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TITLE: Persistent Hormonal Changes in Veterans with Gulf War Illness

PRINCIPAL INVESTIGATOR: Ricardo Jorge, MD

CONTRACTING ORGANIZATION: Baylor College of Medicine
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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The proposed cross-sectional, case-controlled study will assess the association of Gulf War Illness (GWI) with dysregulation of major hormonal systems. A total of 90 Veterans (45 Veterans with GWI and 45 Veterans of comparable age, gender, and military experience who deployed but did not develop GWI) will be recruited from clinical and community sources. Endocrine disorders can be effectively treated by pharmacological interventions currently available, thus, reducing the time it would take for Veterans to access treatment. Consequently, treatment may result in a significant reduction of Veterans' symptomatic burden.

15. SUBJECT TERMS
IRB, HRPO, Gulf War Registry

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1. INTRODUCTION:

The proposed cross-sectional, case-controlled study will assess the association of Gulf War Illness (GWI) with dysregulation of major hormonal systems. The study will assess hormone measures (including the frequency of hormone deficiencies) between Gulf War Veterans with and without GWI, and evaluate the relationship between endocrine measures and neurocognitive function. A total of 90 Veterans (45 Veterans with GWI and 45 Veterans of comparable age, gender, and military experience who deployed but did not develop GWI) will be recruited from clinical and community sources. Assessing hormonal dysregulations in the population has major therapeutic implications because endocrine disorders can be effectively treated by pharmacological interventions currently available, thus, reducing the time it would take for Veterans to access treatment. Consequently, treatment may result in a significant reduction of Veterans' symptomatic burden and maximizing their recovery and quality of life.

2. KEYWORDS:

Endocrine measures; hormonal dysregulation; HPA axis; Gulf War Illness.

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Major Task 1	Target Date	% Complete
Subtask 1: Prepare regulatory documents for IRB submission	12/30/17	100%
Subtask 2: Submit IRB-approved human use protocol and documentation to the DoD HRPO for review and approval	12/31/17 to 3/31/18	100%
Subtask 3: Order medications and materials needed for assessments	12/31/17 to 3/31/18	100%
Subtask 4: Train research team on protocol	12/31/17 to 3/31/18	100%
Major Task 2		
Subtask 1: Identify, recruit, screen, and consent eligible participants	4/1/18 to 4/30/20	Ongoing
Subtask 2: Assess endocrine function at baseline and after stimulation tests	4/1/18 to 4/30/20	Ongoing
Subtask 3: Collect medical, background, neuropsychological, and psychiatric data from subjects in both groups	4/1/18 to 4/30/20	Ongoing

What was accomplished under these goals?

Major Goal 1: Obtain local IRB and HRPO approval to start the study

Efforts during the first quarter were focused on obtaining local and HRPO approvals. The protocol and documents were submitted to Baylor College of Medicine's (BCM) IRB for review on June 13, 2017 and approved on Sept 7, 2017. The request to conduct research at Michael E. DeBakey VA Medical Center (MEDVAMC) was submitted on July 26, 2017 and approved by the Research and Development (RD) Committee on Oct 16, 2017.

The IRB approval letter, protocol, and study related documents were submitted to HRPO for review on Sept 11, 2017. Dr. Susie Stubbs, Program Manager and Human Subjects Protection Scientist at HRPO, completed her review and forwarded her findings to the deputy for concurrence. A request for clarification and modifications was received on Oct 25, 2017. The modifications included: 1) the insertion of a statement to the consent form; 2) clarification regarding BCM's IRB risk determination for the study as less than minimal risk; 3) recommendation to appoint a study monitor. The protocol was subsequently amended and submitted to local IRB on Oct 31, 2017. The amendment was reviewed by BCM IRB on Nov 14, 2017; the IRB approval letter was received on Nov 29, 2017 and forwarded to HRPO on the same day. The official memo with initial approval for the protocol from HRPO was received on Jan 2, 2018.

The second quarter focused on preparing the materials and personnel for the study. The PI worked with the award management office at BCM on creating an account. Once funds were received, testing materials (e.g., test batteries, laboratory and office supplies, etc.) were ordered and personnel hired.

Major Goal 2: Collect Data for Analysis

Efforts during the third quarter were expended on identification, recruitment, and screening study participants. Participant enrollment and data collection began at the end of the third quarter and is ongoing.

