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VOLUME XX Fall 2023

Focus on Research

Aiming to Put Traumatic Nightmares to Rest

Long after their military service ends, many Veterans with post-traumatic stress disorder (PTSD) are haunted by nightmares.

These are not just bad dreams. Post-traumatic nightmares can lead to insomnia and impaired functioning during waking hours, and they can cause severe episodes of panic, anxiety, and depression. Studies have found that nightmares may pose a risk factor for suicide.

Of Veterans with PTSD, 71 to 96 percent may have nightmares, according to the U.S. Department of Veterans Affairs. While sleep disorders and disturbances are common among military personnel and Veterans, much less is understood about nightmares in this population.

“Our Department of Defense-funded research demonstrates that the experience of nightmares is highly variable,” said Anne Richards, MD, MPH, an NCIRE-supported clinician-scientist who focuses on sleep physiology underlying trauma nightmares. “They also wax and wane in frequency and severity for reasons that are not clear.”

“Accurate reporting of nightmares and their content is also clouded by the amnesic effects of sleep, drowsiness, and fatigue on memory,” said Richards, a Clinical Professor in the Department of Psychiatry and Behavioral Sciences and the UCSF Weill Institute for Neurosciences, and Staff Psychiatrist in the PTSD program at the San Francisco VA Health Care System (SFVAHCS).

“With these caveats in mind, nightmares may be



Anne Richards, MD, MPH

*Clinical Professor, Department of Psychiatry and Behavioral Sciences,
UCSF Weill Institute for Neurosciences*

*Staff Psychiatrist, PTSD Program,
San Francisco VA Health Care System*

*Director, Richards Lab
Stress and Health Research Program,
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recalled as exact replays of traumatic experiences or may not seem to have any resemblance to actual lived experiences. Nightmares may go on for years for some, may wax and wane for others, or may occur initially after recent trauma and gradually remit,” she said.

Commitment to stress, trauma research

Richards’ interest in PTSD is rooted in her public

health work, which started two decades ago working with refugees and individuals displaced by armed conflict. During her UCSF psychiatry residency in 2007, she conducted a study in Colombia, a country that was torn apart for many decades by armed conflict.

“At the same time in my training, I started to work at the San Francisco VA Health Care System and realized that I was in an outstanding location to learn about and study the ravages of armed conflict, through a different lens and with a different population,” said Richards.

In her years at the SFVAHCS, Richards has developed expertise in treating male and female Veterans with PTSD and sleep disorders using psychotherapy and medications. Nightmares were a common struggle among her patients.

“Nightmares that manifest in the form of a recurrent, sleep-dependent replay of trauma memories are a fascinating phenomenon with serious clinical implications,” Richards said. “That motivated my interest in understanding the neural processes involved in the consolidation of stressful memories and their replay during sleep, and my interest in developing targeted treatments to eliminate nightmares.”

Combining clinical and laboratory

In 2015—with a VA Career Development Award—Richards shifted from a predominantly clinical role to one with more of a laboratory research lead. Her UCSF lab, where Richards is the Principal Investigator, employs various tools to study PTSD, sleep, and a patient’s physiology. This includes self-reported surveys, a sleep diary mobile app developed by her research team, clinician-administered interviews, video recordings of sleep, cognitive testing, and scalp EEG collected during both sleep and wake neuroscience-based experimental tasks.

Her team conducts research both remotely—by sending measurement devices to participants’ homes—and in person.

“My clinical and scientific interests inform each other,” said Richards. “When I perform clinical treatment research, I am deeply interested in understanding mechanisms through which treatments work. In my observational studies, I seek to understand both the physiology and psychology underlying a behavior. And in my laboratory work, I seek to ensure the translatability of the phenomena observed in the lab to clinically relevant experiences and behaviors.”

The depth and breadth of Richards' research

A key goal of Richards’ research is to better understand the role of sleep in emotional memory processing. “This refers to what the brain does with emotionally salient information,” she said. “We are typically referring to negative emotional information, since that is the type of information that we expect to have negative effects on how a person feels.”

“In real life, we are interested in understanding the brain processes through which life events—such as experienced or witnessed traumatic events—affect people,” said Richards. “One way to study this in controlled laboratory experiments is to expose study participants to visually distressing images, films, or other laboratory stressors and to study reactions to and memory for those images, films or stressors in different contexts to see how context affects emotional reactions and memory.

“For example, after exposure one might assign one group to sleep with a medication and another group to sleep without a medication, to see how things change after sleep, versus without the medication,” she said. “One might also go deeper to determine what aspects of the brain’s physiology are different in the medicated vs. non-medicated group. That would explain the differences in post-sleep reactions and memory. This is just one example of how emotional information processing might be studied.”

