

**AWARD NUMBER: W81XWH-19-1-0138**

**TITLE: PTSD Prevention Using Oral Hydrocortisone in the Immediate Aftermath of Trauma**

**PRINCIPAL INVESTIGATOR: Rachel Yehuda, PhD**

**CONTRACTING ORGANIZATION: Icahn School of Medicine at Mount Sinai  
Bronx, NY**

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**TYPE OF REPORT: Annual Report**

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

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# REPORT DOCUMENTATION PAGE

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<b>13. SUPPLEMENTARY NOTES</b>							
<b>14. ABSTRACT</b> This project, PTSD Prevention Using Oral Hydrocortisone in the Immediate Aftermath of Trauma (PI: Rachel Yehuda), proposes to test a one-time prophylactic pharmacologic intervention – administration of oral hydrocortisone (HCORT) – for the prevention of post-traumatic stress disorder (PTSD) and related mental health disturbances. HCORT is a synthetic glucocorticoid similar to the body's own cortisol, and has numerous clinical uses as an anti-inflammatory agent. In response to acute stress, ample cortisol levels are critical to activating, and then containing, systems mobilized as part of the fight-or-flight response. There is evidence that people with lower cortisol levels at the time of trauma exposure are at elevated risk for PTSD.							
<b>15. SUBJECT TERMS</b> PTSD, prevention, hydrocortisone, trauma							
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## 1. INTRODUCTION:

There is currently no evidence-based intervention for individuals exposed to trauma that is designed to aid recovery and prevent the development of chronic disorders such as post-traumatic stress disorder (PTSD). This project proposes to test a one-time prophylactic treatment for the prevention of symptoms of PTSD and related mental health disturbances and the promotion of resilience using a single dose of hydrocortisone (HCORT), administered within six hours of trauma exposure.

## 2. KEYWORDS:

Trauma; hydrocortisone; PTSD; prevention, prophylaxis

## 3. ACCOMPLISHMENTS

### **What were the major goals of the project?**

*Major Task 1* – establishment of regulatory and data acquisition infrastructure (**100% complete**)

*Major Task 2* – develop and coordinate study staffing for clinical trial (**90% complete**)

*Major Task 3* – participant recruitment, randomization, participant evaluation (**5% complete**)

*Major Task 4* – execution of biomarker assays (each assay performed on samples from 150 subjects batched such that each assay performed across 5 collection time-points)

*Major Task 5* – Data Analysis

*Major Task 6* – Manuscript completion and transition planning

### **What was accomplished under these goals?**

*Major Task 1* – establishment of regulatory and data acquisition infrastructure.

The subaward has been executed between ISMMS and SMC.

IND exemption by the FDA for the study has been received.

Key decisions to finalize study procedures and synchronize procedures across study sites have been made during the reporting period. Procedures to synchronize medication administration between NYC and Israel have been made successfully. Both sites will use hydrocortisone produced by Strides Pharma and will use the same capsule and placebo compound. The dose of hydrocortisone has been standardized to a single dose of 180mg. A new compounding service for SMC has been secured (IMP).

Full IRB study and amendment approval at all institutions have been received. All HRPO inquiries and requirements were addressed and HRPO approval has been received.

Submission for the use of the ISMMS Clinical Research Unit (CRU) and the Investigational Drug Service (IDS) have been completed and submitted

Full R&D approval for the protocol from the James J. Peters VA Medical Center, where all participant biological samples will be analyzed, has been secured.

Submission to Clinicaltrials.gov is has been completed and the study has been successfully listed.

Study SOPs have been finalized and standardized across sites.

### *Major Task 2: Develop and coordinate study staffing for clinical trial*

We have hired personnel required for the study. Training of a clinical research coordinator and a study evaluator has been accomplished. Additional hiring has been intentionally delayed in order to conserve funds given the delays in subject recruitment procedures as the result of the COVID-19 pandemic. New personnel are in the hiring process to replace previous ED staff that left during the pandemic. A new private office at ISMMS has been secured to be used for clinical evaluations.

The study data collection framework and database using REDcap has been created and has undergone troubleshooting of both English and Hebrew measures. Final refinements are being made.

The existing Freezerworks program was incompatible with the Windows 10 update, so a new Freezerworks software version was purchased, and a sample management template was redone. Biological collection and processing procedures were established and staff has been trained on the protocols.

