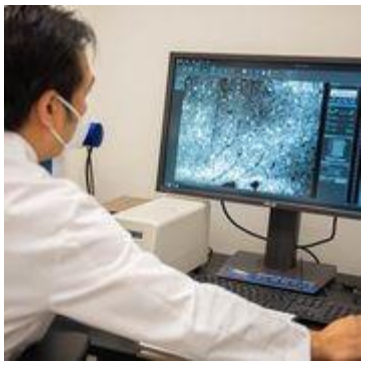

McKnight Brain Research Foundation Annual Report - 2020



University of Florida

1/15/2021

UF | Evelyn F. & William L. McKnight Brain Institute
UNIVERSITY of FLORIDA

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1/12/2021

RE: MBRF Annual Report

Dear Trustees of the McKnight Brain Research Foundation,

It has been a tough year for all of us, but despite the challenges imposed by COVID I am impressed with the resilience of and progress made by our MBRF supported investigators. As outlined in the annual report the MBRF supported programs here at UF continue to flourish, expand and increase their scientific impact. The discovery and translational science efforts have grown and become more impactful. More investigators are being enlisted to work in the area of cognitive brain again, and new educational and training opportunities seem to emerge every month. Efforts to enhance communication, interaction and visibility of the program all our progressing well, and align closely with local objectives of the larger Neuroscience community under the MBI umbrella.

I am delighted that we have formally “reintegrated” the structure and operations of the Age-Related Memory Loss Core Program ("ARML Core Program") and the Cognitive Aging and Memory Clinical Translational Research Program ("CAM-CTRP") into a unified Center for Cognitive Aging and Memory Clinical Translational Research (the "CAM Center") and that Drs. Cohen and Bizon will serve as co-directors. Their leadership efforts in conjunction with the efforts of Drs. Woods and Burke, bode well for the future success and growing footprint of the MBRF programs at UF. With Dr. Bizon potentially poised to become the permanent chair of the Department of Neuroscience, there are likely to be opportunities to recruit new faculty in this area of research in the future. I would like to thank Dr. Foster for his previous leadership of the ARML program, and know that he will continue to be an active investigator in this area.

MBI is currently developing a 5-year strategic plan for the broader Neuroscience and Neuromedicine research programs at UF. The MBRF supported brain and cognitive aging programs will remain a foundational piece of that plan. However, that plan will also highlight the growing connections between the CAM Center and the many other neuroscience research programs here at UF and also initiatives that are designed to continue to move our research towards translation. As a key partner of the MBI’s efforts, we would be delighted to share that plan with you as it is developed over the next six-months, and perhaps even partnering on new initiatives relevant to brain aging that emerge form that plan.

I thank you for your long-lasting support of the program here at UF, and more broadly the MBRF's efforts to increase awareness of brain and cognitive aging.

Sincerely,

Todd E. Golde, M.D., Ph.D.
Director, Evelyn F. and William L. McKnight Brain Institute
Director, 1Florida Alzheimer's Disease Research Center
Member, Center for Translational Research in Neurodegenerative Disease
Professor, Department of Neuroscience, College of Medicine

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McKnight Brain Research Foundation
Center for Cognitive Aging and Memory
Clinical Translational Research
(CAM Center)

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January 13, 2021

Dear Trustees:

Without question, 2020 has been an exceptionally challenging year in which researchers have faced new and unparalleled challenges. During March, the University of Florida ordered a complete cessation of research involving both human subjects and preclinical animal models. The setbacks in our research programs were unavoidable as the health of our faculty, trainees, research subjects and their families took a necessary precedent. Despite these challenges, researchers in the Center for Cognitive Aging and Memory Clinical Translational Research (the "CAM Center") have demonstrated exceptional adaptability and resilience. We have made great strides in integrating the structure and operations of the Age-Related Memory Loss Core Program ("ARML Core Program") and the Cognitive Aging and Memory Clinical Translational Research Program ("CAM-CTRP") into a unified CAM Center that encompasses complementary and collaborative research and educational programs on cognitive aging. Listed below are the primary objectives of the CAM Center as outlined in the MOU with the McKnight Brain Research Foundation. We have highlighted under each objective the activities in the past year that collectively have advanced our mission to uncover the fundamental mechanisms of brain aging that underlie cognitive decline and develop interventions and preventative strategies that promote positive functional outcomes in the process of normal aging.

Objective 1: Maintain and grow the research infrastructure for conducting cutting-edge discovery based cognitive aging research.

A merger to the structure and operations of the Center for Cognitive Aging and Memory Clinical Translational Research (the "CAM Center"), the Age-Related Memory Loss Core Program ("ARML Core Program") and the Cognitive Aging and Memory Clinical Translational Research Program ("CAM-CTRP") programs began towards the end of the last reporting period. Since that time, the leadership of the new CAM Center has met weekly and has been dedicated to laying a solid foundation to support a successful world-class program on cognitive aging that spans preclinical to clinical translational research. We have developed an initial strategic plan that includes taking better advantage of numerous opportunities on the UF campus. This includes expanding existing partnerships with the Brain Rehabilitation Research Center at the VA hospital, the School of Pharmacy and the Alzheimer's Disease Research Center. With respect to the latter, we are particularly focused on collaborating to augment the brain repository by increasing the number of samples of cognitively-intact older adults. Such samples are critical to understand the factors that influence cognitive resiliency. In addition, members of the CAM Center are already working with the Senior Vice President and others in planning for research infrastructure at the Villages, where UF has recently acquired several hospitals.

Research Initiatives

CAM Center researchers have been exceptionally productive, publishing over 75 peer-reviewed manuscripts, advancing their research programs, and securing numerous new awards. Highlights include the fact that Dr. Adam Woods, Associate Director of the CAM Center, received a $700,000 supplement from the National Institutes of Health. This supplement is linked with his ongoing large Phase 3 clinical trial that is designed to test whether transcranial direct current stimulation (tDCS) can amplify benefits of cognitive training in older adults. Specifically, the new study is focused on whether there are factors that make people more or less resilient to the effects of COVID-19 and social isolation. In addition, Dr. Sara Burke, Associate Director of the CAM Center, received a new R01 award from the National Institute on Aging entitled *Metabolic Interventions for Enhancing Cognitive Resilience in Aging and Alzheimer's Disease.* The goal of this award is to determine the mechanisms by which dietary ketosis improves cognition in aged animals. Dr. Burke further received a fundable score on the renewal of her current R01 award entitled *The Contribution of Declines in Functional Connectivity to Cognitive Aging.* The major goal of the next five years of this renewed award will be to determine how alterations in systems-level neural coordination in old animals produce cognitive impairments.

Program Project Grant (PPG) Planning. CAM Center faculty have further made considerable progress towards a Program Project Grant, which we hope to submit to the National Institute on Aging in the upcoming year. This PPG will be focused on non-pharmacological interventions targeting neuroplasticity for cognitive enhancement in older subjects. This program builds on the considerable work from Dr. Woods and colleagues related to using transcranial Direct Current Stimulation (tDCS) to enhance cognition, as well as work from Drs. Bizon, Burke, Porges, Williamson and Lamb investigating cognitively-enhancing effects of vagus nerve stimulation. Dr. Bizon and collaborators Burke, Setlow and Lamb have an R01 on the latter topic pending council review (scored in funding range at National Institute on Aging). The goals of the PPG will be synergistic with the proposal, enabling expansion of our programmatic efforts that span from investigation of mechanism to intervention. We have already spoken with Dr. Molly Wagster at the National Institute on Aging about our plans for this cross-species program and she is enthusiastic about our developing proposal. We are currently holding planning meetings weekly, building our full team of investigators, and initiating the necessary preliminary studies to lay the foundation for this large grant submission.