While Richards’ research mainly targets Veterans with PTSD—and the large majority of study participants are Veterans—her team’s research is highly applicable to the general population. “While the stress of combat is unique and very fortunately only experienced by a limited segment of our population, exposure to adversity and stress is ubiquitous,” she said.

Still, her devotion is indeed to Veterans. “My experiences at the San Francisco VA Health Care System, during residency training and beyond, gave me a more intimate window into the Veteran’s experience, especially with respect to the traumatic life stressors and adversity that combat and non-combat Veterans have been exposed to,” said Richards.

“It is really an honor to be able to support the Veterans I work with in their path of healing. I continue to be blown away by the courage and resilience this extremely diverse group of individuals displays; and I have learned and continue to learn so profoundly from them.”

Current studies by The Richards Lab

The following are examples of the depth and breadth of the Richards's lab's work:

In a study of 45 Veterans who had experienced combat or noncombat trauma, Richards' team showed that sleep spindles—brief bursts of brain activity during one phase of sleep captured by EEG—may regulate anxiety in people with PTSD.

The study, "Sleep Spindles Favor Emotion Regulation Over Memory Consolidation of Stressors in Posttraumatic Stress Disorder", published in May of 2023 in the journal *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, challenged recent work by other researchers that has indicated spindles may heighten intrusive and violent thoughts in people with PTSD.

"These findings may be meaningful not only for people with PTSD, but possibly for those with anxiety disorders," said Richards. "There are non-invasive ways that might harness the benefits of this sleep stage to provide relief from symptoms."

Prescription drugs and electrical brain stimulation are possible treatment options that can induce the positive effects of spindles.

The researchers' next laboratory project is to study the role of spindles in the consolidation and sleep replay of intrusive and violent memories after stress exposure.

The Richards Lab aims to study well-established medications repurposed for use in PTSD and sleep disturbances. The lab currently is conducting a clinical trial to test the effect of doxazosin, an FDA-approved medication, on symptoms of PTSD, including distressing dreams. Participants complete seven nights of home sleep monitoring and then receive doxazosin or matching placebo (sugar pill) for 8 weeks. During that time, participants are closely monitored by a study physician or nurse practitioner.

The team is studying a variant of psychotherapy called narrative-based imagery rehearsal therapy (N-IRT) as a treatment for nightmares in Veterans. N-IRT, which is also called nightmare rescripting, entails choosing a recurring nightmare and picking—or rescripting—the content to make it less intense or distressing. "We believe it's a promising strategy," said Richards.

Distressing Dream Reporting and Effective Ambulatory Measurement of Sleep (DDREAMS)

Sponsored by the U.S. Department of Defense, the Richards Lab is currently conducting a sleep study for those experiencing PTSD.

The goal of this study is to use several approaches to understand sleep disturbance in PTSD. We seek to understand the biology of nightmares, nightmare enactment, and sleep-related violent behaviors and factors that contribute to these problems.

Eligible participants will complete a sleep diary mobile app and wear a motion sensing wristband for 3 weeks. Participants may be eligible for a second part of the study involving several devices to measure their sleep at home. Participants will be compensated for their time with up to \$509 for completion of the study.

Bed partners of participating individuals may also be eligible to participate.

For more information, contact DDREAMSstudy@ncire.org or (415) 221-4810 x25844.

REST Study

Also sponsored by the U.S. Department of Defense, this clinical trial is testing the effect of doxazosin, an FDA-approved medication, on symptoms of Post-traumatic Stress Disorder including distressing dreams. Participants will complete seven nights of home sleep monitoring and then receive doxazosin or matching placebo (sugar pill) for 8 weeks. During that time, participants will be closely monitored by the study physician or nurse practitioner.

You may qualify if you are a Veteran between the ages of 18 and 75 with symptoms including upsetting dreams or sleep difficulties following a life threatening event. Please know that you may qualify even if you have never been diagnosed with PTSD.

Compensation for completing the study is up to \$530.

For more information, contact RESTstudy@ncire.org or (415) 221-4810 x23809.

The Richards Lab is located at the San Francisco VA Health Care System in San Francisco, California. Both studies can be completed remotely.

Q and A: An Interview with Dr. Neal Yuan

Q: Please tell us about your research.

A: As a general cardiologist and Director of our cardiac rehabilitation program, one of my main clinical interests is preventive cardiology, which involves helping patients lower their cardiovascular disease risk factors (high blood pressure, high cholesterol, obesity, etc.).