### *Task 3 – participant recruitment, randomization, participant evaluation*

Both sites agreed to an SOP and flow chart for all study steps and all assessment measurements.

Participant recruitment in the ED is scheduled to begin this summer, contingent upon the COVID-19 rates remaining low.

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

Post-doctoral evaluators are were trained on SCID, CAPS, and MADRS administration and will be supervised by licensed clinical psychologists.

### **How were the results disseminated to communities of interest?**

Nothing to report.

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

Over the next reporting period, if the COVID-19 rates permit, the research team plans to finally initiate subject recruitment and randomization as well as all subject-related study procedures. Participant evaluation and sample collection will be underway.

#### 4. IMPACT:

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

Nothing to report.

**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?** Nothing to report.

#### 5. CHANGES/PROBLEMS:

Nothing to report.

No significant changes in the project of its direction.

##### **Changes in approach and reasons for change**

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

As previously reported, due to the COVID-19 crisis and its impact on New York City and Israel, we have experienced delays in initiating subject recruitment. Due to the fact that study recruitment is planned to be initiated out of the Mount Sinai Emergency Department, we expect additional delays the study recruitment initiation, particularly if COVID-19 rates spike again in the future.

##### **Changes that had a significant impact on expenditures**

Given that study recruitment has not yet begun, study expenditures have been minimal. Expenditures were intentionally and strategically reduced from the original proposal in line with study delays so that the proposed work could still be accomplished within the original budget.

##### **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.** 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.** Nothing to report.

**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.** Nothing to report.

## 7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

### **What individuals have worked on the project?**

Name: Rachel Yehuda, PhD  
Project Role: Principal Investigator  
Researcher Identifier: YEHUDAR01  
Nearest person month worked: 2  
Contribution to Project: As the Study PI of this multi-center project, she will be responsible for overseeing the overall project, working with the Site PI at Chaim Sheba Medical Center (CSMC), and the completion of all tasks on the SOW. She is responsible for the overall decisions on synchronization and finalization of study procedures.

Name: Janine Flory, PhD  
Project Role: Co-Investigator  
Nearest person month worked: 1  
Contribution to Project: Dr. Flory ensures adherence to the protocol by supervising study evaluators and collaboration efforts between the ISMMS and Chaim Sheba Medical Center sites, which includes training and monitoring of rater fidelity.

Name: Linda Bierer, MD  
Project Role: Co-Investigator and Medical Advisor  
Nearest person month worked: .5  
Contribution to Project: Dr. Bierer has assisted with medically relevant decisions, such as medication dosages and exclusion criteria.

Name: Tom Hildebrandt, PhD  
Project Role: Co-Investigator and Statistician  
Nearest person month worked: 1

Contribution to Project: Dr. Hildebrandt has updated the study aims, power analysis, and analytic plans as well as advised on the development of the database.

Name: Joseph Zohar, PhD  
Project Role: Subaward Principal Investigator  
Nearest person month worked: 2  
Contribution to Project: Dr. Zohar has participated in biweekly conference calls with all study staff to finalize and synchronize study procedures.

Name: Lior Carmi, PhD  
Project Role: Co-Investigator  
Nearest person month worked: 3  
Contribution to Project: Dr. Carmi participates in the bi-weekly conference calls and serves as the administrative contact at SMC until a clinical research coordinator is hired.

Name: Heather Bader  
Project Role: Project Manager  
Nearest person month worked: 2  
Contribution to Project: Heather leads the bi-weekly conference calls and initiates discussions about the logistics involved in implementing the study protocol. She has supervised the drafting of all regulatory documents.

Name: Migle Staniskyte  
Project Role: Clinical Research Coordinator  
Nearest person month worked: 1  
Contribution to Project: Migle has drafted the regulatory documents for the ISMMS site and takes notes at the biweekly conference calls.

Name: Stav Cohen  
Project Role: Clinical Research Coordinator  
Nearest person month worked: 1  
Contribution to Project: Stav is organizing the project and will be the primary research coordinator at SMC.

Name: Emmanuel Ruhamyankaka  
Project Role: Data Manager  
Nearest person month worked: 1  
Contribution to Project: Emmanuel has created the REDcap data capture infrastructure for the 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?**

A few projects have ended over the past reporting period. An updated other support document for the PI is included as Appendix A.