Equipment Investment

Light sheet microscope. In September of 2020, CAM Center funds ($25,000) were used to assist in purchasing an UltraMicroscope Blaze BC AO 4.2 Fully-Featured lightsheet microscope (total cost $349,927.00) in partnership with the MBI, Center for Translational Research in Neurodegenerative Disease and the UF Diabetes Institute. This modest investment enables CAM Center faculty access to this powerful research tool. The UltraMicroscope Blaze is a fully motorized light sheet microscope for 3-dimensional imaging of large tissue samples in water, aqueous buffers or organic solvents. All CAM Center faculty will have access to this new light sheet microscope to enhance their research related to the cellular mechanisms of cognitive aging and how this relates to large-scale alterations in structure and function of brain circuits across the lifespan.

Ella system. This automated protein biomarker analysis platform for conducting batch analyses of Elisa assays, including multiple cytokines was purchased from Protein Simple a subsidiary of R&D (Total Cost: $33,000). This system will provide a substitute for Luminex which has reduced accuracy compare to ELLA. It can be run by our phlebotomist and provides results on multiple assays in 60-

70 minutes. We will use this in cytokine and other biomarkers analyses. This system is available to CAM investigators, and others based on collaborative proposal.

Objective 2. Recruit, train and retain high-caliber young scientists interested in neural mechanisms for cognitive aging.

A critical goal for the CAM Center is to train the next generation of neuroscientists and clinicians committed to uncovering the mechanisms of cognitive resilience at advanced ages and maximizing cognitive health across the lifespan. Indeed, CAM Center faculty are dedicated mentors and the impact of their training efforts extend across all academic ranks, including undergraduates, medical and graduate students, residents and postdoctoral fellows, as well as junior faculty. As listed below, over 17 postdoctoral fellows and 25 graduate students are affiliated with the CAM Center. These individuals are supported not only by PI-sponsored extramural awards, but also by several NIH-supported training grants (T32s) that provide stipend support, tuition and travel funds for PhD students. Dr. Bizon, together with MBI co-Deputy Director Dr. Jada Lewis, is a PI on one such T32 (now in its third year) that currently supports six trainees, including PhD students in Drs. Burke and Woods laboratories. In addition, Dr. Woods, together with Dr. Michael Marsiske, was awarded a new T32 this year that supports additional trainees within the CAM Center.

Beyond graduate students and postdocs, we have made a concerted effort to increase the cadre of junior faculty, including clinical faculty focused on research questions relevant to cognitive aging. Through interaction with these individuals who are in the early stages of establishing their research programs, we hope to increase their ability to achieve independent funding in the field of cognitive aging and to inspire a career-long interest and dedication to this research area. Listed below are the junior faculty who are currently affiliated with the CAM Center. We have also attached each individual's Biosketch to this report. Recognizing the interest of the MBRF in increasing clinical faculty in the CAM Center, we have specifically made efforts to increase mentoring efforts of junior clinicians. Thus far, senior members of the CAM Center are mentoring three junior faculty neurologists, two of whom are MD/PhDs.

Matt Burns, MD, PhD
Fellow
Department of Neurology
Member, CAM Center
Clinical Faculty Mentee (Bizon)

Dr. Burns is a physician-scientist who obtained his MD/PhD in 2014 from the University of Illinois at Chicago. He then completed a residency in Neurology in 2018 at the University of Chicago Medical College. In 2018, Dr. Burns started a postdoctoral position supported by a fellowship on movement disorders from the Fixel Center for Neurological Disorders at the University of Florida. Dr. Burns is interested in cognitive dysfunction that occurs as a consequence of normal aging and age-associated diseases such as Parkinson's disease. Dr. Burns was recently selected as a KL2 Pepper Center awardee and has a promising score on a K08, which is currently pending council review at the National Institute on Aging. His mentored awards are focused on determining how aging and synuclein pathology affect executive functioning and decision-making. He is further assessing how deep brain stimulation in the prefrontal cortex may be effective at remediating such cognitive deficits.

Carolina Maciel, MD
Clinical Assistant Professor of Neurology and Neurosurgery; Director of Research, Division of Neurocritical Care
Member, CAM Center
Clinical Faculty Mentee (Burke)

Dr. Maciel is a triple board-certified neurologist with formal training in neurocritical care, electrophysiology, and clinical research. This combination of training enables her to assess mechanisms of secondary brain injury and outcome prediction in acute neurologic injuries and following cardiac arrest, which disproportionately affects older adults. As a diverse scholar selected by the American Academy of Neurology to receive the TRANSCENDS award as first cohort, Dr. Maciel completed formal training in clinical research and clinical trials through a Master of Science program under a comprehensive mentorship for career development. The program offered insight into thriving in a competitive scientific environment, writing successful grant applications and maintaining scholarly productivity. Dr. Maciel mentors trainees during all steps of the scientific process in translational science, from study design to dissemination of findings. She holds volunteer faculty appointments in two other institutions (Yale and the University of Utah), which facilitates recruitment of other sites in multicenter trials and expands the outreach of TRANSCENDS, opening doors to trainees across all phases of their career development.

Alexis Simpkins, MD, PhD, MSCR, FAHA
Clinical Assistant Professor
Department of Neurology
Member, CAM Center
Clinical Faculty Mentee (Woods,Cohen)

Alexis Nétis Simpkins, MD, PhD, MSCR, FAHA is an Assistant Professor of neurology in the University of Florida College of Medicine. Dr. Simpkins first earned a Bachelor of Science degree in chemistry, along with a minor in biology, at Augusta University in Georgia. She was then accepted into the dual doctoral program at the Medical College of Georgia in Augusta, obtaining her medical doctoral degree and a doctorate in vascular biology after investigating utility of a novel agent in vascular and neuroprotection in hypertension and stroke.

She completed her internal medicine internship at the Medical College of Georgia in Augusta. Next, she completed a neurology residency at The Johns Hopkins Hospital in Baltimore. Dr. Simpkins completed her time in Maryland with a combined clinical and research vascular neurology fellowship at the National Institute of Neurological Disorders and Stroke.

Dr. Simpkins is an active member in the American Heart Association and Director of the CREST Initiative for stroke trainee and fellow research and career development in the Vascular Neurology Division.

Karina Alviña, PhD
Research Assistant Professor
Department of Neuroscience
(Mentee of Bizon and Burke)

Dr. Alviña joined the Department of Neuroscience in Fall 2020. After completing her undergraduate degree at Pontifical Catholic University of Chile, she received her PhD in Biological Sciences and Physiology from Albert Einstein College of Medicine in 2008. She then completed postdoctoral research at Columbia and Albert Einstein. Her long-term research goal is to understand how cells in the nervous system communicate with each other in normal and pathological conditions, specifically during aging and age-associated neurodegenerative disorders.

Dr. Alviña has led projects that range from studying intrinsic properties of single brain cells to *in vivo* studies of behavior and mechanisms underlying neurological disorders. She has extensive training in neurophysiology, specifically in the use of acute brain slices to study electrophysiological properties of cells and neural circuits using rodents as animal models. Her first interest is in understanding neural mechanisms that lead to aberrant responses caused by stress and aging-associated processes of neurodegeneration. Her research is also focused on understanding how environmental manipulations such as diet and exercise can be used as resilience agents.

In the short time since Dr. Alviña has been at the University of Florida, she has already been selected as an AlzSTAR Fellow for the 1Florida Alzheimer's Disease Research Center (1FL ADRC; Mentors: Bizon, Lewis and Tansey) and received an Ed and Ethel Moore Alzheimer's Disease Research Program Pilot grant from the Florida Department of Health.

Argyle Bumanglag, PhD
Research Assistant Professor
Department of Neuroscience
(Mentee of Bizon and Burke)

Dr. Bumanglag received his PhD in Neuroscience at the University of Arizona under the mentorship of Dr. Robert Sloviter, and his research career has focused primarily on understanding hippocampal epileptogenesis and the nature of the latent period following brain injury. His finding that granule cell-onset epilepsy is coincident with the initial injury, and not delayed, suggested that selective neuronal injury or dysfunction could be a primary epileptogenic mechanism. Recent experiments based on this hypothesis, in conjunction with years of meticulous epilepsy animal model development, have led to the development of a new model of temporal lobe epilepsy.