My current research administered through NCIRE is the VALOR-QI project which stands for Veterans Affairs Lipid Optimization Reimagined (we love our acronyms in cardiology!). It is a quality improvement project in partnership with the American Heart Association that involves several VA sites and aims to explore ways to help Veterans better control their lipids by using health coaching.

Lipid control is a fundamental part of reducing cardiovascular risk; and we have very effective interventions. There are both lifestyle changes (nutrition, exercise, etc.) as well as medications, with statins being some of the best studied drugs in the field of medicine. While science has brought us many interventions for lipid control, we are still trying to catch up on the clinical side. We know what to do, but convincing patients to make lifestyle changes and take recommended medications remains challenging. It often requires significant time, effort, skill, and can often be difficult for clinicians to fit into patient visits.

To help improve patient engagement, in the VALOR-QI study, we have a dedicated health coach. Additionally, with access to VA's electronic health records systems, we plan to identify patients at high cardiovascular



Neal Yuan, MD

Assistant Professor of Medicine, UCSF

Staff Cardiologist, SFVAHCS

Director of Cardiovascular Stress Testing, SFVAHCS

Director of Cardiac Rehabilitation, SFVAHCS

risk who have uncontrolled lipids and then engage with them about their lipid control. Through a combination of education, motivational interviewing, and other strategies aimed at behavior change, we hope to help increase the number of high cardiovascular risk patients who achieve guideline lipid goals.

Q: You have degrees in molecular biology and engineering biology. One might assume with that background, you would concentrate on technology-related areas of cardiology, but you chose general cardiology. Why?

A: I've had a bit of a journey with regards to my research interests; and I am actually still very involved in "tech-inclined" research. I've always been interested in the cross-section between health information technology and medicine; and for the last few years, I have been involved

in several research projects using deep learning of information-dense data (mainly echocardiograms and electrocardiograms) for predicting cardiovascular diseases.

While this research continues to be an interest of mine—and I believe in its long-term promise—I've also felt a desire to connect my research work a bit more intimately to some of the day-to-day challenges that I encounter when seeing my patients in clinic. In most clinics, I have patients who are grappling with weight gain and are exhausted/overwhelmed by their 10+ prescriptions.

Often, I find myself thinking, "I can prescribe as many medications as I want; but if I can't inspire my patients to take those medications reliably and make real changes to unhealthy lifestyle habits, then really, what am I doing?" It's a "last mile" problem, where we've had so much innovation and research that has led to these fantastic medications and our understanding of how to change disease trajectories; but if we can't go that last distance with the patient, then it all becomes moot.

Q: What influenced you to become most interested in these patient-centered issues?

A: Settling into being an attending physician has heightened my awareness of these issues. There's so much to learn in medicine and during the decade of training it takes to become a cardiologist (or other health provider). You spend so much of your time just practicing the illness scripts and diagnostic schema. It becomes easy (and is likely more expedient) to think of patients through the lens of a medical gaze; whereby individuals

become sums of different diagnoses and risk factors become problems to be learned and solved.

While there's always more to learn as an attending physician, I've felt that I'm finally somewhat caught up; and that has given me the space to really step outside of the medicalization framework and think a bit more about each individual's nuances and what high-touch interventions are needed to tune the medical model to better fit the patient.

Q: Why did you choose the VA for research and clinical practice?

A: During residency, I was lucky to have rotated several months on the inpatient medicine service and had my longitudinal primary care clinic here at the San Francisco VA. I was also part of the residency's Program in Residency Investigation Methods (PRIME) program which is based

at the VA. This site has always been a jewel of the UCSF program and is known for its collaborative and supportive environment for learners and researchers.

As someone who came to the field of medicine through global health, I've always wanted to work with underserved populations. Anyone who's cared for our Veterans knows that they are really some of the most wonderful and deserving people. They have borne the brunt of the ill effects of our country's past wars; and these can be lifelong and have really severe health effects. Fortunately, the VA is a great example of some of the successes of having an integrated, single-payer health system.

Q: What are your career and research goals?

A: My goal is simple (although maybe not all that original): to make

a positive meaningful difference in the best ways I feel I can. For me, that is currently through several different avenues and includes first and foremost, being a really good doctor (what I've spent a decade training to do); and also being an educator/enabler for future medical professionals and hopefully putting out research that matters. I'm excited that VALOR-QI will be an opportunity to pursue a research project with a very immediate and tangible clinical impact.

Q: What would most people be surprised to know about you?

A: For those interested in palmistry, I have a simian crease on my left hand which is associated with fetal alcohol syndrome and a number of genetic chromosomal abnormalities. Thankfully, as far as I know, I am totally fine.