**What other organizations were involved as partners?**

**Organization Name:** Sheba Medical Center  
**Location of Organization:** Tel Hashomer, Ramat Gan, Israel

**Funding:** Grant Funded

**Partner's contribution to the project**

**Facilities:** The Emergency Department at SMC will be used for subject recruitment. Outpatient psychiatry will be used for follow-up visits.

**Collaboration:** Additional recruitment site. Samples will be collected, processed, and sent to JJP VAMC for assay.

**Organization Name:** James J. Peters VAMC

**Location of Organization:** Bronx, NY

**Partner's contribution to the project**

**Facilities:** All participant biological samples will be transported to the James J. Peters VAMC for analysis. This facility is an affiliate of ISMMS.

**Collaboration:** occasionally, VA staff work on this research project.

## 8. SPECIAL REPORTING REQUIREMENTS

**COLLABORATIVE AWARDS:**

**QUAD CHARTS:**

## 9. APPENDICES:

**Appendix A**

### **OTHER SUPPORT**

**YEHUDA, RACHEL**

**ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI**  
**21 HOURS PER WEEK, PART-TIME**

**ACTIVE**

**Title:** PTSD Prevention Using Oral Hydrocortisone in the Immediate Aftermath of Trauma

**Goals:** This project proposes to test a one-time prophylactic pharmacologic intervention – administration of oral hydrocortisone (HCORT) – for the prevention of post-traumatic stress disorder (PTSD) and related mental health disturbances.

**Specific Aims/Tasks:**

- a. Discover an approach that can be used in the immediate aftermath of trauma to promote recovery and resilience
- b. Discover biological markers associated with the prediction of resilience in both HCORT and placebo-treated people
- c. Identify biomarkers that emerge post-treatment in association with recovery and resilience

d. Determine whether and to what extent biological correlates of treatment-induced recovery are similar to, overlap with, or are distinct from biomarkers of resistance to the development of PTSD.

**Supporting Agency:** Dept. of the Army – USAMRAA

**Performance Period:** 05/01/2019- 04/30/2023

**Level of Funding:**

**Time Commitment:** 1.18 CM, .41TPE

**PI:** Yehuda

**Point of Contact:** Claudio D. Ortiz, Ph.D.  
USARMY MEDCOM CDMRP  
1077 Patchel Street  
Fort Detrick, MD 21702  
Phone:  
Claudio.d.ortiz.ctr@mail.mil

**No Scientific or Budgetary Overlap**

**Title:** Evaluation of Prognostic and Diagnostic PTSD Biomarkers

**Goals:** The primary goal of this project is to support the collection of epigenetic and other molecular biomarkers in OEF/OIF combat veterans undergoing CPT-C psychotherapy and resilient controls.

**Specific Aims/Tasks:**

- a. To discover and validate markers, pathways, and networks associated with the *prognosis* of PTSD following treatment.
- b. To discover and validate markers, pathways, and networks associated with state/ severity of PTSD.
- c. To validate biological correlates of PTSD risk and determine which, if any, of these markers improve with recovery.
- d. To identify biomarkers that emerge post-treatment in association with *recovery*.
- e. To determine whether and to what extent biological correlates of recovery are similar to, overlap with, or are distinct from biomarkers of *resistance* to the development of PTSD.

**Supporting Agency:** Dept. of the Army – USAMRAA (Subaward from BVMRP)

**Performance Period:** 09/30/2016-09/29/2021

**Level of Funding:**

**Time Commitment:** 1.87 CM; .64 TPE

**PI:** Yehuda

**Point of Contact:** John Clifford  
john.l.clifford11.civ@mail.mil  
USA Med Research ACQ Activity  
Fort Detrick, MD 21702-5014

**No Scientific or Budgetary Overlap**

**Title:** Assessing Inflammatory and Behavioral Pathways Linking PTSD to Increased Asthma Morbidity in WTC Workers

**Goals:** Workers Asthma and post-traumatic stress disorder (PTSD) are the most common conditions in World Trade Center (WTC) rescue and recovery workers. In this study, we will evaluate the interplay of biological and behavioral mechanisms explaining the relationship of

PTSD with increase asthma morbidity and adapt and pilot test a novel intervention to improve outcomes of WTC workers.

