

AWARD NUMBER: **W81XWH-14-1-0236**

TITLE: "Hippocampal and Cognitive Function, Exercise, and Ovarian Cancer: A Pilot Study"

PRINCIPAL INVESTIGATOR: Richard Sloan, PhD

CONTRACTING ORGANIZATION: Columbia University  
New York, NY 10032

REPORT DATE: August 2017

TYPE OF REPORT: Annual Report

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

DISTRIBUTION STATEMENT: Approved for Public Release;  
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

# REPORT DOCUMENTATION PAGE

*Form Approved*  
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. **PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.**

<b>1. REPORT DATE</b> August 2017		<b>2. REPORT TYPE</b> Annual		<b>3. DATES COVERED</b> 8/1/16 - 7/31/17	
<b>4. TITLE AND SUBTITLE</b>  "Hippocampal and Cognitive Function, Exercise, and Ovarian Cancer: A Pilot Study"			<b>5a. CONTRACT NUMBER</b>		
			<b>5b. GRANT NUMBER</b> W81XWH-14-1-0236		
			<b>5c. PROGRAM ELEMENT NUMBER</b>		
<b>6. AUTHOR(S)</b> Richard Sloan, PhD  Email: rps7@columbia.edu			<b>5d. PROJECT NUMBER</b>		
			<b>5e. TASK NUMBER</b>		
			<b>5f. WORK UNIT NUMBER</b>		
<b>7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)</b>  Columbia University New York, NY 10032			<b>8. PERFORMING ORGANIZATION REPORT NUMBER</b>		
<b>9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)</b>  U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012			<b>10. SPONSOR / MONITOR'S ACRONYM(S)</b>		
			<b>11. SPONSOR / MONITOR'S REPORT NUMBER(S)</b>		
<b>12. DISTRIBUTION / AVAILABILITY STATEMENT</b>  Approved for Public Release; Distribution Unlimited					
<b>13. SUPPLEMENTARY NOTES</b> n/a					
<b>14. ABSTRACT</b> In this application, we propose to address this problem by focusing primarily on a single post-chemotherapy complaint in a single cancer: problems with memory in patients with ovarian cancer. We focus on this problem for three reasons: 1) according to the Ovarian Cancer National Alliance, memory problems are among the most frequently cited by patients; 2) by narrowly targeting our inquiry, we will avoid the "noise" in the data associated with different treatment regimens and correspondingly different cognitive complaints and; 3) there are decades of neuroscience research, some of it from our group, indicating that memory impairment, such as the kind reported in the context of chemotherapy, is mediated primarily by a region of the brain called the hippocampus. In this application, we propose to investigate the possibility that standard chemotherapy regimen used to treat ovarian cancer leads to memory impairment because it arrests the normal processes of neurogenesis, the growth of new nerve cells, in this brain region. In addition, because a growing body of research studies shows that physical exercise leads to improvement in memory and learning and that exercise targets the same brain regions responsible for chemotherapy-induced memory problems, we propose to conduct a pilot study of an intervention to increase patients' physical activity to test whether this will slow this effect of chemotherapy on nerve cell growth in the hippocampus and subsequently offset memory decline.					
<b>15. SUBJECT TERMS</b>  None listed					
<b>16. SECURITY CLASSIFICATION OF:</b>			<b>17. LIMITATION OF ABSTRACT</b>	<b>18. NUMBER OF PAGES</b>	<b>19a. NAME OF RESPONSIBLE PERSON</b> USAMRMC
<b>a. REPORT</b>	<b>b. ABSTRACT</b>	<b>c. THIS PAGE</b>			<b>19b. TELEPHONE NUMBER</b> (include area code)
Unclassified	Unclassified	Unclassified	Unclassified	22	301-619-7649

## Table of Contents

	<u>Page</u>
<b>1. Introduction...</b>	<b>1</b>
<b>2. Keywords...</b>	<b>1</b>
<b>3. Accomplishments...</b>	<b>1 - 2</b>
<b>4. Impact...</b>	<b>2</b>
<b>5.Changes/Problems.....</b>	<b>2-3</b>
<b>6. Products...</b>	<b>3</b>
<b>7.Participants &amp; Other Collaborating Organizations...</b>	<b>3-4</b>
<b>8.Special Reporting Requirements.....</b>	<b>5</b>
<b>9. Appendices.....</b>	<b>5</b>

