

A. OVERALL COVER PAGE

Project Title: Assessing the feasibility and acceptability of using non-invasive transcutaneous auricular vagus nerve stimulation (taVNS) to reduce PTSD symptoms in WTC responders	
Grant Number: 5U01OH012050-02	Project/Grant Period: 07/01/2021 - 06/30/2023
Reporting Period: 07/01/2022 - 06/30/2023	Requested Budget Period: 07/01/2022 - 06/30/2023
Report Term Frequency: Final	Date Submitted: 10/10/2024
Program Director/Principal Investigator Information: REBECCA SCHWARTZ , PHD Phone Number: 516-465-1981 Email: Rschwartz3@northwell.edu	Recipient Organization: FEINSTEIN INSTITUTE FOR MEDICAL RESEARCH 350 Community Drive MANHASSET, NY 110303816 UEI: C5LHMPRJ9J19 EIN: 1112673595A1 RECIPIENT ID:
Change of Contact PD/PI: NA	
Administrative Official: DIANE M MARBURY 350 Community Drive Manhasset, NY 110303816 Phone number: 5164652664 Email: DMarbury@northwell.edu	Signing Official: DIANE M MARBURY 350 Community Drive Manhasset, NY 110303816 Phone number: 5164652664 Email: DMarbury@northwell.edu
Human Subjects: NA	Vertebrate Animals: NA
hESC: No	Inventions/Patents: No

B. OVERALL ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The major goal of the current study is to determine whether the use of a novel, safe, non-invasive form of VNS, transcutaneous auricular VNS (taVNS), would be acceptable and feasible for use with WTC responders who have PTSD and whether the methodology involved with a larger randomized controlled trial (RCT) to test taVNS efficacy would be acceptable and feasible. To accomplish these goals, the current study involves 1) conducting a formative phase evaluation with a focus group of WTC responders with elevated PTSD symptoms to tailor the taVNS intervention and the pilot study methodology and 2) pilot the intervention in a randomized, double-blind placebo controlled parallel-design study with 30 WTC responders who have PTSD. Outcomes include taVNS intervention and study methodology feasibility and acceptability. In addition, differences between baseline and post-treatment MH measures will be used to generate hypotheses for a future larger RCT aimed at evaluating taVNS efficacy in PTSD symptom reduction among a larger sample of WTC responders with PTSD. We will also use results to generate hypotheses regarding potential mechanisms of action including the various inflammatory, neural and cardiovascular changes that correlate with treatment outcomes.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

At the focus group, participants reiterated the fact that current practices of psychotropic medications and talk therapy were not consistently beneficial, and many barriers exist in receiving care, such as transportation and access to care. Participant reactions were extremely positive about the design of the device, and the novelty of a noninvasive and portable earpiece was very exciting. We are disseminating the focus group study findings to the scientific community through a manuscript in a special WTC issue of the International Journal of Environmental Research and Public Health.

Drs Schwartz and Zanos also presented at the World Trade Center Health Program bi-annual meeting that is attended by the scientific community as well as responder community members.

This study was also discussed in numerous newspaper articles as well as podcasts in order to better reach members of the responder community, as outlined in the product section. Our plans for dissemination results of the clinical trial portion of the study will be through publications.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Not Applicable

B.2 - What was accomplished under these goals?

1. Major Activities:

Aim 1: Completed a focus group with six responders, adjusted the methodology and intervention based on feedback, and published the results in a manuscript.

Aim 2: Conducted CAPS interviews and MINI to assess eligibility

Feb 2022 – Nov 2023

Contacted 49 responders; 30 met study criteria. The coordinator reviewed medical conditions and psychiatric exclusions.

Aim 2: Recruited, consented, enrolled, and randomized participants

Mar 2022 – Jan 2024

32 participants were fitted with taVNS devices. If PTSD diagnosis was confirmed via CAPS, participants were randomized into control or sham groups

Aim 2: Conducted baseline visits

Apr 2022 – Jan 2024

32 responders completed baseline assessments, received taVNS devices, and completed self-report surveys on mental health, sleep, and demographics. Blood samples were collected, and a supervised taVNS session was conducted to monitor autonomic function.

Aim 2: Mid-study check-ins

May 2022 – Feb 2024

Project Coordinators conducted regular check-ins to address device-related concerns.

Aim 2: Conducted 8-week follow-up visits

Jun 2022 – Jan 2024

29 responders completed follow-up mental health assessments, biological measurements, and blood draws. CAPS interviews were repeated.

Ongoing: Meetings, manuscripts, and grant preparation

Apr 2023 – Oct 2024

An analysis of outcomes focusing on feasibility and acceptability as well as secondary and tertiary efficacy and mechanistic outcomes has been completed and a manuscript submission is planned for Fall 2024. Grant preparation is in progress.