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

Nothing to Report.

How were the results disseminated to communities of interest?

Nothing to Report.

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

Last quarter, the team began designing a database to organize the data collected and facilitate data analysis in the future. The goal for the next reporting period is to build the database and develop the scripts for data analysis. Additionally, recruitment, enrollment, and data collection will continue per SOW.

Recruitment: Continue to use the directory service to obtain current contact information for veterans on the Gulf War Registry and Clinic Lists to maximize recruitment and screening efforts.

Enrollment: To make-up for the setbacks encountered during the third quarter, the team will increase the enrollment by one-two participants, per quarter.

Data collection: Continue data collection, as planned.

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:

Changes in approach and reasons for change

There were no significant changes in the project approach or its direction.

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

Several set-backs were encountered during the first year.

Personnel Changes: The graduate research assistant originally trained to conduct the neuropsychological and psychiatric assessments moved, and the research coordinator start date was pushed back to June resulting in a shortage of personnel. New personnel were hired and trained. To prevent future delays, the research staff will be cross-trained so the project does not fall behind in the event a team member is out.

Recruitment: Access to the Gulf War Registry took longer than expected. Although the application was submitted in the second quarter, the registry data was not received until the end of the third quarter (June 25, 2018). Gulf War Registry contains the names of Gulf War Veterans in the area and serves as targeted recruitment tool. Without the registry and sufficient personnel to recruit in the community, the team relied on a Gulf War clinic list to identify potential participants.

Recruitment from the clinic list was very tedious because the Gulf War clinic has been inactive for several years, and the information on the list is outdated. To mitigate this problem, a directory service was used to obtain the most current contact information.

Enrollment: To make up for the enrollment shortage encountered during the third quarter, the team plans to increase the subsequent enrollment by 1-2 patients (change enrollment target from 11 to 12 participants) each quarter. The fourth quarter enrollment goal was met, and 11 participants were enrolled. An additional 2 participants were scheduled during the fourth quarter, but the patients rescheduled due to illness.

Changes that had a significant impact on expenditures

There were no significant changes affecting expenditures. The delay in hiring staff reduced the expenditures during the first year. The remaining funds are sufficient to increase staff time to accelerate the data collection process during the next reporting period.

Significant changes in use or care of human subjects

Nothing to Report.

Significant changes in use of biohazards and/or select agents

Not applicable.

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

Publications, conference papers, and presentations

Nothing to Report.

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.

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:	Ricardo Jorge, MD
Project Role:	Principal Investigator
Nearest person month worked:	2.4
Contribution to Project:	Dr. Jorge oversaw all aspects of the research protocol. He negotiated hiring of personnel and managed other financial aspects of the study, submitted regulatory documents for approval, reviewed SOPs, and assessed patients in the study.

Name:	Marco Marcelli, MD
Project Role:	Co-Investigator
Nearest person month worked:	0.6
Contribution to Project:	Dr. Marcelli supervised dynamic testing of all hormonal axes. He is also responsible for the quality and safety of the procedures, evaluating adverse events, and interpreting endocrine test results. Dr. Marcelli contacted patients whose laboratory results were out of range

Name:	Lea Steele, PhD
Project Role:	Co-Investigator
Nearest person month worked:	0.6
Contribution to Project:	Dr. Steele trained provided the materials and trained the team on case/control ascertainment. She edited recruitment materials (patient letter and flyer), guided team on Gulf War Registry access, and helped team come up with recruitment strategies.

Name:	Kankana Chava
Project Role:	Research Nurse
Nearest person month worked:	2.4
Contribution to Project:	Ms. Chava set-up account with laboratory and courier service to transfer specimens, scheduled participant endocrine visits, collected, processed, and submitted blood samples for analysis, and entered study visit notes in patient record.

Name:	Audri Villalon
Project Role:	Coordinator
Nearest person month worked:	2.4
Contribution to Project:	Ms. Villalon developed case report forms, study logs, and SOPs for the project, assisted PI with reports and regulatory requirements (e.g., submitting amendments, as needed), and ordered study materials.
Funding Source:	Unfunded

Name:	Jeanie Hendrickson
Project Role:	Research Coordinator
Nearest person month worked:	2.1
Contribution to Project:	Ms. Hendrickson has worked on recruitment, screening candidates over phone, and scheduling appointments. She has consented participants, administered neuropsychological assessments and questionnaires, and processed payments for participants.