## **“Hippocampal and Cognitive Function, Exercise, and Ovarian Cancer: A Pilot Study”**

**Proposal Log Number OC130386**

**Award Number W81XWH-14-1-0236**

**HRPO Log Number A-18125**

**Reporting Period: 8/1/15 – 7/31/16**

### **1 INTRODUCTION:**

*In this application, we propose to address this problem by focusing primarily on a single post-chemotherapy complaint in a single cancer: problems with memory in patients with ovarian cancer. We focus on this problem for three reasons: 1) according to the Ovarian Cancer National Alliance, memory problems are among the most frequently cited by patients; 2) by narrowly targeting our inquiry, we will avoid the “noise” in the data associated with different treatment regimens and correspondingly different cognitive complaints and; 3) there are decades of neuroscience research, some of it from our group, indicating that memory impairment, such as the kind reported in the context of chemotherapy, is mediated primarily by a region of the brain called the hippocampus. In this application, we propose to investigate the possibility that standard chemotherapy regimen used to treat ovarian cancer leads to memory impairment because it arrests the normal processes of neurogenesis, the growth of new nerve cells, in this brain region. In addition, because a growing body of research studies shows that physical exercise leads to improvement in memory and learning and that exercise targets the same brain regions responsible for chemotherapy-induced memory problems, we propose to conduct a pilot study of an intervention to increase patients’ physical activity to test whether this will slow this effect of chemotherapy on nerve cell growth in the hippocampus and subsequently offset memory decline.*

### **2 KEYWORDS:**

*Physical activity interventions, ovarian cancer treatment, chemotherapy-induced cognitive dysfunction*

### **3 ACCOMPLISHMENTS:**

#### **Major Goals/Objectives:**

1. Approval by CUMC Herbert Irving Comprehensive Cancer Center (HICCC) Protocol Review and Monitoring Committee  
Date of Completion: 4/17/14 (100% completed)
- 1A. Approval of HICCC protocol materials by DoD HRPO; Respond to DoD HRPO questions  
100% completed
2. Approval by New York State Psychiatric Institute (NYSPI) Institutional Review Board  
Date of Completion: 5/15/15 (100% completed)
- 2A. Approval of NYSPI IRB materials by DoD HRPO; Respond to DoD HRPO questions  
Date of Completion: June 1, 2015 (100% completed)
3. Training research assistant “coach” in patient recruitment, retention, delivery of walking intervention  
Date of Completion: July 1, 2015 (100% completed)
4. Training research assistant in administration and scoring of neuropsychology tests  
Date of Completion: July 1, 2015 (100% completed)

5. Training research assistant in image analysis

Date of Completion: July 1, 2015 (100% completed)

6. Recruiting 21 ovarian cancer patients 4-6 weeks post-surgery

July 31, 2016: 5% completed

7. Pre- and post-intervention neuropsychology and imaging data collection and scoring

July 31, 2016: 5% completed

8. Delivering the interventions to the two treatment groups

August 1, 2016: 5% completed

9.Data analysis

July 31, 2016: 5% completed

10.Post-Analysis: Submission of findings to national meetings, proposal to DoD or NIH for definitive study (if appropriate)

July 31, 2016: 0% completed

**What was accomplished under these goals?**

*This is a study to assess the feasibility of recruiting ovarian cancer patients in a pilot study to assess the impact of increasing physical activity on neuropsychological and brain imaging outcomes. The principal finding is that due to changing treatment protocols, it is extremely difficult to recruit patients into the study. The original aim of the study was to recruit patients who were naïve to chemotherapy in order to determine whether an activity increasing intervention could influence the neurocognitive effects of chemotherapy. When the study began, the standard treatment approach was to surgically resect the tumor and then begin chemotherapy. Shortly after, however, many OB/GYN oncologists began to recommend neoadjuvant treatment, in which patients were started on chemotherapy to shrink the tumor, then proceed with surgery, followed by a second round of chemotherapy. While this approach may have been more successful in treating the ovarian cancer, it made it impossible for us to accomplish our research aims because potential patients were no longer naïve to chemotherapy. Additionally, on July 27, 2015, the FDA issued a communication evaluating the risk of brain deposits with repeated use of gadolinium-based contrast agents in MRI studies. Our protocol called for gadolinium-based MRI studies. The combination of this change in treatment approach and FDA notice made it essentially impossible for us to recruit research participants. In an attempt to increase enrollment, we received permission to approach patients with endometrial and uterine cancer but this did not improve enrollment. Over the entire course of the study, we screened the records of 2533 post-operative patients and identified only 4 who met enrollment criteria. Of the 4 who met criteria, only one agreed to participate.*

**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*

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

*NA*

**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*

**CHANGES/PROBLEMS:**

**Changes in approach and reasons for change**

*To increase recruitment, we opened enrollment to endometrial and uterine cancer patients.*

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

*As described above, we have encountered significant problems with recruitment, due in large part to changes in treatment protocols and the FDA notice on brain accumulation of gadolinium.*

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

*Nothing to report*

**Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

*IRB approval to recruit endometrial and uterine cancer patients: January 16, 2016*

*IRB approval to recruit patients receiving both chemotherapy and radiotherapy: May 27, 2016*

**Significant changes in use or care of human subjects**

*IRB approval to recruit endometrial and uterine cancer patients: January 16, 2016*

*IRB approval to recruit patients receiving both chemotherapy and radiotherapy: May 27, 2016*

