.

Cognitive function findings showed that attention improved in the sample as a whole from pre-to-post, with the TRE group showing larger changes than the control group. Likewise, working memory improved from pre-to-post in the sample as a whole, with the TRE group showing larger changes than the Yoga-sham group. These findings are partially consistent with study hypotheses that the TRE group would show more substantial improvements relative to the other two groups.

Findings for measures reflecting changes in executive function were mixed, and not consistent with study hypotheses. Depending on the measure, the sample as a whole improved (i.e., List Fluency), Yoga-sham only improved relative to TRE (i.e., Category Inhibition), the sample as a whole did not change (i.e., Category Switching), or the sample as a whole showed deterioration (i.e. Category Fluency).

Interpretation of findings

The evaluation of study outcomes indicate that the TRE intervention yielded significant benefits over both the Placebo-Yoga and waitlist control groups for learning and working memory, and benefits over the waitlist condition for insomnia symptoms.

On key neurocognitive, symptom, and functional measures, participants in all groups showed improvement, with the magnitude of effects ranging from moderate to large. Thus, it is possible that participating in the trial (including for those in the control condition who were waiting for assignment to treatment) yielded some benefits. We cannot rule out, however, that the passage of time accounted for these changes across groups.

Interpretation of Findings. What is the mechanism that can account for the benefits derived from the tremors in the TRE exercises in comparison to the same exercises without tremors in the Sham-Yoga or the Wait List Control? The literature attributes the tremors induced by TRE to the central pattern generator or CPG (Ingoni, 2015). It supports the production of most rhythmic motor patterns, such as walking, swimming, flying, and breathing. CPGs are neural networks that produce rhythmic patterned outputs without rhythmic sensory input or without higher cerebral involvement that are present in all vertebrae species. Thus, a CPG is a rhythmic movement of neuronal centers of spinal cord origin that may continue without requiring further

movement or sensory feedback to remain self-sustaining (Guertin, 2013). Thus, the basic pattern of taking a step can be produced by the spinal cord without the need of descending commands from the cortex (Kiehn, & Butt, 2003; Whelan, 2003). Ingoni links CPG functions to the salience network for salience detection and the maintenance of homeostasis. The dysregulation of the salience network is associated with PTSD (Lanius et al., 2015), as is impaired context processing (Liberzon & Abelson, 2016); both are large neural networks. The bodily tremors of TRE may restore interoceptive and proprioceptive functions through a normalization of the brain's salience network and, thus, homeostasis and the reduction of such PTSD symptoms as hyper vigilance. According to Ingoni, TRE leads to reorganization of spinal cord neurology and restorative processes that facilitate homeostatic processes between spine and brainstem; these foster brain plasticity related to emotional functions of limbic system. CPG is seen by a number of investigators as having a broadly restorative effect on the brain (Epstein, 1996, Epstein, Senzon, & Lemberger, 2009). Thus, the normalization of the salience network and homeostatic functions has downstream effects in normalizing prefrontal cortical functions that are reflected in the improved working memory, list learning, and sleep found in the TRE intervention. It should be noted that gains in working memory are also found with yoga interventions (Brunner, Abramovic, & Etherton, 2017) but they are significantly greater in the TRE group here in comparison to the Placebo group. It should be noted that list learning is a more complex memory and attention measure in comparison to working memory, as it tests immediate recall, delayed recall, and recognition memory. Another notable finding is the improved sleep, perhaps reflecting improved breathing, a rhythmic activity associated with CPG and, thus, with TRE training.

The gains shown by all three groups call for additional analyses that examine mediators and moderators. All groups improved on the PTSD measure across time, with no between group differences. The cognitive gains over time included episodic memory, complex attention especially for the TRE intervention, and executive function measure for Sham-Yoga. The reduced symptoms over time include post-traumatic stress symptoms, depressive symptoms, and insomnia. Additional secondary analyses will help identify subject groups that particularly benefitted from TRE.

Our findings point to TRE as a potentially useful approach for not only affecting physical functions, such as sleep, but cortical functions associated with trauma. The participants in this study were complex: had multiple psychiatric and medical diagnoses, had received a variety of therapies for some time, had been and were on numerous medications. In a secondary analysis we plan to address these issues more fully with chart reviews of: (1) comorbid psychiatric diagnoses and length of time, (2) mental health treatments and length of time, (3) psychotropic medication and medications with central nervous system effects (4) chronic pain diagnoses and length of time, and (5) interviews as needed. We plan to use regression analyses to help identify mediators that shape the relationship between TRE and intervention gains.

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

The training opportunities provided by the project to staff depended on the position and work activities required of a particular position and of the skill set staff members brought to the study.

Principal Investigator (Martha Kent) this was the first relatively large controlled clinical trial she conducted. Main learning opportunities included an appreciation of the complexity of PTSD diagnosed participants and the requirements of the VA IRB and CDMRP.

Study Coordinator: For both study coordinators (Brigitte Adamsen, Lisa Orozco) who worked on this study, this was the first mental health project they worked on. They learned about Posttraumatic Stress Disorder (PTSD), its characteristics, how to administer the CAPS as a screening tool, how to screen for inclusion/exclusion criteria, appreciate working with a more complex population involving a range of psychiatric symptoms.