**Specific Aims/Tasks:**

1. Assess the relationship of PTSD with systemic and airway inflammatory patterns in WTC workers with asthma and evaluate the association with asthma control
2. Examine the longitudinal association between PTSD and symptom perception in WTC workers with asthma
3. Assess the relationship between PTSD and adherence to asthma SMB (medication adherence, trigger avoidance, and inhaler technique) in WTC workers and identify the pathways linking them
4. Develop and pilot test an integrated intervention for asthma and PTSD by adapting the Relaxation Response Resiliency Program (3RP), a mind-body program, with counseling to promote asthma SMB, and education to correct over-perception of asthma symptoms

**Supporting Agency:** NIOSH/CDC

**Performance Period:** 09/01/2016-08/31/2021

**Level of Funding:**

**Time Commitment:** .32 CM; .11 TPE

**PI:** Wisnivesky

**Point of Contact:** Travis Kubale, Ph.D., , [tek2@cdc.gov](mailto:tek2@cdc.gov)  
World Trade Center Health Program  
National Institute for Occupational Safety and Health  
Centers for Disease Control and Prevention  
4676 Columbia Parkway, MS-R-15  
Cincinnati, Ohio 45226

**No Scientific or Budgetary Overlap**

**Title:** RNA Expression in PTSD in Induced Human Neurons and Blood Cells in Basal and Glucocorticoid-Stimulated Conditions

**Goals:** We will use a new method to induce neuronal cells (iNeurons) from skin cells in combat veterans with and without PTSD and assess RNA expression in these cells and in peripheral blood mononuclear cells (PBMCs) from the same veterans. The overarching hypothesis is that we can identify PTSD molecular pathways in both iNeurons and PBMCs that would (a) be impacted by glucocorticoids and (b) overlap with comparable pathways detected in our blood biomarkers human studies and in blood and brain of animals with PTSD-like phenotypes.

**Specific Aims/Tasks:** (1) To induce and culture iNeurons and in parallel to culture PBMCs from blood of combat veterans with and without PTSD; (2) To identify PTSD associated differential gene expression in iNeurons and PBMCs; (3) To measure PTSD-specific transcriptomic response to glucocorticoid stimulation in iNeurons and PBMCs; (4) To develop PTSD causal gene co-expression network that integrates iNeuron and PBMC gene expression data with previously obtain human/animal data.

**Supporting Agency:** Dept. of the Army – USAMRAA

**Performance Period:** 09/30/2015- 09/29/2021 (NCE)

**Level of Funding:**

**Time Commitment:** 0.12 CM; .04 TPE

**PI:** Yehuda

**Point of Contact:** Claudio D. Ortiz, Ph.D.

USARMY MEDCOM CDMRP  
1077 Patchel Street  
Fort Detrick, MD 21702  
Phone:  
Claudio.d.ortiz.ctr@mail.mil

**No Scientific or Budgetary Overlap**

**Title:** Cognitive and Neural Mechanisms of the Accelerated Aging Phenotype in PTSD

**Goals:** To elucidate the complex interactions between PTSD and aging processes that culminate in poor health outcomes for older adults. The primary focus is to determine whether alterations in brain structure, function, and connectivity lead to premature cognitive decline in older PTSD patients.

**Specific Aims/Tasks:** This study will investigate the influence of chronic PTSD on signatures of aging at neural, cognitive, somatic, and behavioral levels of analysis.

**Supporting Agency:** NIMH/Columbia University

**Performance Period:** 09/01/2017-07/31/2021

**Level of Funding:**

**Time Commitment:** .47 CM; .16 TPE

**PI:** Rutherford (Site PI: Yehuda)

**Point of Contact:** Jovier Evans; jevans1@mail.nih.gov

**No Scientific or Budgetary Overlap**

**PAST**

**Title:** Regulating Emotional Responses to Spoken Comments and Visual Images Across the Affective Instability Spectrum: An fMRI Study

**Goals:** This study uses neuroimaging methods to determine whether emotional instability is associated with an impairment in the ability to use effective emotion regulation mechanisms and whether such impairments are related to disturbances in the activity of the brain systems which typically regulate emotion. Such knowledge could help to develop new treatments specifically targeted to reduce emotional instability.