**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*

**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*

**PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS:**

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

<b>Name:</b>	<b>Richard Sloan, PhD</b>
<b>Project Role:</b>	<i>Principal Investigator</i>
<b>Researcher Identifier (e.g. ORCID ID):</b>	<i>n/a</i>
<b>Nearest person month worked:</b>	<i>1</i>
<b>Contribution to Project:</b>	<i>Dr. Sloan is responsible for all aspects of the study including recruitment of patients, oversight of the activity-increasing program and data analysis</i>
<b>Funding Support:</b>	<i>This project.</i>
<b>Name:</b>	<b>Scott Small, MD</b>
<b>Project Role:</b>	<i>Co-Investigator</i>
<b>Researcher Identifier (e.g. ORCID ID):</b>	<i>n/a</i>
<b>Nearest person month worked:</b>	<i>1</i>
<b>Contribution to Project:</b>	<i>Dr. Small supervises all aspects of the imaging within the proposed project and provides some supervision for the half-time Research Assistant in scoring the imaging data</i>

*Funding Support:*

*This project.*

<b>Name:</b>	<b>Adam Brickman, PhD</b>
<i>Project Role:</i>	<i>Co-Investigator</i>
<i>Researcher Identifier (e.g. ORCID ID):</i>	<i>n/a</i>
<i>Nearest person month worked:</i>	<i>1</i>
<i>Contribution to Project:</i>	<i>Dr. Brickman will oversee the neuropsychological evaluation of participants in the study, including training study personnel on task administration, scoring, quality assurance, and data entry.</i>
<i>Funding Support:</i>	<i>This project.</i>
<b>Name:</b>	<b>Jason Wright, MD</b>
<i>Project Role:</i>	<i>Co-Investigator</i>
<i>Researcher Identifier (e.g. ORCID ID):</i>	<i>n/a</i>
<i>Nearest person month worked:</i>	<i>1</i>
<i>Contribution to Project:</i>	<i>Dr. Wright will be responsible for patient recruitment as well as medical oversight for patients recruited to the study.</i>
<i>Funding Support:</i>	<i>This project.</i>
<b>Name:</b>	<b>Jose Henriquez-Rivera</b>
<i>Project Role:</i>	<i>Research Assistant</i>
<i>Researcher Identifier (e.g. ORCID ID):</i>	<i>n/a</i>
<i>Nearest person month worked:</i>	<i>12</i>
<i>Contribution to Project:</i>	<i>Mr. Henriquez-Rivera is the study “coach” and his responsibilities include patient recruitment, retention, delivery of walking intervention.</i>
<i>Funding Support:</i>	<i>This project.</i>
<b>Name:</b>	<b>Brianna Last</b>
<i>Project Role:</i>	<i>Research Assistant</i>
<i>Researcher Identifier (e.g. ORCID ID):</i>	<i>n/a</i>
<i>Nearest person month worked:</i>	<i>2</i>
<i>Contribution to Project:</i>	<i>Administering and scoring neuropsychological tests under Dr. Brickman's supervision.</i>
<i>Funding Support:</i>	<i>This project.</i>
<b>Name:</b>	<b>Christiane Hale</b>
<i>Project Role:</i>	<i>Research Worker</i>
<i>Researcher Identifier (e.g. ORCID ID):</i>	<i>n/a</i>
<i>Nearest person month worked:</i>	<i>1</i>
<i>Contribution to Project:</i>	<i>Administering and scoring neuropsychological tests under Dr. Brickman's supervision.</i>

<i>Funding Support:</i>	<i>This project.</i>
-------------------------	----------------------

**Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

*Yes, other support attached.*

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

*Nothing to report*

**SPECIAL REPORTING REQUIREMENTS:**

*n/a*

**APPENDICE:**

*n/a*

**Richard Sloan, PhD**

Dr. Sloan has an appointment at the New York State Psychiatric Institute/Research Foundation for Mental Hygiene and Columbia University. This is detailed in a Dual Appointment Agreement between the entities and precludes the possibility of NYSPI/RFMH supporting effort supported by Columbia University and vice versa. Therefore, each project listed below indicates effort at each institution and also Total Professional Effort ('TPE') encompassing the multiple appointments.

**RFMH - ACTIVE AND PENDING****N/A****COLUMBIA UNIVERSITY - ACTIVE**

R01HL139614 (Sumner) 08/01/18-06/30/23 1.2 CM

NHLBI TPE 0.98 CM

*Identifying Early Intervention Targets for Reducing Cardiovascular Risk in Posttraumatic Stress*

This study will help determine whether posttraumatic stress disorder (PTSD) and psychophysiological fear responses, a key component of PTSD, are associated with adverse endothelial cell health, an early cardiovascular disease (CVD) precursor that is responsive to intervention. The results of this study may help trauma-exposed individuals who are at risk of having CVD events.

Role: Co-Investigator

NIH (Sumner)

R33 ES024734-01 (Chillrud and Jack) 03/01/17 - 02/28/20 0.60 CM

NIEHS TPE 0.49 CM

*Potential inhaled dose of particulates, biking and cardiovascular indicators*

This grant seeks to improve our toolkit for measuring human exposure to air pollution by combining data from instruments that measure air pollution concentrations every minute with estimates of how much air a given person drew into their lungs.