Name:	Mohamed Elammari
Project Role:	Graduate Research Assistant
Nearest person month worked:	2.7
Contribution to Project:	Mr. Elammari reviewed Gulf War Clinic List and Gulf War Registry to identify participants eligible for the study. He assists with mailing recruitment letters to candidates, medical record reviews, and endocrine specimen processing, as needed.

Name:	Sangeeth Jeevan
Project Role:	Research Coordinator
Nearest person month worked:	1.5
Contribution to Project:	Mr. Jeevan administered (and trained new personnel on the administration of) neuropsychological assessments and data collection. He also programmed Qualtrics (the platform used to administer questionnaires) and handled other administrative tasks, such as preparing materials for appointments.
Funding Source:	Unfunded

Name:	Ruosha Li
Project Role:	Biostatistician
Nearest person month worked:	1.2
Contribution to Project:	Dr. Li reviewed determined how to code the variables in the study and guided the design of the database 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?

Ricardo Jorge
New: Defining Biotypes of PTSD with resting-state connectivity project funded.
Role: Co-Investigator. Supporting agency: VA CSR&D Merit Review Project Number. No overlap.

Lea Steele
Ended: Understanding Gulf War Illness: An Integrative Modeling Approach
New:

- Assessment of MRI-Based Marker of Dopaminergic Integrity as a Biological Indicator of Gulf War Illness. Supporting agency: CDMRP. No overlap.
- Brain-Immune Interactions as the Basis of Gulf War Illness: Gulf War Illness Consortium (GWIC). Supporting agency: CDMRP. No overlap.
- Examination of Plasma PON1 Paraoxonase Activity and Genotype in Gulf War Veterans. Supporting agency: CDMRP. No overlap.
- Glutamate Receptor and Kynurenine Pathway Functioning in the Pathobiology of Gulf War Illness. Supporting agency: CDMRP. No overlap.
- Investigating Gene-Environment Interactions in Multiple Cohorts of 1990-91 Gulf War Veterans. Supporting agency: CDMRP. No overlap.
- Gulf Coast Center for Precision Environmental Health (GC-CPEH). NIH. No overlap.

Ruosha Li
Ended: Prehospital Rescuscitation On Helicopter Study
New: Modeling and Validation for Tackling Risk Prediction with Competing Risks by Integrating Multiple Longitudinal Biomarkers. Supporting agency: NIH/NIDDK. No overlap.

What other organizations were involved as partners?

Nothing to Report.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: N/A

QUAD CHARTS: N/A

9. APPENDICES:

Ricardo E. Jorge, MD

Recent, Current and Pending Support

ACTIVE

Title: Translational Research Center for TBI and Stress Disorders (TRACTS) Houston (B9268-X)
Supporting Agency: Department of Veteran Affairs
Agency Contracting/Grant Officer: Diana Nieto (Tel. 713-794-7920, email: Nieto.diana@va.gov)
Performance Period: 01/01/2015 - 06/30/2019
Level of Funding:
Time Commitment: 6.0 person months
Project goal: The Translational Research Center for TBI and Stress Disorders or TRACTS, originated at VA Boston Healthcare System, is developing a well characterized cohort of OIF/OEF/OND veterans needed to study how TBI impacts the evaluation and treatment of individuals who carry multiple physical and psychological diagnoses. TRACTS built a strong and well-- defined organizational structure that represents all core elements of the assessment program, including medical and genetic information, structural and functional neuroimaging, clinical, neuropsychological characterization, as well as state of the art data management tools.
Project role: PI
Potential Overlap: There is no overlap

Title: One-Day Life Skills Workshop for Veterans with TBI, Pain, and Psychopathology
Supporting Agency: RR&D Small Projects in Rehabilitation Research (SPIRE)
Agency Contracting / Grant Officer: Diana Nieto (Tel. 713-794-7920, email: Nieto.diana@va.gov)
PI: Lilian Dindo, PhD & Ricardo Jorge MD
Period of Performance: 10/01/2016 - 09/30/2018
Level of Funding:

Project goal: The aim of this proposal is to develop, refine, and evaluate a 1--day trans--diagnostic (i.e., applies to more than one diagnosis) "life skills workshop" to help Veterans develop skills needed to pursue valued goals in the face of life's challenges.
Project role: Mentor
Potential Overlap: There is no overlap

Title: Persistent Hormonal Changes in Veterans with Gulf War Illness
Supporting agency: Department of Defense/CDMRP
Name/contact info agency's procuring Contracting/Grant Officer: Janet Kuhns (Tel. 301-619-2827, email janet.p.kuhns.civ@mail.mil); CDMRP GWIRP Science Officer: Brett Chaney (Tel. 301-619-7511, email. brett.l.chaney.ctr@mail.mil)
Time commitment: 2.4-person months
Performance period: 09/30/2017 – 09/29/2020
Level of Funding:
Project goal: The proposed study will provide a comprehensive assessment of major pituitary hormonal systems in Gulf War veterans, with emphasis on the growth hormone (GH) axis and concurrent evaluation of gonadotropin axes, thyroid hormone axis, and HPA axis. Hormone measures in veterans with GWI will be compared to those of healthy Gulf War veteran controls, with additional evaluations to determine possible differences in endocrine measures in relation to GWI subgroups and experiences and exposures during the Gulf War.
PI: Ricardo Jorge, MD (Gulf War Illness Research Program: New Investigator)

Title: Defining Biotypes of PTSD with resting-state connectivity
Supporting agency: VA CSR&D Merit Review Project Number I01CX001653
Time commitment: 0.5 calendar months
PI: Michael Esterman
Performance period: 10/3/12017 – 09/30/2021
Level of Funding:
Project goal: The overarching goal of this proposal is to use brain imaging to discover subtypes (biotypes) of PTSD that can be identified in individual Veterans' brains. Discovery of these subtypes could lead to treatment development and better prediction of treatment outcomes. These methods are not only applicable to PTSD, but could be used to better understand other mental health problems.
Project role: Co-Investigator
Overlap: There is no overlap.

Past 5 Years
Title: Rivastigmine Patch in Veterans with Cognitive Impairment following TBI (RIVET)
Project goal: This is Multicenter Trial examining the efficacy of a cholinesterase inhibitor (rivastigmine) to remediate memory deficits and improve quality of life among veterans with a history of TBI. CX000239 (CCTA #0001) (Brawman-Mintzer)
Supporting Agency: VA-ORD
Period of Performance: 07/01/2012 - 09/30/2016
Project role: Site PI

Title: Pilot Study of Growth Hormone Deficiency in Veterans with Mild TBI
Project goal: This is a pilot study to determine the endocrinological, neurocognitive, and neuropsychiatric correlated of growth hormone deficiency among OIF/OEF/OND Veterans with a history of mild TBI.
Supporting Agency: Michael E. DeBakey VA Medical Center (MEDVAMC)
Performance of Performance: 03/01/2014 – 09/01/2015
Project role: PI Ricardo Jorge and Jose Manuel Garcia

Title: Treatment of Alcohol Use Disorders in Veterans with TBI
Project goal: This is a phase 2 randomized clinical trial comparing the efficacy of valproate versus naltrexone to prevent relapse among Veterans with alcohol use disorders. In addition, we investigated whether a history of TBI, as well structural and metabolic alterations of the prefrontal cortex and basal ganglia have a moderator effect on treatment response.
Supporting Agency: Veterans Administration – ORD (Merit Research Award)
Performance Period: 05/01/2011-06/01/2015
Project role: PI

Title: Neuro-rehabilitation: Neurons to Networks HFP90-020 (N:N2N) Center of Excellence
Project goal: This was developed by Dr. Harvey Levin in 2009 to study the epidemiology, genetic determinants, neurocognitive correlates, as well as, multimodal neuroimaging findings of military TBI. It resulted in the integration of its resources into the Chronic Effects of Neurotrauma Consortium (CENC).
Project role: Medical Director and Co-PI (2013)
Period of Performance: 07/01/2009 - 06/30/2014

Title: Treatment Strategy to Prevent Mood Disorders Following TBI
Project goal: This is a phase 2 randomized clinical trial testing the efficacy of sertraline versus placebo to prevent the onset of depression during the first 6 months following TBI. In addition, it examined the effect of SSRIs on cognitive recovery following TBI. Supporting agency: NIH, NIMH / R01 NS055827