**Supporting Agency:** NIH/NIMH

**Performance Period:** 09/23/2016 – 05/31/2021

**Level of Funding:**

**Time Commitment:** .13 CM; .04 TPE (Involvement ended 5/31/2020)

**PI:** Koenigsberg

**Point of Contact:** Jovier Evans; jevans1@mail.nih.gov

**No Scientific or Budgetary Overlap**

**Title:** A Randomized Controlled Trial of Internet CBT for PTSD in WTC Responders

**Goals:** We propose to conduct a randomized controlled trial of Internet-based, therapist-assisted CBT in WTC rescue and recovery workers with clinically significant WTC-related PTSD symptoms, compared to a control intervention of Internet-based, therapist-assisted supportive counseling.

**Supporting Agency:** NIH/NIOSH

**Performance Period:** 09/01/2016 – 08/31/2021 (NCE)

**Level of Funding:**

**Time Commitment:** .31 CM; .11 TPE (Involvement ended 8/31/2020)

**PI:** Feder

**Point of Contact:** Travis Kubale, Ph.D., [tek2@cdc.gov](mailto:tek2@cdc.gov)

**No Scientific or Budgetary Overlap**

**Title:** Neuroimaging Biomarkers of Resilience and Treatment Response in PTSD

**Goals:** The specific aims of this project are (1) to identify neural circuits associated with resilience to trauma using multimodal imaging; (2) to identify multimodal neuroimaging biomarkers of treatment response to CPT-C in PTSD; and (3) exploratory aims will investigate the relationship between neuroimaging measures and biological measures available from the parent study including: methylation, gene expression, lysozyme IC50-DEX, and plasma NPY.

**Supporting Agency:** Brain and Behavior Research Foundation

**Performance Period:** 03/15/2017-03/14/2020 NCE

**Level of Funding:**

**Time Commitment:** .06 CM; .02 TPE

**PI:** Yehuda

**Point of Contact:** Sho Tin Chen; [schen@bbrfoundation.org](mailto:schen@bbrfoundation.org)

**No Scientific or Budgetary Overlap**

**Title:** Gene expression profiles as markers of PTSD risk and resilience in WTC responders

**Goals:** The proposed study capitalizes on the existence of this rich and well characterized sample of

WTC responders, recruited from a cohort of over 10,000 WTC responders with diverging longitudinal PTSD symptom trajectories followed at the WTC Health Program

**Specific Aims/Tasks:** To assess gene expression profiles that may indicate PTSD risk and resilience in WTC responders

**Supporting Agency:** NIOSH

**Performance Period:** 07/01/2015-06/30/2018

**Level of Funding:**

**Time Commitment:** .06 CM; .02 TPE

**PI:** Feder

**Point of Contact:** Travis Kubale, Ph.D., [tek2@cdc.gov](mailto:tek2@cdc.gov)

World Trade Center Health Program

National Institute for Occupational Safety and Health

Centers for Disease Control and Prevention

4676 Columbia Parkway, MS-R-15

Cincinnati, Ohio 45226

**No Scientific or Budgetary Overlap**

**Title:** Biomarkers of Psychological Risk and Resilience in World Trade Center Responders

**Goals:** To examine genetic, epigenetic, and neuroendocrine biomarkers of World Trade Center-related posttraumatic stress disorder symptoms among World Trade Center rescue, recovery, and clean-up workers.

**Specific Aims/Tasks:** Employ a multi-level approach to study clinical, psychosocial, neuroendocrine, genotypic, gene-environment interaction, and molecular factors associated with PTSD risk and resilience in WTC responders exhibiting four distinct longitudinal PTSD symptom trajectories: chronic PTSD, delayed-onset PTSD, recovering, and resistant trajectories.

**Supporting Agency:** National Institute For Occupational Safety & Health/CDC/DHHS

**Performance Period:** 09/01/2012-08/31/2018

**Level of Funding:**

**Time Commitment:** 0.19 CM; .07 TPE

**PI:** Feder

**Point of Contact:** Travis Kubale, Ph.D., tek2@cdc.gov

**No Scientific or Budgetary Overlap**

**Title:** Validating Biomarkers for PTSD

**Goals:** This multisite, multidisciplinary study will validate psychological, cognitive, endocrine, genetic, and brain variables in OEF/OIF/OND veterans with and without PTSD.

**Specific Aims/Tasks:** Two samples will be collected including a sample of veterans previously studied and re-assessed for the purpose of examining the stability of clinical and biological markers and an independent sample and in an effort to validate previously identified biomarkers for PTSD.