Dr. Bumanglag joined the laboratories of Drs. Jennifer Bizon and Sara Burke at the University of Florida, where he is focused on understanding and treating disruptions in excitatory/inhibitory balance in the aged brain and its implications to cognitive function. Further, he is interested in understanding behavioral comorbidities associated with temporal lobe epilepsy across the lifespan.

Ruogu Fang, PhD
Assistant Professor
J. Crayton Pruitt Family Department of Biomedical Engineering
(Mentee of Woods)

Dr. Fang is the Director of Smart Medical Informatics Learning and Evaluation (SMILE) Lab in the Biomedical Engineering Department. Dr. Fang is also a tenure-track Assistant Professor in the Department of Biomedical Engineering, with affiliation to Electrical and Computer Engineering, Computer and Information Science and Engineering, and Radiology. She is a biomedical data scientist with expertise in machine learning, neuroimaging, and brain dynamics modeling for neurological diseases. She is a pioneer in multimodal neuroimage analysis using machine learning and artificial intelligence, publishing a survey paper on health informatics in big data age, and multiple pioneering papers on dictionary learning, sparse representation, tensor total variation, and evolutionary deep learning for neuroimage analytics in flagship journals and leading, developing toolboxes on neuroimage analysis used by tens of laboratories worldwide, and serving as guest editor of Journal Computerized Medical Imaging and Graphics. Dr. Fang's work has been highlighted as the top 25 Hottest Papers in Medical Image Analysis Journal and won the Best Paper Award at International Conference on Image Processing. Dr. Fang's research specifically focuses on discovery and application of novel machine learning approaches for enhancing neuroimaging precision and brain dynamics quantification in adults with neurological diseases. Dr. Fang has expertise in multi-disciplinary neuroimaging analysis methodologies (optimization, sparsity, dictionary learning, machine learning, deep learning), extensive experience with hemodynamics-related neurological disorders, image restoration applications, and recent research with neurodegenerative diseases. Dr. Fang is the PI of the National Science Foundation CRII (Pre-CAREER) Award (NSF 1564892), NSF III Award (NSF 1908299), National Institute of Health Clinical Translational and Science Institute Award on brain dynamics modeling in multimodal neuroimaging.

Joseph Gullett, PhD
Research Assistant Professor
Department of Clinical Health Psychology
(Mentee of Cohen, Woods)

Dr. Gullett is a licensed neuropsychologist and Research Assistant Professor with the University of Florida Center for Cognitive Aging and Memory. He received his PhD in clinical psychology from the University of Florida in August of 2017 after the completion of a one-year clinical internship in psychology at the West Los Angeles VA Medical Center. He has worked extensively in multimodal neuroimaging, including functional MRI and Diffusion methods to study populations with white matter pathology including older adults, Veterans with mild traumatic brain injury (mTBI), and people living with HIV (PLWH). His current work applies the methods of multimodal neuroimaging and neuropsychology to the study of cognitive aging as well as in Veterans with mTBI and PLWH and alcohol use disorders. He remain clinically-involved in the neuropsychological assessment of various populations, and collaborate as a licensed neuropsychologist both on a weekly clinical service as well as on a number of NIAAA-funded U-01 and R-01 grants focused on aging and PLWH. He recently completed a 1Florida Alzheimer's Disease Research Pilot Grant which generated the pilot data being included in a K-23 Clinical Trial submission to the National Institute of Aging, Neuroscience. This new area of focus, which includes the use of multi-modal neuroimaging to predict cognitive and intervention outcomes in older adults, is developing into his current area of research expertise.

Ashok Kumar, PhD
Research Associate Professor
Department of Neuroscience
(Mentee of Foster)

Over the past two decades, Dr. Kumar's research has been focused on delineating the mechanisms contributing to age-related cognitive impairment. Toward this goal, a central focus of his research involves the role of various interventions such as environmental enrichment, exercise, viral vector, and anti-inflammatory compounds in restoring/reversing age-associated impaired cognition, synaptic plasticity, and cell excitability. Along with Dr. Thomas Foster, he has been instrumental in characterizing N-methyl-D-aspartate receptor (NMDAR) hypofunction during aging and its relationship with cognitive impairment (PMID: 20884759, PMID: 24089479, PMID: 21942371, PMID: 25740525, PMID: 27180169, PMID: 26732087, PMID: 30031231, PMID: 28467718, PMID: 30209673, PMID: 30504275); this work highlights a link between age-associated impaired cognition and a redox-mediated decline in NMDAR function. Their recent research findings (PMID: 30031231, PMID: 28928652) demonstrate that nonsteroidal anti-inflammatory compound improves neurogenesis, spatial memory, and NMDAR synaptic function. For aging, by far the main risk factor for neurodegenerative disease including Alzheimer's disease (AD), the question remains "why are the elderly more vulnerable to AD?" Aging decreases NMDAR function at the synapse. His current work is testing the hypothesis that an oxidized redox state associated with aging influences GluN2B NMDAR synaptic localization/trafficking, particularly the extrasynaptic ones.

Objective 3. Expand the scientific community at UF pursuing research relevant to age-related cognitive decline and memory loss.

We have made progress in expanding our community at UF. Beyond those faculty and trainees mentioned within this report (who received funding from the CAM Center), we have many more UF faculty who affiliate with the CAM Center and conduct research on related topics. A full list of these affiliate faculty can be found on our website: https://cam.mbi.ufl.edu/faculty/.

One key activity that locally raises visibility for the mission of the CAM Center is the annual William G. Luttge Lectureship that is supported by a generous endowment provided by the McKnight Brain Research Foundation almost ten years ago. The 8th Annual William G. Luttge Lectureship in Neuroscience was planned for April 2020. **Dr. Carla J. Shatz, PhD**, Sapp Family Provostial Professor, David Starr Jordan Director of Stanford Bio-X, and Professor of Biology and of Neurobiology at Stanford University, was our confirmed invitee and her visit was planned in conjunction with the 50th anniversary of the Department of Neuroscience. Unfortunately, due to the COVID-19 pandemic, Dr. Shatz's lecture had to be postponed. We will be rescheduling this Luttge Lecture in the fall of 2021, when we anticipate it being safe to host Dr. Shatz and other attendees in person.

Despite our inability to host the annual Luttge Lecture, we have been proactive in bringing our community together virtually by inviting seminar speakers throughout the semester. Since **March 2020 and continuing through April 2021**, the weekly joint Department of Neuroscience-MBI Seminar is being offered in a virtual format through Zoom. Due to the reduced cost of hosting speakers 'virtually', the CAM Center has had the opportunity to invite prominent and diverse scientists from around the world to give seminars related to cognitive aging and/or learning and memory. Moreover, the cancellation of the 2020 Luttge Lecture left funds available to host speakers by giving a modest honorarium (approved at the November MBRF trustee meeting). These seminars

have been well attended, with participant numbers ranging between 70 -100 each week. Moreover, discussions have been lively and served to provide cohesion to the CAM Center and UF Neuromedicine communities during a difficult time for our research community. Seminar speakers have also joined for a virtual “coffee hour” with our trainees each week. Below is a summary of Dr. Shatz’s research as well as our past and upcoming virtual seminar speakers sponsored by the CAM Center. In the upcoming spring semester, we intend to invite other McKnight Institutes to “tune in” to our virtual seminars.

Annual William G. Luttge Lecture Series

The 8th Annual William G. Luttge Lecture, now planned for Fall 2021, will be delivered by **Dr. Carla J. Shatz, PhD**, Sapp Family Provostial Professor, David Starr Jordan Director of Stanford Bio-X, and Professor of Biology and of Neurobiology at Stanford University.

Dr. Shatz’s research is focused on understanding how developing brain circuits are transformed into adult connections during critical periods of development. Her work, which focuses on the development of the mammalian visual system, has relevance not only for treating disorders such as autism and schizophrenia, but also for understanding how the nervous and immune systems interact. Dr. Shatz is a Howard Hughes Investigator and from 2000-2007 she was Chair of the Department of Neurobiology at Harvard Medical School and the Nathan Marsh Pusey Professor of Neurobiology. Dr. Shatz has received many awards, including the Gill Prize in Neuroscience in 2006. In 1992, she was elected to the American Academy of Arts and Sciences, in 1995 to the National Academy of Sciences, in 1997 to the American Philosophical Society, in 1999 to the Institute of Medicine, and in 2011 she was elected as a Foreign Member of the Royal Society of London. Dr. Shatz was awarded the Gerard Prize in Neuroscience from the Society for Neuroscience, and in 2015, the Gruber Prize in Neuroscience. In 2016, she was the recipient of the Champalimaud Vision Prize, and the Kavli Prize in Neuroscience for the discovery of mechanisms that allow experience and neural activity to remodel brain circuits. In 2018, she received the Harvey Prize in Science and Technology.