Role: Co-Investigator

5R01HL128310-02 (Edmondson) 07/15/15 - 03/31/19 0.60 CM

NIH/NHLBI TPE 0.49 CM

*Test of a new theory to explain excess risk in cardiac PTSD*

The goal of the proposed research is to identify targets for new interventions to reduce the doubled cardiac event recurrence and mortality risk faced by the 1 in 8 survivors of non-ST elevation myocardial infarction and unstable angina who develop PTSD secondary to their life-threatening cardiac event.

Role: Co-Investigator

2P01AG003949-32 (Lipton) 09/01/17 - 05/31/21 1.80 CM

Albert Einstein College of Medicine (NIH) TPE 1.47 CM

*Einstein Aging Study*

To identify risk factors and protective factors that influence both normative cognitive aging and the earliest onset of Alzheimer's Disease.

Role: Subcontract - Principal Investigator

1U19AG051426-01A1 (WISC) (Ryff) 07/25/16 - 05/31/21 0.60 CM

NIH (WISC) TPE 0.49 CM

*Integrative Pathways to Health & Illness*

The overall objective of MIDUS is to study health, broadly defined, as an integrated biopsychosocial process that unfolds across the decades of adult life.

Role: Subcontract - Principal Investigator

W81XWH-14-1-0236 (NCE) (Sloan) 08/01/14 - 07/31/18 0.25 CM

DOD(OC130386) TPE 0.20 CM

*Hippocampal and Cognitive Function, Exercise and Ovarian Cancer: A Pilot Study*

We propose to examine whether carboplatin and paclitaxel-based chemotherapy for ovarian cancer induces cognitive dysfunction and reduced DG CBV and to test whether an individually based walking intervention may attenuate this chemotherapy-induced cognitive and DG dysfunction.

Role: Principal Investigator

5P50AG008702-27 (Small) 06/01/15 - 05/31/20 0.12 CM

NIH TPE 0.10 CM

*Alzheimer's Disease Research Center*

This project supports a wide spectrum of research on Alzheimer's disease.

Role: Co-Investigator

NIH (Kimhy) 04/01/17 - 03/31/21 0.30 CM

NIH TPE 0.24 CM

*Improving Cognition via Exercise in Schizophrenia*

Individuals with schizophrenia (SZ) display substantial cognitive deficits across multiple domains. These deficits have been identified as major determinants of poor functioning and disability, representing a serious public health concern and an important target for interventions. At present, available pharmacological and cognitive-remediation treatments offer only minimal to limited benefits to ameliorate these deficits. Thus, there remains an urgent need to identify novel treatments for cognitive deficits in people with SZ.

Role: Co-Investigator

### **COLUMBIA UNIVERSITY - PENDING**

1 R01 AG058417 (Sloan) 04/01/18 - 03/31/23 3.0 CM

NIA TPE 2.45 CM

*Dietary Modulation of Neuroinflammation in Age-Related Memory Disorders*

In a small study, we showed that consumption of cocoa flavanols led to improved cognitive function and an increase in the function of a region of the brain responsible for memory and learning. Promising pilot data from this study suggest that one mechanism of this effect is the capacity of cocoa flavanols to reduce systemic and neuroinflammation, which in turn improves the function of this brain region. In this application, we propose to test this mechanism in a randomized controlled trial in which healthy older adults receive cocoa flavanols or placebo daily for a 12-week period, with pre- and post-intervention MRIs to assess the function of this brain region and blood draws to measure key inflammatory markers.

1R01MH116298-01 (Rutherford) 04/01/18 - 03/31/23 1.0 CM

NIMH TPE 0.98 CM

*Mitochondrial Function and Fatigue in Late Life Depression*

This exercise RCT will investigate the role of mitochondrial changes in the progression of sarcopenia.

Role: Co-I

NIH (Diaz) 07/01/18 - 06/30/23 0.60 CM

NIH TPE 0.23 CM

*Breaking up prolonged sitting: a factorial trial to evaluate the efficacy of multiple components of a sitting interruption intervention for improving endothelial health*

This study is designed to investigate the effects of a sitting interruption intervention in real world conditions over an extended period.

Role: Co-Investigator

PR160029 (Picard) 06/01/18 - 05/31/21 0.65 CM

Department of Defense TPE 0.53 CM

*Stress Reactivity in Mitochondrial Disease: Physiological, Neural, and Epigenetic Mechanisms*

This project will test the hypothesis that mitochondrial dysfunction in patients with the m.3243A>G mutation exhibit abnormal neural connectivity within the brain, which mediates exaggerated neuroendocrine, cardiovascular, and inflammatory responses to psychological stress, and abnormal epigenetic regulation of gene expression.

Role: Co-Investigator

R01HL141494-01 (Shechter) 04/01/18-03/31/23 0.48 CM

NIH TPE 0.39 CM

*Poor Sleep, Sedentary Behavior, and Secondary Cardiovascular Risk in Stroke and TIA Patients*

The goal of this ancillary R01 is to evaluate sleep and sedentary behavior after stroke or transient ischemic attack (TIA) as potential therapeutic targets to reduce risk of secondary cardiovascular disease (CVD).