**Supporting Agency:** NYU- DOD/USAMRAA

**Performance Period:** 04/01/2014-03/31/2017

**Level of Funding:**

**Time Commitment:** .95 CM; .33 TPE

**PI:** Marmar (Site PI: Yehuda)

**Point of Contact:** Pamela Nevels, , pamela.nevels@us.army.mil

**No Scientific or Budgetary Overlap**

**BRONX VETERANS MEDICAL RESEARCH FOUNDATION/ JAMES J. PETERS  
VAMC**

**VA APPOINTMENT: 8/8<sup>th</sup> , FULL-TIME**

**ACTIVE**

**Title:** Evaluation of Prognostic and Diagnostic PTSD Biomarkers

**Goals:** The primary goal of this project is to support the collection of epigenetic and other molecular biomarkers in OEF/OIF combat veterans undergoing CPT-C psychotherapy and resilient controls.

**Specific Aims/Tasks:**

- a. To discover and validate markers, pathways, and networks associated with the *prognosis* of PTSD following treatment.
- b. To discover and validate markers, pathways, and networks associated with state/ severity of PTSD.
- c. To validate biological correlates of PTSD risk and determine which, if any, of these markers improve with recovery.
- d. To identify biomarkers that emerge post-treatment in association with *recovery*.

e. To determine whether and to what extent biological correlates of recovery are similar to, overlap with, or are distinct from biomarkers of *resistance* to the development of PTSD.

**Supporting Agency:** Dept. of the Army – USAMRAA

**Performance Period:** 09/30/2016-09/29/2021

**Level of Funding:**

**Time Commitment:** 1.2 CM; .80 TPE

**PI:** Yehuda

**Point of Contact:** John Clifford  
john.l.clifford11.civ@mail.mil  
USA Med Research ACQ Activity  
Fort Detrick, MD 21702-5014

**No Scientific or Budgetary Overlap**

**Title:** DNA Methylation and Inflammatory Signatures with Suicide Risk and Treatment in US Veterans.

**Goals:** This study compares DNA methylation patterns and inflammatory markers in veterans with suicide, depression and healthy comparison subjects, followed longitudinally and examines changes with treatment.

**Specific Aims/Tasks:** To assess DNA methylation patterns and inflammatory markers in veterans with psychiatric conditions longitudinally.

**Supporting Agency:** VA MERIT CSR&D

**Performance Period:** 7/1/16-05/15/21 (NCE)

**Level of Funding:**

**Time Commitment:** .30 CM; .20 TPE

**PI:** Haghighi

**Point of Contact:** Gleason, Theresa, [theresa.gleason@va.gov](mailto:theresa.gleason@va.gov)

**No Scientific or Budgetary Overlap**

**Title:** Neurobiology of Affective Instability in Veterans at Low and High Risk for Suicide

**Goals:** The major goals of this project are to identify behavioral, neurobiological, and psychophysiological features underlying suicidal behavior in veterans and determine whether baseline psychophysiological measures predict suicidal behavior at 12-month follow-up.

**Supporting Agency:** VA ORD MERIT

**Performance Period:** 04/1/17 - 03/31/21

**Level of Funding:**

**Time Commitment:** .60 CM; .39 TPE

**PI:** Hazlett

**Point of Contact:** Gleason, Theresa, [theresa.gleason@va.gov](mailto:theresa.gleason@va.gov)

**No Scientific or Budgetary Overlap**

**Title:** Using Telehealth to Improve Outcomes in Veterans at Risk for Suicide

**Goals:** This is a 3-site randomized controlled trial at the VA Pittsburgh Healthcare System (VAPHS), the VA New York Harbor Health Care System (VANY) and James J Peters VA Medical Center (JJPVA) to evaluate a telehealth intervention for suicide prevention in a diverse group of Veterans at risk for suicide.

**Supporting Agency:** American Foundation for Suicide Prevention

**Performance Period:** 12/14/18 - 01/15/22

**Level of Funding:**

**Time Commitment:** .60CM; .39TPE

**PI:** Haas

**Point of Contact:** Carl Niedzielski, grantsmanager@afsp.org

**No Scientific or Budgetary Overlap**

**Title:** Predicting Suicidal Behavior in Veterans with Bipolar Disorder using Behavioral and Neuroimaging Based Impulsivity Phenotypes

**Goals:** This project aims to assess both trait and state measures of impulsivity using self-report measures and functional magnetic resonance imaging to predict the occurrence of suicidal behavior longitudinally over 1 year in Veterans with bipolar disorder.