Spring 2020 CAM Center-Sponsored Seminar

Jamie Near, PhD Assistant Professor of Psychiatry, McGill University) was the CAM Center-sponsored seminar speaker on **February 27, 2020.** Dr. Near was the last speaker that the CAM Center was able to host in person before UF sponsored travel was paused due to the COVID-19 pandemic. Dr. Near’s research is focused on the development of advanced magnetic resonance spectroscopy (MRS) techniques to accurately measure metabolite concentrations in the brain. Specific activities in Dr. Near's laboratory include: pulse sequence programming, data processing and analysis, radiofrequency coil development, and quantum mechanical simulation of MRS experiments. Dr. Jamie Near works closely with clinicians and neuroscientists to investigate the neurochemical basis of cognitive aging and is currently collaborating with CAM Center faculty (Porges and Burke) to examine how advanced age and diet impact glutamate and GABA levels, as well as markers of neuroinflammation using MRS.

Fall 2020 CAM Center-Sponsored Speakers

Dr. Rosanna Olsen, PhD (Assistant Professor, Rotman Research Institute, University of Toronto) was the seminar speaker on **October 8, 2020**. Dr. Olsen's research is directed toward understanding the representational nature and neural organization of human memories using high-resolution structural and functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG), eye movement monitoring, and amnesia patient studies to investigate memory formation, retention, and retrieval. Her recent work has examined the structural changes that occur in older adults who are exhibiting early signs of cognitive decline. This work indicated that a specific region of the medial temporal lobe (MTL) is one of the earliest brain regions affected by Alzheimer's disease and that MTL structural changes can precede subjective memory complaints in community-dwelling older adults.

Dr. Gina Poe, PhD (Professor, Department of Integrative Biology and Physiology University of California, Los Angeles) was the seminar speaker on **October 22, 2020**. Dr. Poe was a former trainee of Dr. Carol A. Barnes and her current research lab investigates the mechanisms by which sleep traits serve learning and memory consolidation. Memories are encoded by the pattern of synaptic connections between neurons. Her lab employs neurophysiological recording and optogenetic techniques in behaving animals to see how neural patterns underlying learning are reactivated during sleep, and how activity during sleep influences the neural memory code. Both strengthening and weakening of synapses is important to the process of sculpting a network when we make new memories and integrate them into old schema. Dr. Poe's research has shown that while synaptic strengthening can be efficiently accomplished during the waking learning process, the synaptic weakening part of memory integration requires conditions unique to sleep. The absence of noradrenaline during sleep spindles and REM sleep as well as the low levels of serotonin during REM sleep allow the brain to integrate new memories and to refresh and renew old synapses so that we are ready to build new associations the next waking period. Memory difficulties involved in post-traumatic stress disorder, Schizophrenia, and advanced age involve abnormalities in the sleep-dependent memory consolidation process that her lab studies.

Dr. Farida Sohrabji, PhD (Interim Department Chair, Department of Neuroscience and Experimental Therapeutics, Professor, Department of Neuroscience and Experimental Therapeutics Director, Women's Health in Neuroscience Program, Texas A&M University) was the seminar speaker on **November 5, 2020**. Dr. Sohrabji's research program focuses on brain-immune interactions regulated by estrogen and its implications for neuro-inflammatory diseases such as stroke in women. Additionally, her laboratory also examines estrogen's interactions with other endogenous and environmental endocrine mediators, including Vitamin D hormone and the peptide hormone Insulin-like Growth Factor (IGF)-1. Her current studies use an animal model to examine age and sex differences in recovery from stroke, focusing at the cellular level on the endothelium and astrocytes, which are the principal components of the blood brain barrier. At the molecular level, her research program examines sex and age differences in micro RNA and epigenetic markers, with a view to developing biomarkers for diseases and uncovering new therapeutic targets.

Dr. Catrina Robinson, PhD (Assistant Professor Department of Neurology, Medical University of South Carolina) was the seminar speaker on **December 3, 2020**. Dr. Robinson's research focuses on understanding the role of metabolic disorders (such as prediabetes, diabetes, and obesity) on brain health and aging. Current experiments are focused on studying the impact of diet and obesity on memory function. Her research also examines mechanisms that link metabolic disorders to an increased risk of Alzheimer's disease and the role of prediabetes on stroke recovery. The overall goal of her laboratory is to understand the metabolic pathways involved in cognitive function in order to develop novel therapeutic targets to improve brain health in older adults.

Upcoming Spring 2021 CAM Center-sponsored Seminar Speakers

Dr. Elizabeth Head, PhD (Professor, Vice Chair for Research Department of Pathology and Laboratory Medicine Director, Experimental Pathology Program) is scheduled to be the CAM Center-sponsored seminar speaker on **January 28, 2021**. The overarching goal of her laboratory is to identify interventions for people with Down syndrome (DS) to slow or prevent the development of Alzheimer's disease (AD). Moreover, other current research projects are focused on several collaborative longitudinal studies of aging in adults with Down syndrome to test the hypothesis that white matter integrity, cerebrovascular dysfunction and neuroinflammation contribute to cognitive decline and dementia. By identifying key factors modifying or associated with the development of dementia in Down syndrome, Dr. Head's primary goal is to identify novel targets for intervention that are highly likely to be unique to this vulnerable group of people.

Dr. Rune Berg, PhD (Associate Professor, University of Copenhagen) is scheduled to be the CAM Center-sponsored seminar speaker on **February 4, 2021**. The primary research areas of the Berg Lab are to examine neuronal population activity in the spinal cord and brain using large array electrophysiology, development of novel probe technology, classify the network architecture in motor circuits, histological clearing techniques for large sample imaging for network reconstruction, as well as awake electrophysiology with chronic implantation of electrodes and optical fibers in the central nervous system.

Dr. Greg Quirk, PhD (Professor, Department of Psychiatry and Anatomy & Neurobiology, University of Puerto Rico School of Medicine) is scheduled to be the CAM Center-sponsored seminar speaker on **February 25, 2021**. The primary mission of the Quirk laboratory is to increase understanding of how the brain overcomes fear using behavioral, optogenetic and neurophysiological approaches in rodent and nonhuman primate models. The Quirk lab also aims to train effective scientific thinkers who value collaboration and to increase neuroscience practice in historically underrepresented countries.

Dr. Karen Duff, PhD (Center Director, Dementia Research Institute, University College London) will be the CAM Center-sponsored speaker on **March 18, 2021**. Her research is focused on understanding how the abnormal aggregation of tau protein in the brain exacerbates cognitive aging. Intraneuronal neurofibrillary tangles (NFTs), consisting of hyperphosphorylated tau protein, are a hallmark of several neurodegenerative conditions including Alzheimer's disease (AD) and Frontotemporal dementia (FTD). The accumulation of abnormal (argyrophilic) tau starts in the transentorhinal cortex in the earliest stages of AD and spreads through the limbic and association cortices via the trisynaptic circuit in a precise and defined manner, correlating with the cognitive deficits that develop in the condition. To better understand the causes and consequences of abnormal tau accumulation and the propagation of tauopathy, Dr. Duff's research has used a plethora of methods, and cell and animal models, including a novel transgenic mouse that differentially expresses pathological human tau in the entorhinal cortex (EC-Tau).