Period of Performance: 02/01/2008 - 04/01/2014
Project role: Principal Investigator

PENDING
Title: Translational Research Center for TBI and Stress Disorders (TRACTS) Houston (B9268-X)
Supporting Agency: Department of Veteran Affairs
Agency Contracting/Grant Officer: Diana Nieto (Tel. 713-794-7920, email: Nieto.diana@va.gov)
Performance Period: 07/01/2019 - 06/30/2024
Level of Funding:
Time Commitment: 6.0-person months
Renewal of the Center mentioned Above. No Overlap

Title: Multisite RCT of STEP-Home: A Skill Based Community Reintegration Program
ID1 RX002907-01A1 VA RR&D
PI: Catherine B. Fortier PhD & Ricardo Jorge MD (Houston PI)
Dates of Funding: 04/01/2019-03/31/2023
Total Direct Costs:
Houston Direct Costs:
This RCT examines the efficacy of an integrated rehabilitation program designed to address the most frequent morbidities affecting OIF/OEF/OND Veterans: TBI, PTSD and chronic pain.

Lea Steele, Ph.D.
Other Support | October 2018

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1. Title: Assessment of Diverse Biological Indicators in Gulf War Illness: Are they Replicable? Are They Related?
Role: PI
Time commitment: 10%
Supporting agency: Department of Defense/CDMRP
Performance period: 9/1/2016 – 8/31/2019
DOD #: W81XWH-11-1-0812
CDMRP Log #: GW100068
Brief description of study objectives: This project will determine whether diverse previously-identified findings associated with Gulf War illness (GWI) can be replicated in a single, well-characterized sample of veterans, and the extent to which those findings are associated with one another. The study will compare GWI cases to veteran controls using brain imaging, neuropsychological testing, psychiatric assessments, and evaluation of neuroendocrine (dexamethasone suppression test) function, immune parameters, and the coagulation cascade.

2. Title: Assessment of MRI-Based Marker of Dopaminergic Integrity as a Biological Indicator of Gulf War Illness
Primary award currently being transferred to Baylor College of Medicine
PI: Deborah Little, Ph.D.
Role: Co-I
Time commitment: 5%
Supporting agency: Department of Defense/CDMRP
Performance period: 10/01/2017 – 9/30/2019
CDMRP Log #: GW130063
Brief description of study objectives: This project will leverage existing brain imaging data from a well-characterized sample of 1990-91 Gulf War veterans to assess brain structures and processes of high interest for understanding GWI, but not previously studied in ill Gulf War veterans. This includes an in-depth, detailed analysis of the integrity of the corticostriatal circuit using high resolution diffusion imaging. Investigators will use cutting edge applications of existing imaging tools to provide information on the microstructure within these regions.

3. Title: Brain-Immune Interactions as the Basis of Gulf War Illness: Gulf War Illness Consortium (GWIC)
Multisite consortium grant to Boston University Medical Campus; PI: Kim Sullivan, Ph.D.
Role: Co-I (Texas Site PI)
Time commitment: 25%
Supporting agency: Department of Defense/CDMRP (via subaward from Boston University)
Performance period: 10/1/2013 – 9/29/19 [pending final approval of no cost extension]
CDMRP Log #: GW120037
Brief description of consortium objectives: This multisite consortium will undertake a coordinated series of clinical and preclinical studies aimed at providing a comprehensive understanding of the pathobiology of GWI. This will include clinical studies conducted in parallel at three sites (Boston, Miami, and Central Texas). Parallel preclinical studies will evaluate persistent effects of GW neurotoxicants *in vitro* and in rodent models of GWI. Findings from clinical and preclinical studies will be compared and used to identify specific brain-immune pathways that can be targeted for treatment intervention.

4. Title: Examination of Plasma PON1 Paraoxonase Activity and Genotype in Gulf War Veterans
Primary award to Northern CA institute for Research and Education (NCIRE)
Role: Co-I
Time commitment: 5% Year 1, 10% Year 2, 10% Year 3
Supporting agency: Department of Defense/CDMRP (via subaward from NCIRE)
Performance period: 9/01/16 – 8/31/19
CDMRP Log #: GW150037
Brief description of study objectives: This study will evaluate the extent to which interactions between paraoxonase (PON1) and Gulf War (GW)-related exposures contributed to the risk for developing Gulf War Illness (GWI) in a large (>800) sample of GW veterans. The project leverages existing PON1 paraoxon activity and PON1192 genotype data and GW-related exposure data in 4 independent cohorts of GW veterans.