**Supporting Agency:** VA CSR&D

**Performance Period:** 1/01/20- 12/31/23

**Level of Funding:**

**Time Commitment:** .60CM; .39TPE

**PI:** Szeszko

**Point of Contact:** Mark Roltsch, PhD

**No Scientific or Budgetary Overlap**

## **PAST**

**Title:** Evaluation of Glucocorticoid-Related Prognostic and Diagnostic PTSD Biomarkers

**Goals:** This project is designed to investigate genetic, epigenetic, gene expression and neuroendocrine differences between combat veterans who no longer meet criteria for PTSD following psychotherapy and those who retain the diagnosis post-treatment. It will also compare the biology of similarly exposed veterans who did not develop PTSD with those who recover following treatment, in order to identify biological systems that are activated in recovery.

**Specific Aims/Tasks:** Cognitive processing therapy (cognitions only) will be the treatment. Genome wide methylation will be examined in concert with a focused study of glucocorticoid receptor regulation and function so as to identify predictors and correlates of PTSD risk, recovery, persistence, and resistance. The aim is to facilitate the development of novel targets for prophylaxis and treatment, and to appreciate blood markers that could be used to predict clinical prognosis, so as to promote more effective treatment planning in veterans with PTSD.

**Supporting Agency:** VA MERIT

**Performance Period:** 01/01/16 to 12/31/20

**Level of Funding:**

**Time Commitment:** 1.2 CM, 1.00 TPE

**PI:** Yehuda

**Point of Contact:** Smith, Samantha, samantha.smith10@va.gov  
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Cube 11E  
Washington, D.C. 20002

**No Scientific or Budgetary Overlap**

**Title:** Suicide Safety Planning Group Treatment - "Project Life Force"

**Goals:** This project pilots a new treatment intervention for suicidal Veterans incorporating emotion regulation skills training with suicide safety planning.

**Specific Aims/Tasks:** To pilot a new treatment intervention for suicidal Veterans incorporating emotion regulation skills training with suicide safety planning.

**Supporting Agency:** VA Rehabilitation R&D

**Performance Period:** 9/30/15-09/29/20 NCE

**Level of Funding**

**Time Commitment:** .30 CM; .20 TPE

**PI:** Goodman

**Point of Contact:** Gleason, Theresa, [theresa.gleason@va.gov](mailto:theresa.gleason@va.gov)

**No Scientific or Budgetary Overlap**

**Title:** Glucocorticoid functioning in OEF/OIF/OND Veterans with mTBI and PTSD

**Goals:** Enhance coordination of diagnosis and treatment of combat veterans who receive care at VA.

**Specific Aims/Tasks:** To investigate the effects of mTBI, PTSD and their interaction on measures of HPA axis functioning. People with PTSD will show evidence of enhanced GR sensitivity (e.g., greater CORT and ACTH suppression to dexamethasone, lower lysozyme IC<sub>50</sub>-DEX) while people with a history of mTBI will show lower cortisol, higher basal ACTH and a suppressed ACTH response to GCT. People with both disorders will resemble the PTSD only group on measures of enhanced GR sensitivity.

**Secondary Aim:** To investigate the response to GC administration in mTBI and PTSD, and their interaction, on memory and learning using a randomized, placebo-controlled design. We hypothesize that GC administration will be associated with deficits in learning in people with mTBI, but improvements in attention and working memory for people with PTSD, and possibly with PTSD and mTBI. Affective responses to the challenge (anger and anxiety) will be examined.

**Supporting Agency:** VA MERIT CSR&D

**Performance Period:** 01/01/2014-12/31/2019 NCE

**Level of Funding:**

**Time Commitment:** .60 CM; .39 TPE

**PI:** Flory

**Point of Contact:** Gleason, Theresa, [theresa.gleason@va.gov](mailto:theresa.gleason@va.gov)

**No Scientific or Budgetary Overlap**

**Title:** Intranasal Insulin: A Novel Treatment for Gulf War Multisymptom Illness

**Goals:** The major goal is to assess the efficacy of two different doses (10 IU BID and 20 IU BID) of daily intranasal insulin for eight weeks on memory and attention functioning, on overall physical health and mood, and on other symptoms that are characteristic of or associated with CMI (e.g., fatigue, pain, sleep quality, subjective cognitive function) in Gulf War Veterans with CMI.