Dr. Duke Han, PhD (Professor of Family Medicine, Keck School of Medicine, USC) will be the CAM Center-sponsored speaker on **March 25, 2021**. Dr. Han's research examines the factors that impact cognition and decision making in aging. He also has special interests in using novel neuroimaging and statistical approaches to better understand these factors. He was the recipient of the prestigious Paul B. Beeson Career Development Award in aging research, which is supported by the National Institute on Aging (NIA), the American Federation of Aging Research (AFAR), and the John A. Hartford Foundation. Dr. Han is also an inaugural Governance Committee member of the Global Council for Brain Health, an independent science collaborative convened by the AARP with support from "AgeUK", which is tasked to summarize scientific knowledge regarding brain health topics for the aging public.

Dr. Roy Hamilton, PhD (Associate Professor in the departments of Neurology and Physical Medicine and Rehabilitation at the University of Pennsylvania) will be the CAM Center-sponsored speaker on **April 1, 2021**. Dr. Hamilton's research is focused on using brain stimulation to augment cognitive function in aging. He has employed TMS and tDCS in a range of studies to examine the neural network organization of cognitive control, visuospatial processing, language production, semantic memory, and creativity. He is a clinically trained behavioral neurologist and cognitive neuroscientist, and as such, has dedicated his career to exploring the structure-function and network-function relationships that underpin complex human behaviors.

Dr. Sunil Gandhi, PhD (Associate Professor, Neurobiology and Behavior School of Biological Sciences, Associate Director of the Center for the Neurobiology of Learning and Memory, UCI) will be the CAM Center-sponsored speaker on **April 8, 2021**. Dr. Gandhi's research focuses on understanding how local interneurons control cortical plasticity. His laboratory employs a combination of techniques, including two-photon functional imaging, in vivo patch-clamp recordings, the transplantation of neuronal precursors, and mouse genetic tools that identify, stimulate/silence defined neural circuits. Dr. Gandhi is also focused on developing new techniques for the visualization of long-range connections in the visual system using whole brain clearing, viral tracing and light sheet imaging.

Dr. Andre Fenton, PhD (Professor of Neural Science, NYU) will be the CAM Center-sponsored speaker on **April 15, 2021**. Dr. Fenton's research examines how brains store experiences as memories, and how the expression of knowledge activates information that is relevant without activating what is irrelevant. His laboratory uses molecular, electrophysiological, behavioral, engineering, and theoretical methods to investigate these fundamental and interrelated issues in neuroscience. Relevant to cognitive aging, the Fenton laboratory is currently examining the role of the hippocampus in controlling how relevant and irrelevant information are differentially processed. While rats and mice solve problems that require using relevant information and ignoring distractions, the Fenton Laboratory obtains neurophysiological recordings from multiple sites and uses computational tools to decode information from these recordings.

Objective 4. Increase visibility of the research and develop messaging at local, national, and international levels.

Website. Increasing visibility of the CAM Center's research and affiliated faculty is an important goal and we have begun laying the initial groundwork for a communications plan for the Center. One effort to date is to create a new website, which was very recently launched: https://cam.mbi.ufl.edu/. We have spent considerable time creating content, faculty directories, and templates to assist with Center branding. Nevertheless, maintaining such a site with the large (and growing) number of faculty and trainees requires considerable time and regular daily attention. To prioritize this effort and ensure current website content and maintenance, we will be moving forward with hiring a CAM Center communications intern in the coming months. This individual will manage updates and coordinate CAM Center news across UF outlets.

LinkedIn. One effort that we also plan to undertake in the next year is to improve tracking of our current and former trainees. We will be asking all of our CAM Center faculty and trainees to create LinkedIn accounts to assist with maintaining contact and assessment of long-term outcomes. Moving forward, these professional groups will also provide networking opportunities for our former trainees looking for academic and private sector positions.

Social Media. In addition to the website, we have also recently completed the process of acquiring a UF-sanctioned CAM Center Twitter account @UF_CAMcenter. From an academic and scientific standpoint, Twitter is a large community for publicizing our accomplishments and recruiting top students and faculty. To date, we have vastly underutilized this network and I believe that efforts to do so will improve our applicant pool for academic programs and any future faculty openings. Our future CAM Center communications intern will be charged with generating weekly content for the Twitter account, which will include publicizing newly published papers, student accomplishments and faculty and student awards. We will work with other McKnight Institutes and the MBRF Communications Working Group to coordinate our efforts and ensure we use our account to also amplify research accomplishments from our McKnight partners.

Objective 5. Increase interactions and cohesion within the CAM Center, other UF Centers and industry partners to facilitate bidirectional (discovery to translation) cognitive aging and memory research at UF.

A major goal of our now integrated CAM Center is to increase cohesion between our discovery and translational research programs. While many community building efforts have been hindered by the COVID-19 pandemic, the CAM Center leadership has continued to meet weekly all of this past reporting period. We have developed an initial draft of a strategic plan that provides a clear guide for continuing to move forward with our vision of a truly cohesive, world-class program on cognitive

aging at the University of Florida. We will be working in the next several months with MBI and College leadership to ensure our plan is fully integrated with larger initiatives in the broad neuroscience community and takes full advantage of all opportunities in the Colleges of Medicine and Public Health and Human Performance at UF.

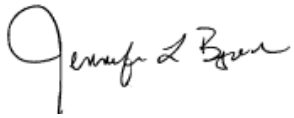
Objective 6. Increase interactions with the other McKnight Brain Institutes and increase visibility of ARML and CTRP Core Programs.

Many of the efforts described above are focused on increasing interactions among CAM Center faculty and our Core Programs (both ARML and CAM-CTRP). We have made a conscious decision to "brand" ourselves as the CAM Center, rather than use the core program names in our University or outward facing communications. We feel that this approach is consistent with our goal of forming one integrated Center and will serve to increase recognition of our mission outside of the University of Florida.

As described above, we have begun to work with leaders at the Brain Rehabilitation Research Center at the VA hospital, the School of Pharmacy and with the Alzheimer's Disease Research Center to discuss ways that the CAM Center can partner to maximize resources that facilitate shared missions. We have also invited directors of numerous UF Centers to affiliate with the CAM Center. These include Dr. Sara Jo Nixon (Center for Addiction Research and Education); Malú Tansey (Center for Translational Research and Neurological Disease); and Dr. Gordon Mitchell (Breathing Research and Therapeutics). Each of these Centers house investigators conducting research on co-morbidities of aging that can significantly impact cognition in older adults. Through these efforts, we hope to facilitate collaborations between CAM Center faculty and investigators at UF working on topics such as sleep apnea, cannabis and other substance use, and age-associated diseases such as Alzheimer's and Parkinson's diseases.

In addition to long-standing projects that extend across McKnight Institutes, we also describe in this year's report a number of new inter-institutional collaborations. These collaborations include multiple MBRF Cognitive Aging and Memory Intervention Pilot Core Awards led by investigators at the University of Florida. Dr. Natalie Ebner is collaborating with members of the University of Arizona and University of Miami to develop novel paradigms for understanding decision-making and susceptibility to scamming in older adults. In addition to publishing several collaborative studies enabled by this award, Dr. Ebner and her collaborators have now submitted a new R01 to the National Institute on Aging on this topic. Dr. John Williamson is collaborating with Dr. Gene Alexander at the University of Arizona to conduct a cross-institution study investigating vagus nerve stimulation in older adults.

We are proud of our many accomplishments during this challenging year, and are confident that with the distribution of vaccines and the continued support of the University of Florida Administration and the McKnight Brain Research Foundation, we are poised for continued growth and productivity in 2021.



Jennifer L Bizon, PhD
Co-Director, CAM Center
Professor and Interim Chair
Department of Neuroscience

Ron Cohen, PhD
Co-Director, CAM Center
Professor and Evelyn McKnight Chair of Clinical Translation in Cognitive Aging and Memory
Department of Clinical and Health Psychology

Annual Report
McKnight Brain Research Foundation
Sponsored Institutes and Research Programs
Report Period: **January 2020-December 2020**

SUMMARY OF SCIENTIFIC ACHIEVEMENTS IN THE PAST YEAR

Jennifer L Bizon, PhD
Professor and Interim Chair
Department of Neuroscience
Co-Director, Center for Cognitive Aging and Memory Clinical Translational Research (CAM Center)

Despite the significant challenges in 2020, the Bizon lab continued to make progress in advancing our understanding of the neural mechanisms that contribute to decline of cognition in aging. As part of one of our funded R01s from National Institute on Aging (NIA) focused on understanding drivers of age-associated changes in decision making, we published two new studies showing that male and female sex hormones play differing roles in risk-taking inclinations and the ability to delay gratification. The findings from these rodent-model studies were reported in the journals Neuropsychopharmacology (Impact Factor 7.9) and eLife (Impact Factor 7.4). Our data could provide useful insight for why decision making is altered in aging and for development of approaches to optimize decisions in older adults.