Role: Co-Investigator

R01 (Chang) 07/01/18-06/30/23 0.60 CM

NIH TPE 0.49 CM

*The Impact of an Alternative Emergency Department Management Strategy on PTSD and Cardiovascular*

*Risk In Survivors of Tia and Minor Stroke*

The aim of this study is to study the impact of emergency department discharge to rapid outpatient neurology clinic on TIA/stroke-induced PTSD, cardiovascular disease outcomes and 30-day rehospitalization in a sample of TIA and minor stroke patients seen in the emergency department.

Role: Co-Investigator

DoD (Rauh) 01/01/18-12/31/18 0.30 CM

Department of Defense

TPE 0.24

*Pre-motor Brain and Behavioral signs of Parkinson's Disease in an environmentally at-risk birth cohort*

The proposed study addresses several important questions about the causes and progression of Parkinson's disease (PD) over the life course, including the role of toxic exposures that may contribute to the risk of disease.

We propose to study a unique community cohort of urban minority children, who are now reaching the age of 18 years, and who were routinely exposed to indoor and outdoor residential sprays, to try to identify the very earliest signs of risk for later PD that may appear long before clinical and motor symptoms can be seen.

R01HL142921 (Sloan) 04/01/19-03/31/24 3.0 CM

NIH TPE 2.45 CM

Pro-Inflammatory Effects of Exercise Training: A Mechanistic Study

The goal of this project is to test and to identify the biochemical mediators of this exercise-induced effect, leading to the identification of potential targets for other health-promotional interventions.

Overlap Statement: There is no scientific, budgetary or commitment overlap.

**SCOTT A. SMALL, M.D.****Other Support****Active**

MARS 2015 (Small)	04/01/15 - 03/31/18	3.94
CM		

**MARS**

Understanding the Potential Role of CF With Regard To Brain Function and Cognition

To study the role of cocoa flavanol [CF] consumption in the context of brain function, cognition, and age-related memory decline.

P50AG008702 (Small)	09/29/89-05/31/20	1.16
CM		

NIH/NIA

**Alzheimer's Disease Research Center**

This project supports a wide spectrum of research on Alzheimer's disease.

U01AG016976 (Small)	07/01/98-06/30/19	0.26
CM		

University of Washington Subcontract

**NACC**

Goals are to coordinate activities of Alzheimer's Centers by working with and supplying data to national center.

W81XWH-14-1-0236 (Sloan)	8/1/14 - 7/31/18	0.12
CM		

DoD

**Hippocampal and Cognitive Function, Exercise and Ovarian Cancer: A Pilot Study**

In this application, we propose to investigate the possibility that standard chemotherapy regimen used to treat ovarian cancer leads to memory impairment because it arrests the normal processes of neurogenesis, the growth of new nerve cells, in this brain region.

R01MH105355 (Small, Neria)	07/01/15 - 05/31/2018	0.60
CM		

NIH/NIA

**Neural Signature of Fear Overgeneralization in Trauma Exposed Adults**

The overarching goal of the study is to use a functional magnetic resonance imaging (fMRI) paradigm of conditioned-fear generalization, skin conductance response (SCR), and machine learning analytic methods in order to identify a neural signature of trauma-related psychopathology that can potentially serve as an objective measure of pathology and functional impairment, and a novel target for neuroscience informed treatments of functionally impaired trauma exposed populations.

1R61 MH112800 (Small)	07/05/2017 - 06/30/2019	1.20
CM		

NIMH

**Glutamate reducing interventions in schizophrenia**

To test the effectiveness of the medication Pomaglumetad in the reduction of psychotic symptoms on prodromal subjects.

Role: Co-Investigator

**Pending**

PAR-16-365 (Sloan/Small)	9/1/2017-08/31/2022	
1.20 CM		

NIH

**Dietary Modulation of Neuroinflammation in Age-Related Memory Disorders**

Role: PI

R01AG057507 (Marquer)	04/01/2018 - 03/31/2023	0.36 CM
NIH		

Arf6 and the pathogenesis of Alzheimer's Disease

The major goal of this project is to investigate the role of the small GTP-ase ARF6 in the progression of late-onset Alzheimer's disease.

Role: Co-Investigator

R01 (Sloan)  
1.20 CM

4/1/2018 - 3/31/2023

NIH  
In a small study, we showed that consumption of cocoa flavanols led to improved cognitive function and an increase in the function of a region of the brain responsible for memory and learning. Promising pilot data from this study suggest that one mechanism of this effect is the capacity of cocoa flavanols to reduce systemic and neuroinflammation, which in turn improves the function of this brain region. In this application, we propose to test this mechanism in a randomized controlled trial in which healthy older adults receive cocoa flavanols or placebo daily for a 12-week period, with pre- and post-intervention MRIs to assess the function of this brain region and blood draws to measure key inflammatory markers.