**Supporting Agency:** DoD/ Dept. of the Army – USAMRAA

**Performance Period:** 09/30/2012-09/29/2019 NCE

**Level of Funding:**

**Time Commitment:** .60CM; .39TPE

**PI:** Golier

**Point of Contact:** Brett Chaney, brett.l.chaney.ctr@mail.mil  
Congressionally Directed Medical Research Programs (CDMRP)  
1077 Patchel Street  
Fort Detrick, MD 21702

**No Scientific or Budgetary Overlap**

**Title:** Improving PTSD Outcomes in OIF/OEF Returnees: A Randomized Clinical Trial of Hydrocortisone Augmentation of Prolonged Exposure Therapy - Additional Biomarkers

**Goals:** This project supports the collection of epigenetic and other molecular biomarkers in OEF/OIF combat veterans undergoing prolonged exposure therapy, with or without hydrocortisone augmentation. Additionally, it adds a relevant animal model component to this research.

**Specific Aims/Tasks:** Conduct assays for urinary catecholamines, urinary cortisol metabolites and creatinine, GR gene methylation and gene expression, isolation of lymphocytes, plasma endocannabinoids, genome wide association and expression, and genome wide gene methylation.

**Supporting Agency:** Dept. of the Army – USAMRAA/ DOD

**Performance Period:** 02/20/2013-02/19/2018

**Level of Funding:**

**Time Commitment:** 1.2 CM; 0.79 TPE

**PI:** Yehuda

**Point of Contact:** Holly Campbell-Rosen  
USA Med Research ACQ Activity  
Fort Detrick, MD 21702-5014

**No Scientific or Budgetary Overlap**

**Title:** Novel Therapeutics in PTSD: A Randomized Clinical Trial of Mifepristone

**Goals:** Determine whether mifepristone administration yields a sufficiently high proportion of clinical responders to warrant more extensive and definitive research as part of a Phase III trial.

**Specific Aims/Tasks:** Conduct a Phase IIa, multi-site, double-blind, placebo-controlled trial of mifepristone in veterans with PTSD, evaluating after one month.

**Supporting Agency:** VA CCTA (CCTA 0004)

**Performance Period:** 04/01/2012-12/31/2017

**Level of Funding:**

**Time Commitment:** 0.60 CM; 0.39 TPE

**PI:** Golier

**Point of Contact:** Lisa M. Robin, M.A., LPC, Lisa.robin@va.gov

**No Scientific or Budgetary Overlap**

**Title:** CSP #589 Veterans Individual Placement and Support Towards Advancing Recovery (VIP-STAR)

**Goals:** Determine how Individual Placement and Support (IPS) model of supported employment compares to Compensated Work Therapy (CWT).

**Specific Aims/Tasks:** Compare veterans in the two work programs on occupational functioning, PTSD symptoms, self-esteem, quality of life, and health outcomes.

**Supporting Agency:** VA Cooperative Studies Program (CSP)

**Performance Period:** 11/01/2014-10/31/2017

**Level of Funding:**

**Time Commitment:** 1.80 CM; 1.18 TPE

**PI:** Davis

**Site PI:** Yehuda/Berger

**Point of Contact:** Peter Guarino, , peter.guarino@va.gov

**No Scientific or Budgetary Overlap**

**Title:** Improving PTSD Outcomes in OIF/OEF Returnees: A Randomized Clinical Trial of Hydrocortisone Augmentation of Prolonged Exposure Therapy

**Goals:** Evaluate the effects of hydrocortisone (Hcort) augmentation to improve the ability of prolonged exposure therapy (PE) to reduce PTSD symptoms in veterans with PTSD.

**Specific Aims/Tasks:** This study consists of a pre-treatment evaluation, eleven weekly sessions of hydrocortisone (or placebo) augmented Prolonged Exposure Therapy, post treatment evaluation, and a follow-up evaluation

**Supporting Agency:** Dept. of the Army – USAMRAA/ DOD

**Performance Period:** 07/26/2010-07/25/2016

**Level of Funding:**

**Time Commitment:** 2.40 CM; 1.58 TPE

**PI:** Yehuda

**Point of Contact:** Lisa Wells Roark  
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**No Scientific or Budgetary Overlap**