In addition, our laboratory acquired promising new findings from preclinical rat models which show that vagus nerve stimulation can enhance forms of cognition that decline in aging. These data have formed the foundation for a new R01 proposal entitled “Mechanisms and therapeutic potential of vagus nerve stimulation in aging and Alzheimer’s Disease” that is focused on using vagus nerve stimulation to treat cognitive decline in aging. This grant (which represents a collaboration with other CAM investigators: Setlow (MPI), Burke (co-I) and Lamb(co-I)) has scored within the funding range at the National Institute on Aging, and will be reviewed at council in January 2021. Our first paper on this topic also will be published next year as part of a special issue in *Neurobiology of Learning and Memory*. These data, together with those from the Burke lab, are also providing the foundation from which to bridge preclinical rodent and human studies (from Dr. Porges and others) in a larger cross-species Program Project Grant (PPG) that is currently under development and targeted for submission later this year.

Building on our long-time collaboration with Dr. Barry Setlow, we have further completed preliminary studies evaluating the acute and long-term effects of cannabis on cognition in old rats. We believe these studies are of critical importance given that older adults represent the demographic in which the largest increase of cannabis use has been observed in the past five years. Almost no studies, however, have evaluated effects of this drug in aging. Our initial data show that acute cannabis can *enhance* working memory in aged (but not young) rats. These preliminary findings have formed the basis for a new grant awarded in December 2020 (Setlow and Bizon PIs) from the Florida Department of Health (DoH) Ed and Ethel Moore Alzheimer’s Disease Research Foundation. In addition, both R21 and R01 proposals (Setlow and Bizon MPIs) were submitted in 2020 on this topic and will be reviewed in February 2021. In addition to these projects, we have also continued our

long-time collaborations with Dr. Sara Burke and Dr. Jason Frazier, both of which have resulted in collaborative manuscripts (one is published and two others are under review).

Trainees in the Bizon lab have also made considerable progress in the past year. Our prior postdoctoral fellow, Dr. Joseph McQuail accepted a tenure-track Assistant Professor position at University of South Carolina Medical school where he is now establishing his own independent research program investigating neural mechanisms of age-associated decline. Our former student and postdoc, Dr. Caesar Hernandez is now a postdoc at our fellow McKnight Institute (University of Alabama Birmingham) working in Dr. Lori McMahon's laboratory. We have recruited a new pre-doctoral student, Wonn Pyon, who was an undergraduate research and technician for several years with Dr. Carol Barnes. Wonn is establishing in vivo calcium imaging in our laboratory and will be evaluating the status of neuromodulatory brain systems in relation to decision making in our aged rat models. We further recruited a new Postdoctoral Research Associate (Dr. Mojdeh Faraji, PhD) who has an exceptional quantitative background and is working on our NIA R01 entitled "Decision making and basolateral amygdala dysfunction in aging". Finally, Dr. Setlow and I are mentors of a MD/PhD Fellow, Dr. Matt Burns, who has received a Pepper Center KL2 to study the cognitive consequences of age-associated alpha synuclein pathology. Dr. Burns also has a promising score on a K08 application pending at council review at NIA.

My lab has continued to disseminate our research findings. I gave several presentations on my lab's research including at the Winter Brain Conference in Big Sky. Montana, University of Kansas (invited seminar), and was a speaker at "iNAV 2020, 3rd Interdisciplinary Navigation Symposium (my talk was viewed by over 700 attendees). I also served as a discussant at the "Second workshop on research definitions for reserve and resilience in cognitive aging and dementia**.** My lab will be presenting three posters at the upcoming Society for Neuroscience meeting.

Notably, I accepted the role of Interim Chair of the Department of Neuroscience. I was also honored to be selected to be the College of Medicine nomination and ultimately accepted as a Fellow in the Hedwig van Amerigen Executive Leadership in Academic Medicine. I have been attending this year long course since June 2020.

Ron Cohen, PhD
Evelyn McKnight Chair of Clinical Translation in Cognitive Aging and Memory
Professor, Clinical and Health Psychology
Co-Director, Center for Cognitive Aging and Memory
Clinical Translational Research (CAM Center)

The following is a review of activities over the past year in my capacity as the Evelyn McKnight Chair of Clinical Translation in Cognitive Aging and Memory. With respect to research and publications, my activities: 1) Publishing manuscripts based on prior studies; 2) Overseeing ongoing research studies including several R01-U01 projects; 3) Grant writing to obtain funding for continuing lines of research; and 4) Directing the Cognitive Ageing and Memory – Clinical Translational and Research Program. Published research includes 11 manuscripts, and four others that have been accepted for publication. This brings my total number of peer reviewed publications to over 330. There have also been multiple abstracts presented by my graduate students and fellows at scientific meetings.

Several noteworthy studies will be highlighted that make significant contributions to the scientific literature on successful cognitive and brain aging. On most of these studies, I have served as the senior author, while students or junior faculty members have served as the first author. Together with Talia Seider, PhD (dissertation) and other CAM colleagues, we have conducted analyses on

neuroimaging data focused on neural activation and functional connectivity of brain systems involved in shape, location, and velocity discrimination in the context of cognitive and aging. The first manuscript has been published which demonstrates preservation of functional capacity and brain response with advanced age, but with spread of activation to frontal cortical regions. Two other manuscripts are either submitted or will soon be submitted for publication: 1) The relationship between performance on the Visual Assessment Battery (VAB – paradigm developed for this study) and performance on commonly used neuropsychological measures of visual perception (Benton's Judgement of Line Orientation and Facial Recognition tests); and 2) Another manuscript demonstrates the dedifferentiation of neural activation across cortical visual areas on fMRI in older adults is associated with stronger visual discrimination performance. Another line of research came to fruition as well, as Amanda Garcia's dissertation project has yielded very interesting findings regarding semantic processing and representation relative to associative strength and concreteness in the context of older adults who are aging successfully. These findings are being prepared for submission. This fMRI study also shows preservation in the neural response within cortical hubs responsible for semantic functions, but changes in the magnitude and spread of activation with advanced age. Both the visual discrimination and semantic studies are important as they address how neural response of the brain changes for cognitive functions that remain stable at advanced age. An interesting study was published on which Dr. Gullett of the Center for Aging and Cognitive Memory (CAM) is first author that shows how specific mRNAs are associated with age and cognitive performance in older adults who are aging successfully. This study extends an earlier work conducted with Dr. Foster on this topic, employs machine learning algorithms to determine what may be optimal predictors from this epigenetic data. Data collection on the McKnight Brain Aging Registry is largely completed (except a few participants who could not be imaged given COVID), and findings from this initiative are being prepared for manuscripts across the four MBIs. Multiple secondary analyses submitted by other faculty and graduate students have been approved and are also underway. We also are collecting COVID related data in the interim. Along with these studies, there are multiple manuscripts resulting from the ACT study on which Drs. Woods, Marsiske and I are MPIs.