2. Specific Objectives:

The primary outcome measure for this study was feasibility, which was assessed by (1) recruitment rates, (2) adherence to the taVNS intervention, (3) 8-week retention rates, and (4) completion rates of study assessments. Feasibility was defined by a 75% recruitment rate among eligible participants and adherence and retention rates of 70%.

The secondary outcome measure focused on acceptability, evaluated by (1) the time required to complete questionnaires, (2) missing data rates, (3) the time required for biological data collection, (4) refusal rates for biological measures, and (5) scores on the taVNS Satisfaction and Usefulness Questionnaire.

Tertiary outcomes included mental health symptoms and biological measures, assessed at baseline and the 8-week follow-up. Mental health was measured using self-report instruments (PCL-5, GAD-7, PHQ-9, PSQI), and demographic and mental health treatment data were collected. Biological measures (HRV, EEG, GSR, inflammatory markers, etc.) were collected before and after device use, both at baseline and follow-up.

3. Significant Results:

Results indicated that daily taVNS was feasible and acceptable for the population studied. 65.3% of eligible participants enrolled, with a 90.6% retention rate and 80% adherence to the treatment protocol. 98.5% of participants reported positive feedback on the device's comfort and ease of use, meeting the study's benchmarks.

Preliminary effectiveness analyses showed a 40% improvement in PTSD symptoms in the treatment group, compared to 28.5% in the sham group. Reductions were observed in intrusion, mood disturbances, and arousal symptoms, although there were no significant changes in biological and physiological markers.

4. Key Outcomes or Other Achievements:

The preliminary findings demonstrated that taVNS is both feasible and acceptable as a treatment intervention for WTC responders with PTSD. The high adherence rate and overall positive feedback regarding the device's usability and comfort underscore the practicality of integrating this non-invasive therapy into clinical settings.

The reductions in PTSD, depression, and anxiety symptoms, alongside improvements in quality of life observed in this study, suggest that taVNS holds promise as an effective treatment option for PTSD. Given that many PTSD patients discontinue traditional therapies, taVNS offers a potential alternative for populations at risk of high dropout rates.

There is significant interest in the community regarding alternative treatments for PTSD, with our study being cited as one of the top five medical research innovations projects emerging from the Feinstein Institutes for Medical Research in 2021. The use of personalized, handheld devices for home use exemplifies how technology can be integrated into mental health treatment to improve patient adherence and outcomes.

C. OVERALL PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

Yes

Publications Reported for this Reporting Period

Public Access Compliance	Citation
N/A: Not NIH Funded	Schwartz RM, Shaam P, Williams MS, McCann-Pineo M, Ryniker L, Debnath S, Zanos TP. Understanding Mental Health Needs and Gathering Feedback on Transcutaneous Auricular Vagus Nerve Stimulation as a Potential PTSD Treatment among 9/11 Responders Living with PTSD Symptoms 20 Years Later: A Qualitative Approach. International journal of environmental research and public health. 2022 April 16;19(8). PubMed PMID: 35457714; PubMed Central PMCID: PMC9029393; DOI: 10.3390/ijerph19084847.
N/A: Not NIH Funded	Schwartz RM, Shaam P, Williams MS, McCann-Pineo M, Ryniker L, Debnath S, Zanos TP. Understanding Mental Health Needs and Gathering Feedback on Transcutaneous Auricular Vagus Nerve Stimulation as a Potential PTSD Treatment among 9/11 Responders Living with PTSD Symptoms 20 Years Later: A Qualitative Approach. International journal of environmental research and public health. 2022 April 16;19(8). PubMed PMID: 35457714; PubMed Central PMCID: PMC9029393; DOI: 10.3390/ijerph19084847.

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Category	Explanation
Other	https://www.bioworld.com/articles/511308-9-11-first-responders-with-ptsd-may-get-help-from-vagus-nerve-stimulator?v=preview
Other	https://medicalxpress.com/news/2021-09-terrorism-years-minute-doses-electricity.html
Other	https://www.newsday.com/business/technology/world-trade-center-ptsd-feinstein-clinical-trial-1.50356722
Other	https://www.northwell.edu/news/the-latest/5-research-advances-2021
Other	https://www.northwell.edu/news/the-latest/wtc-health-program-improves-survival-longevity-for-9/11-heroes