R01 MH113861-01 (Girgis)  
NIMH

7/1/17 - 6/30/22

1.80 CM

The Neurobiology of Violence in a Psychosis-Risk Cohort  
The goal is to determine how to best ask about thoughts of violence, obtain comprehensive assessment of symptom correlates of violent thoughts and actions, and investigate relationships between violent thoughts and brain abnormalities  
Role: Co-Investigator

### **Overlap**

There is no scientific overlap between any of the grants listed above and the application under consideration. If the pending grants are funded, efforts will be adjusted accordingly.

---

**For New and Competing Applications (PHS 398) – DO NOT SUBMIT UNLESS REQUESTED  
For Non-competing Progress Reports (PHS 2590) – Submit only Active Support for Key Personnel**

---

**PHS 398/2590 OTHER SUPPORT**

---

**Jason D. Wright**

ACTIVE

NCI R01 CA169121-01A1 (Wright, PI) National Cancer Institute The Influence of Hospital Variability on the Management of Cancer-Associated Complications To evaluate common complications from cancer therapy using administrative data.	1/1/13-12/31/18	3.0 calendar
--	-----------------	--------------

SAC 160066 (Hershman, PI) Susan G. Komen Foundation Comorbidity, Toxicity, and Breast Cancer Survival Among Women On and Off Clinical Trials. The goal of this project is to examine the effect of comorbidities on survival for women with breast cancer treated on cooperative group trials and in general practice.	5/1/16-4/30/19	1.2 calendar
---	----------------	--------------

American Cancer Society (Kukafka, PI) Decision Support for BRCA Testing in Ethnically Diverse Women The goal of this project is to test a decision support tool to promote genetic testing in women at risk for breast and ovarian cancer.	6/1/17-5/31/21	
--	----------------	--

OVERLAP

There is no scientific or budgetary overlap on any current project.

PENDING

NCI (Hershman, PI) National Cancer Institute Treatment Delay and Non-Adherence to Oral Antineoplastic Agents To evaluate barriers to use, adherence, cost and comparative effectiveness of oral anti-cancer drugs.	9/1/18-3/31/23	1.2 calendar
---	----------------	--------------

**Adam Brickman**  
**Other support**

**Active**

R56AG034189 (Brickman) NIH/NIA <i>White Matter Hyperintensities in Aging and Dementia</i> This project will examine the degree to which small vessel cerebrovascular contributes independently or interactively to the development and clinical expression of AD across racial and ethnic groups. It will provide novel mechanistic insight into the disease and help identify new targets for intervention Role on Project: Principal Investigator	09/01/2016 – 08/31/2018	0.54 calendar
RF1AG054070 (Manly, Brickman) NIH/NIA <i>Offspring Study of Mechanisms for Racial Disparities in Alzheimer's Disease</i> The overall aim of this study is to identify biological and sociocultural mechanisms of racial/ethnic disparities in cognitive function among middle-aged people with and without a parent with Alzheimer's Disease Role on Project: Principal Investigator	09/01/2016 - 07/31/2021	1.38 calendar
R01AG054520 (Brickman, Zahodne) NIH/NIA <i>Resilience Mechanisms Underlying Racial/Ethnic Disparities in Alzheimer's Disease</i> The overall aim of this longitudinal study is to identify new, modifiable mechanisms of racial/ethnic disparities in Alzheimer's disease (AD) among a multi-ethnic cohort of approximately 2,000 older adults. Role on Project: Principal Investigator	08/01/2017-05/31/2022	1.20 calendar
R25AG059557 (Brickman/Cosentino) NIH <i>Summer of Translational Aging Research for Undergraduates (STAR U)</i> This program seeks to overcome historic barriers that have prevented undergraduate students, from underrepresented minority backgrounds, from pursuing careers in scientific and aging research. Role on Project: Co-Investigator	07/01/2018-6/30/2023	0.60 calendar
P50AG008702 (Small/Brickman-Project Leader) NIH/NIA <i>Alzheimer's Disease Research Center</i> This project supports a wide spectrum of research on Alzheimer's disease. Role on Project: Project Principal Investigator	06/01/2015 - 05/31/2020	1.20 calendar
RF1AG051556 (Brickman, Luchsinger, Moreno) NIA <i>Interdisciplinary Research to Understand the Interplay of Diabetes, Cerebrovascular disease and Alzheimer's Disease</i> To conduct studies in humans and mice relating diabetes to Alzheimer's and vascular mechanisms. Role on Project: Principal Investigator	09/30/2015 - 08/31/2020	0.90 calendar
1RF1AG051556-01S2 (Brickman, Luchsinger, Moreno) NIA <i>Interdisciplinary Research to Understand the Interplay of Diabetes, Cerebrovascular disease and Alzheimer's Disease</i> To conduct studies in humans and mice relating diabetes to Alzheimer's and vascular mechanisms. Role on Project: Principal Investigator	09/30/2017 - 08/31/2018	0.30 calendar
R01AG049810 (Bondi) NIH	03/15/2016-02/28/2021	0.24 calendar

*Re-visiting Methods for MCI Diagnosis to Improve Biomarker and Trial Findings*

Subcontract site is to provide collaborative support for the aims and goals of the UCSD-based research project