Several manuscripts are in preparation and abstracts presented by graduate students at meetings from data resulting from the WISE study (bariatric surgery effects on cognition). This R01 study is nearing completion with respect to longitudinal data collection. Findings to date show that MRS and other neuroimaging measures, along with laboratory biomarkers (e.g., cytokines) are associated with BMI and A1C reduction, and changes in cognition. Analyses addressing baseline MRS metabolite levels predicting BMI and A1C reduction which will likely have considerable scientific impact is submitted to Obesity the major journal on this field. A continuing line of research focuses on alcohol and marijuana use in the context of HIV and aging continue with exciting data emerging from the 30-day challenge U01 grant. This study focuses on the effects of alcohol reduction via contingency management on cognition and brain among heavy drinkers who are over the age of 50. The ROGUE study is an R01, which examines the gut-liver-brain effects in older adults with HIV is proceeding well, with initial microbiome data providing evidence linking HIV and age with microbiome disturbances. This work together with other collaborative research with Drs. Porges and Williamson on vagal nerve stimulation led to a PO1 program project submission to NIAAA that has an excellent chance of being funded. There are other ongoing studies which cannot be reviewed in detail in this report.

With respect to my role in the directing the CAM-CTRP, it is very gratified that the faculty members who have been recruited over my time at UF are extremely productive, well-funded, and are either now independent researchers or on their way towards this objective. The center continues to grow with over 45 study coordinators, graduate students, and post-doctoral fellows. This growth has resulted from the success of the group in obtaining external funding. In fact, CAM faculty now provide support for a significant percentage of graduate students in neuropsychology within the CHP. In addition, the merger of the CAM-CTRP and ARML programs has essentially doubled the size of our

center and is likely to result in submission of a P01 project in 2021 on neuroplasticity and neuromodulation in the context of cognitive and brain aging. It reflects the successful integration of our groups. Our core faculty is sought out to serve as primary mentor/advisor for graduate students in the Departments of Clinical and Health Psychology, and in the Neuroscience department. Collaborations with CAM faculty in other departments has grown. My involvement in the Brain Rehabilitation Research Center is an example of this. Drs. Williamson, Lamb, and I are collaborating on several lines of research. I played a major role in conceptualizing the VA BRRC renewal, which was successful in being funded. We are translating our CAM database and neuroimaging protocols for data collection with a particular focus on traumatic brain injury in the context of an aging VA population. In sum, the CAM is flourishing at UF and I anticipate significant scientific contributions by our center in the coming years.

Sara N Burke, PhD
Associate Professor
Department of Neuroscience
Associate Director, CAM Center

The year 2020 was marked by a number of scientific achievements and challenges for the Burke laboratory. My research program continues to focus on understanding the systems-level mechanisms of age-related cognitive decline as well as developing and testing diet-based interventions for improving cognitive outcomes in old age. In support of this, I received a fundable score on the competitive renewal for my NIH/NIA R01 "*The Contribution of Declines in Functional Connectivity to Cognitive Aging*," and the renewal of this award is pending. Moreover, I obtained new funding from the Florida Department of Health Ed and Ethel Moore Alzheimer's Disease Research Foundation to examine if cyclic (1 week on carbohydrate restriction/1 week on standard diet) ketogenic diet therapy can improve cognitive function in old rats. If successful, this work will identify a novel and translatable dietary intervention that could improve cognitive outcomes in older adults. Despite the challenges presented by the COVID-19 pandemic and my lab's mandatory closure from March 17th to May 15th, 2020, I recruited a new Postdoctoral Research Associate (Dr. Carly Logan), who is bringing to the lab expertise with *in vivo* micro dialysis, and a new graduate student (Samm Smith). Furthermore, my current graduate student (Tara Cooper) was awarded a position on an institutional training grant that is focused on examining non-pharmacological interventions for cognitive aging (PIs: Drs. Woods and Marsiske).

This past year was also a time of transition with several my lab members leaving to pursue the next stage of their careers. Dr. Sarah A. Johnson transitioned to a tenure-track faculty position at Rosalind Franklin Medical University and Dr. Abbi Hernandez is currently in a postdoctoral position at the University of Alabama, Birmingham (UAB) and supported by a training grant to examine mechanisms of aging in relation to the gut-brain axis. Dr. Hernandez's move to UAB facilitated a new collaboration for my and Dr. Bizon's labs with EMBI researchers at UAB (Drs. Carter and Burford). We are currently working on review papers that will highlight the virtues of combining geroscience with neuroscience to understand and treat cognitive aging. We also submitted and collaborative pilot grant to the McKnight Brain Research Foundation to examine how vagus nerve stimulation and a ketogenic diet impact the gut microbiome.

I have also continued to disseminate my research findings regarding mechanisms of cognitive aging both with research publications and with formal seminars and research symposia. This past year, my laboratory has published 7 papers on the topic of cognitive aging. Moreover, prior to COVID-19, I organized and presented in a symposium at the International Winter Conference on Neural

Plasticity (February 13, 2020) on Neurometabolism in Healthy Aging and Disease that included 2 National Academy of Science Members (Dr. Gyuri Buzsaki and Marcus Raichle) as well as Drs. Donno Korol and Paul Gold. Drs. Korol and Gold have been instrumental in showing how impaired glucose metabolism in the aged brain leads to cognitive deficits. While travel has not been possible since March, I have had the opportunity to present virtual seminars online at the University of Texas, Austin and at Ruhr-Universität Bochum in Germany. My lab will also be presenting 4 posters at the Society for Neuroscience Virtual Conference in January. Finally, in February 2020, I became an Associate Editor at the journal *Behavioural Brain Research*. My editorial responsibilities focus on handling papers that relate to brain function and behavior in relation to aging and age-related diseases. Importantly, this journal has an international readership.

Adam Woods, PhD
Associate Professor
Department of Clinical Health Psychology
Associate Director, CAM Center

Since last report, I have acquired additional funding for my research on novel non-invasive interventions for remediating cognitive aging. At present, I have 16 funded projects as PI, MPI and Co-I. In addition to existing funds for two multisite R01 randomized clinical trial across two of the McKnight Brain Institutes (the R01 ACT study, n=360), (the R01 REVITALIZE trial, n=168), a K01 performing a dose response companion study to ACT (Stimulated Brain, n=80), two R21s (1 PI, 1 Co-I), an RF1 (Co-I), an R37 (Co-I), U01 (site PI), a VA Merit Grant (Co-I), and MBRF pilot (MPI), I recently received a fundable score on my third R01 as PI. This R01 will leverage the ongoing ACT trial and employ novel artificial intelligence-based analytic methods combined with computational neuroscience techniques to a) predict transcranial direct current stimulation (tDCS) and cognitive training treatment response and b) develop a deployable method for precision-dosing of tDCS to optimize behavioral outcomes in older adults. In addition, I was awarded as MPI, along with Michael Marsiske and Glenn Smith, a T32 pre-doctoral training grant titled *Research Training in Non-Pharmacological Interventions for Cognition in Aging, MCI, and Alzheimer's Disease.* This training grant will afford 6 PhD students with dedicated training in non-invasive intervention methods (behavioral, lifestyle, brain stimulation) for remediating cognitive aging and improving function in patients with MCI or AD. My research program to find and implement novel non-invasive methods for intervening on cognitive aging and the prevention of dementia continues to thrive, receiving over $15 million in funding from NIH awards in the past 5 years and over 2.5 million in the past year alone. For the 4th year, I have been the top grant recipient in my department and one of the top 5 grant recipients in my college. Collectively, this body of work represents the CAM's efforts to pioneer novel non-invasive interventions for combating cognitive aging in older adults. My lab has grown to 28 lab members and continues to expand with funding success. In addition, my lab produced 26 peer-reviewed publications this year, many in journals with impact factors of 6 or higher. Of note, this year we published the largest finite element computational modeling study in older adults for prediction of tDCS current flow, a novel method for combining computational modeling with artificial intelligence methods to predict treatment outcomes from tDCS and calculate precision dosing in older adults as well as seminal papers in cognitive aging and brain function (working memory [*Cerebral Cortex]*, hippocampal [*Front. in Aging Neuroscience*], speed of processing [*Front. in Aging Neuroscience*], white matter structural integrity [*NeuroImage*]).

In the past year, I have also joined the editorial boards of *Frontiers in Aging Neuroscience* (Associate Editor) and *Contemporary Clinical Trials*. Finally, I was honored to receive the Excellence in

Research Mentorship Award from the Department of Clinical and Health Psychology, an award nominated and voted for by graduate students in the department.