Psychology Technicians: Several psychology technicians participated in the study. For all of them, it was the first exposure for working on a study. Thus, they had to learn a range of skills, starting from simple to complex ones: Recruitment of subjects, consenting, screening, pre-testing that involved the administration of scales and individually administered neuropsychological tests. They learned to score the scales and cognitive tests and enter data into a spread sheet.
Intervention Trainers/Therapists (Travis Webb, Beth Dietrich) were trained in implementing TRE and Placebo conditions to participants. This included them actually experiencing the training themselves through training provided by Dr. Berceli, the developer of TRE. They were able to apply the approaches with sensitivity and accuracy.
Study staff members professional achievements: Since completing their work with the study, two study staff members have graduated from nursing school (Brigitte Adamsen, Dominique Gandy), one is enrolled in medical school (Barnwell Taylor), two are enrolled in doctoral programs in psychology (Morgan Regalado Hustead, Ashley Knobloch). Two staff members have completed their pre-med undergraduate studies and are in the process preparing for and applying to medical schools (Gabriela Avila, Amer Marji), two have graduated from master's level counseling programs (Morgan Regalado Hustead, Danielle Ruberto). This study has contributed significantly to the professional development of these staff members.

How were the results disseminated to communities of interest?
1.Poster Presentation:
Neuromuscular Tremors as Tension and Trauma Releasing (TRE): From Cultural Practices to Controlled Clinical Trial (RCT) of TRE
Mary C. Davis, Morgan Hustead, Beth Dietrich, David Berceli, Martha Kent
Abstract was submitted to and accepted by the 2018 conference of the International Society for Traumatic Stress Studies (ISTSS), meeting in Washington, DC, November, 2018.
2. Veterans Video Project:
Arizona Republic Video Journalist videotaped the TRE exercises and interviewed involved staff for a detailed documentary on TRE. Participants included PI Martha Kent, Consultants David Berceli, Professor Mary Davis, Study Coordinator Brigitte Adamsen, Research Assistant Morgan Regalado Hustead, with hospital media consultant Paul Coupad. The Video Journalist is Hannah Gaber Saletan <hgabersale@arizonarepublic.com> Contact telephones 602-444-8604; 480-223-3922. We do not know when this documentary will air.
What do you plan to do during the next reporting period to accomplish the goals?
Nothing to Report.
We are at the beginning phase of analyzing and understanding our data. We anticipate more interactions with the local and larger community, once our work is fully completed and has appeared in print. We plan to develop further presentations and journal publications.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?
We are at the beginning phase of analyzing and understanding our data. We anticipate more interactions with the local and larger community and will develop further presentations and journal publications.
Dr. Berceli has had very good international success in training TRE to provider groups in numerous countries where he developed TRE in workshops and presentations over the past 20-30 years. His work is well known internationally and he has made inroads in attracting funding and recognition in the US. Please see his summary of training and presentations with Active

Duty and Veteran organizations listed in **Appendix 9**. We plan to engage his expertise in making TRE known in the relevant treatment communities in the US.

What was the impact on other disciplines?

In progress.

What was the impact on technology transfer?

In progress.

What was the impact on society beyond science and technology?

In progress.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

Nothing to Report.

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

Nothing to Report.

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

Nothing to Report.

Significant changes in use or care of human subjects

Nothing to Report.

Significant changes in use or care of vertebrate animals

Nothing to Report.

Significant changes in use of biohazards and/or select agents

Nothing to Report.

6. PRODUCTS:

Publications, conference papers, and presentations

Journal publications.

Kent, M., Rivers, C. T., & Wrenn, G. (2015). (2015). Goal-directed Resilience in Training (GRIT): A biopsychosocial model of self-regulation, executive functions, and personal growth (*eudaimonia*) in evocative contexts of PTSD, obesity, and chronic pain. *Behavioral Sciences*, 5, 2015, 264-304.

Quirin, M., Kent, M., Boksem, M. A. S., & Tops, M (2015). Integration of negative experiences: A neuropsychological framework for human resilience. *Behavioral and Brain Sciences, 38*, 44-45.

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

Nothing to Report.

Other publications, conference papers, and presentations.

Poster Presentation:

Mary C. Davis, Morgan Hustead, Beth Dietrich, David Berceli, Martha Kent. Neuromuscular Tremors as Tension and Trauma Releasing (TRE): From Cultural Practices to Controlled Clinical Trial (RCT) of TRE. Accepted for presentation at the International Society for Traumatic Stress Studies annual conference. Washington, D.C., November, 2018.

Morgan Regalado, Northern Arizona University; Frank Infurna, Arizona State University; Aram Mardian, Phoenix VA Health Care System; Martha Kent, Phoenix VA Health Care System. Test-Taking Effort while Exploring a Resilience Mechanism of the Environment x Biobehavioral Control Model. International Resilience Symposium. Mainz, Germany. September, 2017.