In the Helix



Tiffany Murphy

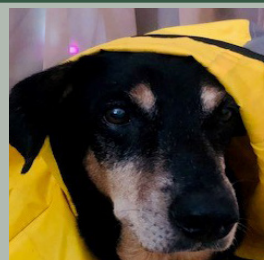
NCIRE Contracts and Grants Specialist II

Q: What is something you love doing? Why?

A: I adore being out in nature, away from the hustle and bustle. Being able to disconnect, listen to birds chirping, as opposed to the ever-present cell phone or incoming email pings, breathes new life into my soul.

Q: If you could be any fictional character, who would you be and why?

A: Jane Jetson! She was always such a stylish mom, loved shopping and was the backbone of her family. I'm most envious however of her deadliest weapon: Rosie! What I wouldn't do to have my very own Rosie to help get me through the days.



Cynthia Huynh, RN

NCIRE Research Nurse

Q: What is something you love doing? Why?

A: I love being a hermit. I love having "Cyn" time—disappear from the world and just be with me, myself and I. This is how I center myself.

Q: If you could be any fictional character, who would you be and why?

A: I don't know, there are so many great characters. But, I wouldn't mind being be our doggie, Cayman. He is so spoiled and cute with so much personality! Sometimes he's more of a toddler than a dog.

If you or someone you know is an NCIRE employee and would like to be featured in *In the Helix*, contact us at dna@ncire.org.

Department Updates

NCIRE Office of Sponsored Research Update

We are pleased to introduce our newest member of NCIRE's Office of Sponsored Research, OSR staff, Ms. Asha Payda, Staff Research Associate III (Clinical Research Coordinator).

Asha fills the newly created clinical research coordinator position within NCIRE's Administrative Core to help fulfill the ever-growing need for an on-site clinical research coordinator to support our research community. She brings decades of research experience from phase I-IV industry sponsored trials to federal clinical trials.

If you are interested in learning more about NCIRE's clinical coordinator services, please contact Newton.Ong@ncire.org for additional information.

Funding Opportunities

Industry Opportunities

Please contact Newton Ong, newton.ong@ncire.org, or Adan Pinedo, adan.pinedo@ncire.org, for further information on the following Industry Opportunities.

GlaxoSmithKline

Phase 3, Randomized, Open-Label Study of Dostarlimab as Sequential Therapy in Patients with Locally Advanced, Unresectable Non-Small Cell Lung Cancer (Stage III) Who Have Not Progressed Following Definitive, Platinum-based, Concurrent Chemoradiation Therapy versus Durvalumab

Horizon Therapeutics

A Phase 4, Open-label Study of KRYSTEXXA® (Pegloticase) Co-administered With Methotrexate (MTX) in Patients With Uncontrolled Gout (FORWARD OL)

Novartis

A Phase II multicenter, open-label, single-arm dose escalation study of Asciminib monotherapy in 2nd and 1st Line Chronic Phase – Chronic Myelogenous Leukemia (ASC2ESCALATE)

Please visit the Office of Sponsored Research page on the NCIRE SharePoint at <https://ncire.sharepoint.com/> or click [here](#) for the full list of Industry Opportunities.

Federal Funding Opportunities

Please contact Jessica Schmidt, jessica.schmidt@ncire.org, for further information on the following Federal Funding Opportunities.

NIH: Research Supplements to Promote Diversity in Health-Related Research (Admin Supp - Clinical Trial Not Allowed) <https://grants.nih.gov/grants/guide/pa-files/PA-21-071.html>

NIH: NEI Translational Research Program for Therapeutics (R61/R33 Clinical Trial Not Allowed) (PAR-23-200) National Eye Institute <https://grants.nih.gov/grants/guide/pa-files/PAR-23-200.html>

- Due Dates for New Applications: February 16, 2024; February 16, 2025

Please visit the Office of Sponsored Research page on the NCIRE SharePoint at <https://ncire.sharepoint.com/> or click [here](#) for the full list of Federal Funding Opportunities.

New Federal Funding Awards

Congratulations to the following Principal Investigators for your recently funded awards!