Role on Project: Co-Investigator

R00AG47963 (Zahodne) 09/01/2016 - 08/31/2019 0.24 calendar  
NIH/NIA

*Psychosocial protective factors in cognitive and brain aging*

Characterizing potential intervention targets to reduce age-related cognitive morbidity in diverse elders is of critical importance to the U.S. aging population. This project aims to determine which positive psychosocial factors (1) buffer the impact of brain pathology on cognition and (2) protect against cognitive decline in older adults of different racial/ethnic backgrounds and with different cognitive abilities

Role on Project: Co-Investigator

U01AG051412 Schupf, Lott, Silverman) 10/01/2015 - 09/30/2020 0.96 calendar  
NIA

*Biomarkers of Alzheimer's Disease in adults with Down Syndrome*

The goal of this interinstitutional/collaborative study focuses on a longitudinal and multidisciplinary determination of key biomarkers that are likely to define this progression, including levels and rates of change in blood based biomarkers such as  $\beta$ -amyloid peptides, protein and lipid profiles, and measures of amyloid and tau concentration in cerebrospinal fluid, neuroimaging-based changes and genetic polymorphisms

Role on Project: Co-investigator

RF1AG054023 (Mayeux) 08/01/2016 - 06/30/2021 0.60 calendar  
NIH

*Genetic Epidemiology of Cerebrovascular Factors in Alzheimer's Disease*

The overall goal of this project is to test hypotheses concerning how genetic variants, cardiovascular risk factors, and cerebrovascular disease predispose to Late Onset Alzheimer's disease and whether these relationships differ by ethnic group

Role on Project: Co-Investigator

R01AG057962 (Razlighi) 09/1/2018-08/31/2023 0.12 calendar  
NIH/NIA *Functional connectivity network in default mode regions provides the underlying infrastructure for task-based functional co-de/activation networks*

While functional connectivity and task-based co-deactivation networks in default mode regions both reported to be disrupted in different stages of Alzheimer's disease, we aim to show that disruption of functional connectivity cannot precede the disruption of task-based deactivation network.

Role on Project: Co-Investigator

R01MH102293 (Rutherford) 12/01/2014 – 12/31/2018 0.60 calendar  
NIH/NIMH

*Mechanisms of Antidepressant Non-Response in Late-Life Depression*

The purpose of this study is to examine the mechanisms that mediate non-responsiveness to anti-depressant treatment in late life depression, including presence and severity of small vessel cerebrovascular disease

Role on Project: Co-Investigator

R01MH111596 (Rutherford) 09/01/2017 – 07/31/2022 0.60 calendar  
NIH/NIMH

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

This study investigates the influence of chronic post-traumatic stress disorder (PTSD) on signatures of aging at neural, cognitive, somatic, and behavioral levels of analysis. One hundred fifty individuals, older than age 50 and diagnosed with PTSD will be studied along with 150 age-, sex-, and trauma exposure-matched subjects without PTSD. Procedures include structural and functional neuroimaging, neuropsychological testing, and analysis of fluid and physical biomarkers.

Role Project: Co-Investigator

R01MH114980 (Brown, Rutherford) 9/18/2017 – 7/31/2022 0.60 calendar NIH/  
NIMH

*Neurocognitive and neuroimaging biomarkers: predicting progression towards dementia in patients with treatment resistant late-life depression*

This study examines how late life depression and response to medication might be linked to cognitive aging and dementia

Role on Project: Co-Investigator

R01AG050440-03 (Luchsinger) 09/01/2015 - 05/31/2020 0.24 calendar NIH/  
NIA

*Diabetes Status and Brain Amyloid in Middle Aged Hispanics*

The main goal of this proposal is to study whether diabetes status (type 2 diabetes [referred to as diabetes] and pre-diabetes, compared with normal glucose tolerance [NGT]), is related to increased amyloid  $\beta$  ( $A\beta$ ) deposition in the brain, one of the culprits of Alzheimer's disease (AD), in a community sample of 150 middle aged Hispanics with a mean age of 63 years.

Role on Project: Co-Investigator, site PI

R01AG055299 (Luchsinger) 08/01/2017-04/30/2022 0.48 calendar NIH/  
NIA

*Are there ethnic differences in brain amyloid and tau in the seventh decade of life?*

Goals: to compare in-vivo Alzheimer's neuropathology across Blacks, Hispanics, and Whites in Northern Manhattan

Role: Co-Investigator

### **Pending**

R01AG058767 (Devanand) 04/01/2018-3/31/2023 0.60 calendar  
NIH

*Olfactory Impairment in Offspring Study of Racial Disparities in Alzheimer's Disease*

We plan to test the 12-item Brief Smell Identification Test (BSIT) in 3,000 offspring as an add-on study to the recently funded project "Offspring study of mechanisms for racial disparities in Alzheimer's disease".