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization? No

C.5 OTHER PRODUCTS AND RESOURCE SHARING

NOTHING TO REPORT

D. OVERALL PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	Sr/Key	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
REBECCASCHWARTZ	Y	Schwartz, Rebecca	PHD	PD/PI	1.1	0.0	0.0			NA
ZANOSTHEODOROS	Y	Zanos, Theodoros	BS,MS,PHD	PD/PI	1.1	0.0	0.0			NA
JMOLINE	N	Moline, Jacqueline	BA,MD,MS	Co- Investigator	0.6	0.0	0.0			NA
KMDELIGIANNIDIS	N	Deligiannidis, Kristina Marie	BS,BS,MD	Co- Investigator	0.2	0.0	0.0			NA
SDEBNATH	N	Debnath, Shubham	PhD	Postdoctoral Scholar, Fellow, or Other Postdoctoral Position	4.2	0.0	0.0			NA
MBELLEHSEN	N	Bellehesen, Mayer H	PhD	Co- Investigator	0.2	0.0	0.0			NA
MMCCANN4	N	McCann, Molly	PHD,MS,BS	Postdoctoral Scholar, Fellow, or Other Postdoctoral Position	0.8	0.0	0.0			NA
WILLIAM_M	N	Williams, Myia	PhD	Co- Investigator	0.3	0.0	0.0			NA
PSHAAM	N	Shaam, Pooja	MA	Project Coordinator	12.0	0.0	0.0			NA
	N	Lieberman, Lynne	PhD	Licensed Clinical Psychologist	0.8	0.0	0.0			NA
	N	Ryniker, Laura	MPH	Associate Project Manager	2.4	0.0	0.0			NA

Glossary of acronyms:

Sr/Key - Senior/Key

Cal - Person Months (Calendar)

Aca - Person Months (Academic)

Sum - Person Months (Summer)

Foreign Org - Foreign Organization Affiliation

SS - Supplement Support

RS - Reentry Supplement

DS - Diversity Supplement

OT - Other

NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Not Applicable

D.2.b New Senior/Key Personnel

Not Applicable
D.2.c Changes in Other Support
Not Applicable
D.2.d New Other Significant Contributors
Not Applicable
D.2.e Multi-PI (MPI) Leadership Plan
Not Applicable

E. OVERALL IMPACT**E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?**

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

G. OVERALL SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND NOTICE OF FUNDING OPPORTUNITIES REPORTING REQUIREMENTS NOTHING TO REPORT
G.2 RESPONSIBLE CONDUCT OF RESEARCH Not Applicable
G.3 MENTOR'S REPORT OR SPONSOR COMMENTS Not Applicable
G.4 HUMAN SUBJECTS G.4.a Does the project involve human subjects? Not Applicable G.4.b Inclusion Enrollment Data File(s) uploaded: CumulativeInclusionEnrollmentReport Completed.pdf G.4.c ClinicalTrials.gov Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?
G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT NOT APPLICABLE
G.6 HUMAN EMBRYONIC STEM CELLS (HESCS) Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)? No
G.7 VERTEBRATE ANIMALS Not Applicable
G.8 PROJECT/PERFORMANCE SITES Not Applicable
G.9 FOREIGN COMPONENT No foreign component
G.10 ESTIMATED UNOBLIGATED BALANCE Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

Cumulative Inclusion Enrollment Report

This report format should NOT be used for collecting data from study participants.

Study Title:

Comments:

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/ Alaska Native										
Asian										
Native Hawaiian or Other Pacific Islander										
Black or African American										
White										
More Than One Race										
Unknown or Not Reported										
Total										

I. OVERALL OUTCOMES

I.1 What were the outcomes of the award?

This study investigated the feasibility and acceptability of transcutaneous auricular vagus nerve stimulation (taVNS). This noninvasive neurostimulation technique delivers electrical pulses via the cymba conchae region of the ear to help reduce post-traumatic stress disorder (PTSD) symptoms among World Trade Center Health Program (WTCHP) responders. Participants were placed in treatment (n = 20) and sham (n = 7) groups and underwent daily 15-minute treatment sessions for eight weeks. The stimulation group used a handheld device that stimulated the auricular branch of the vagus nerve, while the sham group received a similar device without active stimulation.

The study found that daily taVNS was a feasible and acceptable intervention for WTC responders. Participants were eligible for the study based on elevated PTSD symptoms on specific screening test scores. Of those eligible, 65.3% enrolled in the study and completed the necessary steps to fit the device and take baseline measurements. The study had a 90.6% retention rate, meaning that most participants remained in the study, and participants used the device about 80% as instructed. Feedback about the device's usability and comfort was generally positive, with 98.5% of participants expressing satisfaction in the follow-up questionnaire. The study readily met our feasibility and acceptability goals.

The preliminary effectiveness of the treatment was measured by comparing mental health scores before and after the study. In the treatment group, 40% of participants saw an improvement in their PTSD symptoms, compared to 28.5% in the sham group. On average, the treatment group also showed more reductions in specific areas, including intrusions, thoughts and mood, and arousal symptoms. However, there were no significant changes in biological markers.

These results suggest that taVNS could be a promising, easy-to-use treatment option for PTSD. Optimal and personalized stimulation parameters can be investigated to improve therapeutic efficacy, as well as treat other mental health disorders.