Theodora Mauro, MD

Project Title: Emollient therapy for improved survival and growth of very low birth weight infants in Zimbabwe
Sponsor: NIH via subcontract from Stanford University
Activation Date: 4/1/2023

Wenhan Chang, PhD

Project Title: Vitamin D and Beta-Amyloid Signaling in Hyperparathyroidism
Sponsor: NIH via subcontract from UCSF
Activation Date: 7/6/2023

Thomas Neylan, MD

Project Title: Investigating Fear System Myelination in PTSD Using In Vivo and Post Mortem Data
Sponsor: NIH
Activation Date: 7/6/2023

Vasanth Jotwani, MD

Project Title: Mitochondrial health, cardiovascular risk, and blood pressure targets in hypertensive adults
Sponsor: NIH (Supplement)
Activation Date: 8/16/2021

Robert Nissenon, PhD

Project Title: Novel Strategies for Understanding and Treating Fibrous Dysplasia
Sponsor: NIH via subcontract from UCSF
Activation Date: 9/12/2023

Sei Lee, MD

Project Title: Prognostic Indices for Hospitalized Older Adults with and without Alzheimer's Disease and Related Dementias
Sponsor: NIH
Activation Date: TBD

Shira Maguen, PhD

Project Title: SCC-CIVIC-FA Track B: Participatory Action Research to Enhance Equity and Prevent Moral

Injury in Community Paramedicine

Sponsor: NSF via subaward from San Jose State University
Activation Date: TBD

Renuka Nayak, MD

Project Title: From here to eternity: gut microbial response to drug therapy and inflammation
Sponsor: NIH
Activation Date: TBD

Alison Rustagi, MD

Project Title: Identifying Older Adults who Benefit from Lung Cancer Screening
Sponsor: NIH
Activation Date: TBD

Irina Strigo, PhD

Project Title: Dynamic Evaluation of Neural Mechanisms for Affective Touch: Pathways for Touch-induced Pleasantness and Pain Modulation
Sponsor: NIH via subcontract from UCSD
Activation Date: TBD

Michael Weiner, MD

Project Title: Blood Biomarker Development and Validation in Chronic Traumatic Encephalopathy and Alzheimer's Disease and Alzheimer's Disease Related Dementias
Sponsor: NIH via subcontract from Boston University
Activation Date: 7/3/2023

Annie Li Wong, RN

Project Title: Feasibility of Project Nurse Lead Social Prescription Program to Decrease Loneliness and Social Isolation in People with Parkinson's Disease
Sponsor: Gerontological Advanced Practice Nurses Association Foundation, Inc.
Activation Date: TBD

New Cooperative Research and Development Agreements (CRADAs)

Congratulations to the following Principal Investigators for your recently signed CRADAs!

James Brown, MD

Brian Feeley, MD

Alexander Monto MD

Kendrick Shunk MD, PhD

Neel Singhal MD, PhD

Elaine Tseng, MD

Arthur Wallace MD, PhD

Sunny Wang MD

Joseph Yang MD

Neal Yuan, MD

Message from the Chief Executive Officer

This publication marks our twentieth volume, quite a milestone! We have a very dedicated committee and a scientific writer who help make the DNA Newsletter possible. I am thankful for their diligent and thoughtful contributions over the past five years. It is our goal to share research and relevant updates to the SFVAHCS Community.

With our 20th volume, we have remarkable contributors for the Fall 2023 Newsletter: Anne Richards, MD, MPH and Neal Yuan, MD. We appreciate the time they have allocated to share details on their research. If you have suggestions for future stories, please contact the DNA Newsletter Committee at dna@ncire.org.

We are approaching fall and I am looking forward to this magical season—the colors and changes in sunrise and sunset are always a marvel to behold.

NCIRE is approaching the end of fiscal year 2023, ending on 9/30/2023. Through the end of December, we will be working to close the 2023 financials, build the fiscal 2024 financial projections/budget, and begin work on the 2023 financial audit.

The 2023 annual NCIRE Principal Investigator and Research Community Satisfaction Survey was completed on June 23, 2023. The response rate was 38%, a bit short of the 50% goal. The full 2023 survey results can be found on the NCIRE SharePoint at <https://ncire.sharepoint.com/> or [here](#). Over the next year, we will continue facilitating and supporting research by providing consistent administrative, technological, and systems support. We will also offer training opportunities for research and grant administration and compliance. We will hold training opportunities at least every quarter that will cover a variety of areas.

Thank you for taking time to read our Fall 2023 Newsletter. Please let me know if you have any questions or comments.



Rebecca Rosales, MBA, CRA
Chief Executive Officer

About NCIRE

NCIRE - The Northern California Institute for Research and Education has one mission and one goal: Advancing Veterans Health. We sustain a scientific community of clinicians and researchers and support nearly 200 researchers who have joint faculty appointments at the University of California, San Francisco (UCSF) and the San Francisco VA Health Care System (SFVAHCS) and are working to foster innovation through leadership in the field of Veterans health research. Our broad portfolio of projects receives generous support from the National Institutes of Health, the Department of Defense, and individual donors, making us the largest nonprofit research institute devoted to Veterans health in the US.

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