5. Title: Persistent Hormonal Changes in Gulf War Veterans
Role: Co-I; PI: Ricardo Jorge, MD, Baylor College of Medicine
Time commitment: 5% Y1-2, 10% Y3.
Supporting agency: Department of Defense/CDMRP
Performance period: 9/30/2017 – 9/29/2020
CDMRP Log #: GW160106
Brief description of study objectives: This study will assess the association of GWI with dysregulation of the major pituitary hormonal systems: the growth hormone (GH) axis, gonadotropin axes, thyroid hormone axis, and HPA axis. Hormone measures in veterans with GWI will be compared to those of healthy Gulf War veteran controls. Additional analyses will evaluate endocrine measures in relation to neurocognitive function and in veteran subgroups defined by symptom severity and deployment experiences.

6. Title: **Glutamate Receptor and Kynurenine Pathway Functioning in the Pathobiology of Gulf War Illness**.
Role: Co-I; PI: Marijn Lijffijt, PhD, Baylor College of Medicine
Time commitment: 2.5% Y1-2, 5% Y3.
Supporting agency: Department of Defense/CDMRP
Performance period: 9/30/2017 – 9/29/2020
CDMRP Log #: GW160077
Brief description of study objectives: A major goal of this project is to test neuroinflammatory pathways and NMDA receptor functioning in a well-characterized group of 1990-1991 Gulf War veterans. Exploratory analyses will test interrelationships among biomarkers obtained in cerebrospinal fluid, and NMDA receptor functioning using a challenge with NMDA receptor antagonist ketamine.

7. Title: Investigating Gene-Environment Interactions in Multiple Cohorts of 1990-91 Gulf War Veterans
Primary award to Boston University; PI: Patricia Janulewicz Loyd, PhD
Role: Co-I
Time commitment: 0% Y1, 2.5% Y2-3.
Supporting agency: Department of Defense/CDMRP (via subaward from Boston University)
Performance period: 9/01/17 – 8/31/20
CDMRP Log #: GW160013
Brief description of study objectives: This case-control study will investigate genetic-exposure interactions (BCHE genotype and PON1 status) and the risk of developing GWI using 4 separate cohorts of 1990-1991 Gulf War veterans. This will clarify the extent to which predisposing factors lead to some GW veterans getting sick while others with similar deployment exposures remained healthy.

8. Title: Gulf Coast Center for Precision Environmental Health (GC-CPEH)
Primary award to Baylor College of Medicine; PI: Cheryl Walker, PhD
Role: Co-I
Time commitment: 5%
Supporting agency: NIH/National Institute of Environmental Health Sciences
Performance period: award notice August 2018, est. performance period: 4/2019-4/2024
Brief description of study objectives: This NIEHS P30 award will establish the multi-institutional and multidisciplinary Gulf Coast Center for Precision Environmental Health. The GC-CPEH will provide the resources, expertise, and infrastructure to develop and support impactful environmental health research in the region, including mechanisms for community outreach and education concerning environmental health issues relevant to target constituencies in the Gulf Coast region. This includes development of a Military Exposures and Health resource for military personnel and veterans in the Gulf Coast region.

UTHealth | School of Public Health
The University of Texas Health Science Center at Houston

Ruosha Li, PhD

Active

Title: Dynamic Prediction of Time to Next Failure Event
Supporting agency: NSF
Name/contact info of agency's procuring Contracting/Grants Officer: Nandini Kannan (nakannan@nsf.gov)
Performance Period: 9/1/2016-8/31/2019
Level of effort (in percentage or calendar months): 1.0 cal. Month (8.3% FTE)
Brief description of project goals: This project focuses on the development of novel statistical methods to conduct dynamic prediction of disease outcomes, on the basis of patients' post-baseline longitudinal biomarker trajectories.
PI: Xuelin Huang, PhD. Ruosha Li, PhD.
Role: co-PI.
Potential Overlap: no-overlap