Role on Project: Co-Investigator

R01AG057709-01A1 (Gutierrez) 08/15/2018 – 04/30/2023 0.60 calendar  
NIH/NIA

*Genetic Contribution to Brain Arterial Dilatation and its Role in Cognition and dementia*

The goal of this study is to determine the role of brain arterial dilatation IN Alzheimer dementia.

R01AG58067 (Brickman/Manly) 07/01/2018 - 06/30/2023 2.40 calendar  
NIH/NIA

*Tau PET imaging in racially/ethnically diverse middle-aged adults*

The purpose of this study is to examine the extent to which tau deposition is related to cognitive function, to determine whether tau deposition varies across racial/ethnic groups, and to determine the extent to which cerebrovascular disease is associated with tau pathology in midlife

Role on Project: Principal Investigator

R01AG054066 (Berkman) 09/01/2018 – 08/31/2023 1.20 calendar  
NIH/NIA

*Cognitive Function, Alzheimer's Disease and Related Disorders in the HAALSI Cohort*

The HAALSI Dementia Study will make significant strides toward understanding the prevalence, incidence, and underlying mechanisms contributing to dementia in rural South Africa. We will explore specific genetic, medical, and psychosocial risk factors for dementia in the HAALSI cohort, and use magnetic resonance imaging (MRI) to better characterize the relationship between cognitive and brain aging. Role: Co-Investigator

Role on Project: Co-Investigator, Subcontract PI

R01NS110045 (Brickman/Barone)	09/01/2018-8/31/2023	1.80 calendar
NIH/NIA		
<i>Mechanistic links between diffuse white matter injury and Alzheimer's disease</i>		
The purpose of this project is to clarify the nature of the relationship between diffuse white matter injury and AD, and to understand the cellular mechanisms involved.		
Role on Project: Principal Investigator		
R01AG061817 (Luchsinger, Devanand, Rao)	09/01/18-08/31/23	0.60 calendar
NIH/NIA		
<i>Auditory, olfactory, and motor correlates of in-vivo AD neuropathology and cognitive decline in late-middle age</i>		
Goals: To compare the auditory, olfaction, and motor correlates of Alzheimer's disease (AD) biomarkers of Amyloid, Tau, and Neurodegeneration (ATN) and cognitive performance in community dwelling adults in late middle age.		
Role on Project: Co-Investigator		
R01AG062268 (Huey)	09/01/2018-08/31/2023	0.30 calendar
NIH		
<i>Neuroanatomical associations with the factor structure underlying neuropsychiatric symptoms in Alzheimer's disease</i>		
Neuropsychiatric symptoms in Alzheimer's disease and related dementias are a major public health problem as they are common, greatly increase the cost of and difficulty of care, and our pharmacological treatments are inadequate. We propose to use a data-driven approach to determine the factors underlying neuropsychiatric symptoms in participants with Alzheimer's disease, the brain networks associated with these factors, and test a novel brief global measure of neuropsychiatric symptoms. The goals are to improve the measurement and classification of neuropsychiatric symptoms in studies of participants with Alzheimer's disease and related dementias, and to identify measures to use and brain networks to target with anatomically-based treatments of neuropsychiatric symptoms, including Transcranial Magnetic Stimulation (TMS).		
Role on Project: Co-Investigator		
U01AG061363 (Verghese)	09/01/2018-08/31/2023	1.20 calendar
NIH/NIA		
<i>Central Neural Control of Mobility – Evolution, Biology and Clinical Consequences</i>		
We propose a multidisciplinary team science approach to investigate central neural control of mobility: cognitive processes and underlying brain substrates that control locomotion. Our approach seeks to establish evolution of central neural control of mobility in aging including the earliest brain changes in ambulatory high functioning older adults without overt neurological disease that precede mobility decline		
Role on Project: Co-Investigator, Subcontract PI		
R01AG061885 (Rutherford)	09/01/2018-08/31/2023	1.20 calendar
NIH/NIA		
<i>From the Age-Related Positivity Effect to Alzheimer's Disease: Developing Normative and Amyloid-Associated Neuromarkers of Emotional Reactivity and Regulation</i>		
The proposed studies seek to understand normal changes in the brain's processing of emotions over the lifespan and to investigate how Alzheimer's brain pathology interrupts this normal emotion processing and causes distressing behavioral symptoms.		
Role on Project: Co-Investigator, Subcontract PI		
R01AG058417 (Sloan)	09/01/17-08/31/22	0.60 calendar
NIH		
<i>Dietary Modulation of Neuroinflammation in Age-Related Memory Disorders</i>		
We propose to test this mechanism in a randomized controlled trial in which healthy older adults receive cocoa flavanols or placebo daily for a 12-week period, with pre- and post-intervention MRIs to assess the function of this brain region and blood draws to measure key inflammatory markers.		

Role on Project: Co-Investigator

R01AG051346 (Goldberg)  
NIH/NIA

04/01/2018-03/31/2023

0.60 calendar

*Novel Cognitive and Functional Measures for Alzheimer's Disease Prevention Trials*

This proposal focuses on novel measures of cognition and everyday function that have robust psychometrics and reduced practiced effects.

Role on Project: Co-Investigator