Conference Papers:

Martha Kent, Excellence in Living in the Presence of Extremes: Environment x Biobehavioral Control Model. Sponsored Workshop on Understanding the Origins of Combat Stress and Moral Injury through Cross-cultural Research. Arizona State University Center for Evolution & Medicine. Tempe, AZ, March 1-2, 2017.

Martha Kent. When Science Does not Know Anything About Your Life, Who Is the Doctor? From the Personal to the Scientific. 3rd Bi_Annual Community Health Matters Forum *"Understanding Resilience in Underserved Communities; From Research to Reality*". Atlanta Clinical & Translational Science Institute: Emory, Morehouse, Georgia Institute of Technology. Atlanta, April 27, 2017.

Website(s) or other Internet site(s)

The website for TRE by Dr. David Berceli is http://www.traumaprevention.com.
He is currently exploring with the nonprofit organization ***TRE for All*** the possibility of creating website for Veteran and Active Duty TRE.

Technologies or techniques

Nothing to Report.

Inventions, patent applications, and/or licenses

Nothing to Report.

Other Products

Nothing to Report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	**Martha Kent**
Role:	PI
Research Identifier:	
Person Months:	24 as months as Department of Defense (DoD) appointment, 12 months as Without Compensation appointment (WOC)
Contribution to Project:	Project oversight, training of staff, progress reports, IRB contact
Funding Support:	DoD
Name:	**Brigitte Adamsen**
Role:	Coordinator (student)
Research Identifier:	
Person Months	24
Contributions to Project:	Recruitment, consenting, reporting, scheduling
Funding Support:	DoD
Name:	**Lisa Orozco**
Role:	Coordinator
Research Identifier:	
Person Months:	3
Contributions to Project:	Recruitment, preparation of initial study documents
Funding Support:	DoD
Name:	**Travis Webb**
Role:	Trainer/therapist
Research Identifier:	
Person Months:	2
Contribution to Project:	Training of patients, progress notes, patient education
Funding Support:	DoD

Name:	**Beth Dietrich**
Role:	Trainer/therapist
Research Identifier:	
Person Months:	18
Contribution to Project:	Training of patients, progress notes, patient education
Funding Support:	DoD
Name:	**Taylor Barnwell**
Role:	Psychology Technician (student)
Research Identifier:	
Person Months:	12
Contribution to Project:	Testing, scoring, data entry, consenting
Funding Support:	DoD
Name:	**Jinah Kim**
Role:	Psychology Technician (student)
Research Identifier:	
Person Months:	4
Contribution to Project:	Testing, scoring, data entry, consenting
Funding Support:	DoD
Name:	**Ashley Knobloch**
Role:	Psychology Technician (student)
Research Identifier>	
Person Months:	2
Contribution to Project:	Testing, scoring, data entry, consenting
Funding Support:	DoD
Name:	**Danielle Ruberto**
Role:	Psychology Technician (student)
Research Identifier:	
Person Months:	4
Contribution to Project:	Testing, scoring, data entry, consenting
Funding Support:	DoD
Name:	**Dominique Gandy**
Role:	Psychology Technician (student)
Research Identifier:	
Person Months:	3
Contribution to Project:	Testing, scoring, data entry, consenting
Funding Support:	DoD
Name:	**Morgan Regalado Hustead**
Role:	Psychology Technician, Coordinator (student)
Research Identifier:	
Person Months:	36
Contributions to Project:	Testing, scoring, data entry, consenting, recruitment, reporting
Funding Support:	DoD, WOC
Name:	**Gabriela Avila**
Role:	Psychology Technician (student)
Research Identifier:	
Person Months:	6
Contributions to Project:	Testing, scoring, data entry, consenting
Funding Support:	WOC
Name:	**Amer Marji**

Role:	Psychology Technician
Research Identifier:	
Person Months:	6
Contributions to Project:	Testing, scoring, data entry, consenting
Funding Support:	WOC
Name:	**Mary Davis**
Role:	Statistician Consultant
Research Identifier:	
Person Months:	24
Contributions to Project:	Methodology consultant, statistical analysis
Funding Support:	DoD
Name:	**David Berceli**
Role:	TRE consultant
Research Identifier:	
Person Months:	24
Contributions to Project:	Training therapists in TRE and Placebo approaches
Funding Support:	DoD
Name:	**Charles Hoge**
Role:	Intervention consultant
Research Identifier:	
Person Months:	3
Contribution to Project:	Design of Placebo condition, intervention consultation
Funding Support:	No compensation

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 participants?
None were involved.

8. SPECIFIC REPORTING REQUIREMENTS

Collaborative Awards
There are no collaborative awards.
Quad Chart
Is updated and included.

9. APPENDICES

List of Appendices:
Appendix 1. References
Appendix 2. Training Manuals for the Training of Trainers/Therapists
Appendix 3. Monitor Questionnaires
Appendix 4. Source documents
Appendix 5. Diaries
Appendix 6. Eligibility Screening Scales
Appendix 7. Flow Diagram for Implementing the Main Intervention in Four Waves
Appendix 8. Table of Outcome Measures

Appendix 9. David Berceli TRE Presentations and Training: U.S.A.and Global
Appendix 10. Texts of Presentations and Publications