Title: Persistent Hormonal Changes in Veterans with Gulf War Illness
Supporting agency: Department of Defense/CDMRP
Name/contact info agency's procuring Contracting/Grant Officer: Janet Kuhns (Tel. 301-619-2827, email janet.p.kuhns.civ@mail.mil); CDMRP GWIRP Science Officer: Brett Chaney (Tel. 301-619-7511, email. brett.l.chaney.ctr@mail.mil)
Time commitment: 1.2 person months
Performance period: 09/30/2017 – 09/29/2020
Level of Funding:
Project goal: The proposed study will provide a comprehensive assessment of major pituitary hormonal systems in Gulf War veterans, with emphasis on the growth hormone (GH) axis and concurrent evaluation of gonadotropin axes, thyroid hormone axis, and HPA axis. Hormone measures in veterans with GWI will be compared to those of healthy Gulf War veteran controls, with additional evaluations to determine possible differences in endocrine measures in relation to GWI subgroups and experiences and exposures during the Gulf War.
PI: Ricardo Jorge, MD (Gulf War Illness Research Program: New Investigator)
Role: Co-I (statistician)

Title: Modeling and Validation for Tackling Risk Prediction with Competing Risks by Integrating Multiple Longitudinal Biomarkers
Supporting agency: NIH/NIDDK
Name/contact info agency's procuring Contracting/Grant Officer: Sherker, Averell H (averell.sherker@nih.gov)
Time commitment: 3.0 person months
Performance period: 06/19/2018– 04/30/2022
Level of Funding:
Project goal: The proposed study will develop modeling, validation and inference procedures to handle

competing risks data with multiple longitudinal biomarkers. The proposed statistical methods will be applied to a registry study on pediatric acute liver failure (PALF), to develop and validate a prediction tool.
PI: Ruosha Li, PhD
Role: PI
Potential Overlap: no-overlap

Pending

Title: Statistical methods for regression modeling of global percentile outcome in neurological diseases
Supporting agency: NIH/NINDS
Name/contact info of agency's procuring Contracting/Grants Officer: ADENIYI, OLAMIDE A (olokool@mail.nih.gov)
Performance Period: 04/01/2019-- 03/31/2021
Level of effort (in percentage or calendar months): 1.3 calendar month
Brief description of project goals: The proposed study will develop novel statistical methods to achieve regression modeling of the global percentile outcome, for both cross-sectional and longitudinal data. The proposed methods will be applied to existing datasets from two neurological clinical trials.
PI: Ruosha Li
Level of funding:
Role: PI
Potential Overlap: no-overlap

Previous (Past 5 years)

Title: Prehospital Rescuscitation On Helicopter Study
Supporting agency: University of Washington / NIH
Name/contact info of agency's procuring Contracting/Grants Officer: Vivian Sun vivsun@uw.edu
Performance Period: 4/15/2017-12/31/2017
Level of effort (in percentage or calendar months): 20% FTE
Brief description of project goals: The Prehospital Resuscitation On Helicopter Study (PROHS) is a pragmatic, multicenter, prospective observational study of air ambulance-based prehospital resuscitation regimens currently utilized at the participating sites. Patients will be enrolled at participating sites that currently have blood products available on air ambulances and other sites that do not.
PI: John B. Holcomb
Role: co-investigator
Potential Overlap: no-overlap

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Ruosha Li, PhD

Title of award/support: PARKINSON'S DISEASE CLINICAL TRIAL: STATISTICAL CENTER
Supporting Agency: NIH/ NINDS
Name/contact info of agency's procuring Contracting/Grants Officer: MOY, CLAUDIA S (moyc@ninds.nih.gov)
Performance Period: Dec 2014—Nov 2016
Level of effort (in percentage or calendar months): 21% FTE
Brief description of project goals: Provide statistical support to the NINDS Exploratory Trials in Parkinson's disease (NET-PD) network.
PI: Barbara Tilley, PhD and Sheng Luo, PhD.
Role: co-investigator

Title of award/support: HEPATITIS B RESEARCH NETWORK - DATA COORDINATION CENTER
Supporting Agency: NIH/NIDDK
Name/contact info of agency's procuring Contracting/Grants Officer: DOO, EDWARD (dooe@niddk.nih.gov)
Performance Period: Aug 2011—Nov 2014
Level of effort (in percentage or calendar months: 40% FTE
Brief description of project goals: DCC works with the HBRN members to support all aspects of study design, study conduct, and data analysis for the various studies. In collaboration with HBRN personnel, we developed data collection instruments and processes to facilitate collecting complete and accurate data.
PI: Belle, Steven H.
Role: Statistician

Title of award/support: PHASE III TRIAL OF POCKET PATH: A COMPUTERIZED INTERVENTION TO PROMOTE SELF-CARE
Supporting Agency: NIH/ NATIONAL INSTITUTE OF NURSING RESEARCH
Name/contact info of agency's procuring Contracting/Grants Officer: TULLY, LOIS (tullyla@mail.nih.gov)
Performance Period: May 2012-Apr 2014
Level of effort (in percentage or calendar months): 10% FTE
Brief description of project goals: The purpose of this proposed phase III is to compare the efficacy of a novel intervention, Pocket PATH (Personal Assistant for Tracking Health) for promoting self-care and improving health outcomes relative to standard care after lung transplantation.
PI: DE VITO DABBS, ANNETTE J
Role: co-investigator

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Ruosha Li, PhD

Title of award/support: A MULTI-CENTER GROUP TO STUDY ACUTE LIVER FAILURE IN CHILDREN
Supporting Agency: NIH/NIDDK
Name/contact info of agency's procuring Contracting/Grants Officer: SHERKER, AVERELL (averell.sherker@nih.gov)
Performance Period: 2013- Nov 2014
Level of effort (in percentage or calendar months: 10% FTE
Brief description of project goals: The goal is to improve short- and long-term outcomes for pediatric acute liver failure (PALF) through a better understanding of patient phenotypes, reassessment of risk classifications, and associating early events to outcome at one year.
PI: Squires, Robert
Role: Statistician

Safety Monitor Report
10/24/18

IRB Protocol Number	H-41120
Title	Persistent Hormonal Changes in Veterans with Gulf War Illness
Principal Investigator (PI)	Ricardo Jorge, MD
Study Sponsor	DoD
Proposal Number	GW160106
Award Number	W81XWH-17-1-0368
HRPO Log Number	A-20301.a and A-20301.b

Independent Safety Monitor:
Sanjay Mediwala, MD
Board Certified Endocrinologist
Michael E. DeBakey VA Medical Center

H-41120 Summary

Year 1 Quarter 1 (Oct 2017 – Dec 2017)

No patients were enrolled during the first quarter.

Year 1 Quarter 2 (Jan 2018 – Mar 2018)

No patients were enrolled during the first quarter.

Year 1 Quarter 3 (April 2018 – June 2018)

# of patients enrolled during this quarter:	2
# who completed endocrine tests:	1
# of patients with AE:	0
# of patients with UPIRTSO:	0

Year 1 Quarter 4 (July 2018 – Sept 2018)

# of patients enrolled during this quarter:	11
# who completed endocrine tests:	8
# of patients with AE:	1
# of patients with UPIRTSO:	0

Protocol Evaluation

The purpose of this study is to assess hormonal dysregulation in Gulf War veterans and evaluate the association of Gulf War Illness in major hormonal systems. The dynamic tests used in this study (Glucagon Stimulation Test for growth hormone deficiency and the ACTH stimulation test for adrenal insufficiency) are routine endocrine tests. The testing protocol used in this study is consistent with clinical guidelines and standard publications.

The risks of adverse events (AE) from stimulation tests in Gulf War veterans is the same as general population.

Adverse Events

Of the nine patients who underwent testing, one patient reported nausea and chills. The symptoms were mild in nature and present before endocrine testing began. The patient vomited one time during the adrenal insufficiency stimulation test and reported feeling better after he vomited. Dr. Marcelli, endocrinologist on this protocol, evaluated the patient. The research nurse monitored the patient. The patient was allowed to leave the room once the symptoms resolved.

Reporting Requirements

Reporting requirements met. The AE was documented in the patient's study folder and reviewed by the endocrinologist and PI. The event does not require IRB reporting since it is not a serious adverse event nor unanticipated problem.

Unanticipated Problems Involving Risk to Subjects or Others (UPIRTSO)

There were no unanticipated problems (in terms of nature, severity, or frequency) involving risks to subjects or others. There is no new literature or findings suggesting that the research places subjects or others at greater risk of harm than was previously known or recognized.

Sanjay K Wadhwa MD.