Tom C Foster, PhD
Professor
Department of Neuroscience
Evelyn F. McKnight Chair for Research on Cognitive Aging and Memory

The following is a review of activities over the past year in my capacity as the Evelyn F. McKnight Chair for Research on Cognitive Aging and Memory. In the past year, most of our studies have been directed at the idea that preservation of cognitive function during aging occurs through two processes: *maintenance*, which slows or prevents age-related brain changes and associated cognitive decline, and *reserve or resilience*, which represents plastic properties in response to the stressors of aging, which preserves cognition through compensation. **i**) We published a manuscript in the *Journal of Neuroscience* on molecular markers of altered strategy selection (Smith et al., 2020). In this case, the biomarkers permitted the identification of changes in the activation of different brain regions as a compensatory mechanism to adapt to a decline in the function of the brain region that normally underlies the cognitive process of interest (i.e. pattern separation). **ii)** We (Yegla and Foster) received a small grant to examine molecular markers of cognitive reserve using public data sets of gene expression. **iii)** As a member of the Reserve and Resilience: Animal studies working group, I took the lead role in producing a manuscript Cognitive reserve in model systems for mechanistic discovery: importance of longitudinal studies (in press). **iv**) The importance of longitudinal studies was also emphasized in a published manuscript by my group, which longitudinally characterized predictors of the trajectory of cognitive decline, and included brain imaging, a minimally invasive measure that can be translated to humans (Febo et al., 2020).

The second major area of research also involves minimally invasive measures, blood samples that can be employed in human studies. **i)** In this case, blood based biomarkers (i.e. microRNA) were related to cognition, and brain changes (i.e. neuroimaging) in older adults (Gullett 2020). **ii)** In addition, a grant was funded (Cruz-Almeida, PI) to examine epigenetic markers in blood of older humans, in relation to pain and cognition. A third area of research examined the role of peripheral inflammation and neuroinflammation in brain aging and cognitive decline (Barter et al., 2020; Shaeradeh et al., 2020). A program project grant will be submitted in January examining biomarkers (blood) and proxies of cognitive reserve on cognitive impairment in older sepsis patients and brain mechanisms for age x sepsis cognitive impairment in a mouse model. Finally, Dr Ashok Kumar received a NIA grant, which attempts to enhance or correct impaired memory through viral/pharmacological regulation of NMDA receptor function.

Dawn Bowers, PhD, ABPP-CN
Professor
Departments of Clinical and Health Psychology and Neurology
Member, CAM Center
MBRF Cognitive Aging and Memory Intervention Pilot Core Awardee

We are continuing to recruit and enroll older adults in an ongoing randomized clinical trial between UF and the University of Arizona, *A Pilot Intervention with Near Infrared Simulation Revitalizing Cognition in Older Adults.* The goal of this 12-week clinical intervention is to test the viability of near-infrared photobiomodulation in improving cognition and brain health in older

adults. Outcomes include pre-post intervention changes in experimental cognitive measures and neuroimaging (resting state fMRI, MRS spectroscopy). Approximately 1/3 of anticipated participant have completed the study to date, with delays due to research shutdown related to the COVID-19 epidemic. In addition, the REVITALIZE R01 funded based on this pilot is ready for initiation across both study sites (UF and UA).

Yenisel Cruz-Almeida, PhD
Associate Professor
Department of Dentistry
Member, CAM Center
Awarded supplemental funding from the ARML core program to support R01 shared with Dr. Ebner

In this reporting period, we have made significant progress on our NIA-funded R01 entitled "*Mechanisms of Oxytocin's Analgesia in Older Adults*" for which we receive CAM funds to augment our neuroimaging project. Specifically, have refined our IRB protocol for the study and the IND for the drug compound has been updated. Both the drug and the placebo have been compounded at the Investigational Drug Services at UF and spray supplies (spray bottles and pumps) have been received from collaborating companies (SGD-Pharma and Aptar Pharma). We have fully trained study staff including several trainees from under-represented backgrounds. We have started recruitment efforts including using UF's Consent2Share as well as community newspaper advertisements, which have been very effective in study enrollment. For example, two months of newspaper advertisements have yielded over 55 older individuals that have directly contacted us to be part of the study. Of those 30 have been screened and 24 have started the enrollment process. Although we are on track for study enrollment, we have been impacted since December by the seasonal flu, where experimental sessions were canceled by participants experiencing flu-symptoms. More recently starting in February, we have experienced cancellations by participants concerned with the coronavirus COVID-19.

Steven T DeKosky, MD
Deputy Director, McKnight Brain Institute
Aerts-Cosper Professor of Alzheimer's Research
Departments of Neurology and Neuroscience
Member, CAM Center

We have made significant progress in studies looking at memory changes in normal aging and with the more severe abnormalities that extend to other cognitive domains and may lead to dementia. This work involves detailed neuropsychological testing, quantitative neuroimaging, and pathology-specific PET scans. Indeed, subjects from the Alzheimer's Disease Research Center who are normal or have varying levels of memory impairment but who are negative for amyloid on PET scan are the ideal candidates to study normal aging, without the concern that some of them are on the way to AD and are just entering the early phases. Therapeutic efforts are directed a both magnetic brain stimulation and transcranial direct stimulation, assessing for level of improvement and tolerance of the procedure. Finally, I am working with the ADRC in our Mt Sinai Medical center (Miami Beach) to look at memory loss in Hispanic participants and determine differences between this group and non-Hispanic Whites. I continue to work within the ADRC to utilize highly sensitive memory assessments

to determine how helpful they are in differentiating normal aging changes in memory from the initial manifestations of vascular or AD dementia, or, as is frequently the case, both vascular and Alzheimer pathology.

Natalie C. Ebner, PhD
Associate Professor
Department of Psychology
Member, CAM Center
MBRF Cognitive Aging and Memory Intervention Pilot Core Awardee

We have made significant progress on our intervention pilot award entitled "*Uncovering Risk Profiles of Deception and Mitigating Susceptibility to Scamming in Midlife and Older Age: A Novel Intervention Tool*". During the past year, we have developed a novel ecologically valid, behavior-based data collection infrastructure (PHIT; PHishing Internet Task) as well as its controlled in-lab equivalent (PEST; Phishing Email Suspicion Test). We have collected data from over 300 young and older participants in this last reporting period using these new paradigms. Further, we have published the paradigms and made them available to the scientific community. Additional data collection and data analysis are currently underway.

Joseph Gullett, PhD
Research Assistant Professor
Department of Clinical Health Psychology
Member, CAM Center

Since the last report, two first-author manuscripts have been published in high-tier journals (Average IF = 5.5). Both of these publications focused on cognitive aging. The first examined the contribution of a novel white matter integrity marker to cognitive functions specific to a number of pathways in the brain. The second used machine learning to examine the ability of blood-derived micro RNA to predict cognitive functioning on the MoCA and NIH Toolbox. I completed my 1Florida Alzheimer's Disease Research Center 2019 Pilot Grant project in September of 2020. From this project, I was able to generate pilot data demonstrating the ability of a multi-modal neuroimaging machine learning pipeline to predict whether a patient with mild cognitive impairment would progress to dementia after one year. A first-author manuscript is currently being revised for submission to the *Journal of Alzheimer's Disease*. I have submitted a K23 Clinical Trial proposal to the NIA-Neuroscience division, which was scored but not funded. I am currently awaiting data collection on a related project to complete, which will be used as pilot data to improve the K23 proposal for the February submission period in 2021. Lastly, I have also submitted a VA CDA-2 application investigating the ability of a machine learning pipeline to predict whether a Veteran with chronic cognitive difficulties after mild traumatic brain injury can benefit from a planned cognitive training intervention.

Ruogu Fang, PhD
Assistant Professor
J. Crayton Pruitt Family Department of Biomedical Engineering
College of Engineering
Member, CAM Center

Through productive collaboration with CAM and College of Health and Human Performance, our team has built artificial intelligence (AI) systems for understanding mechanism and individual variability in tDCS for cognitive aging and spinal cord stimulation for chronic pain. We have also developed AI system for diagnosing Alzheimer's Disease and Parkinson's Disease via eye scans (featured by a number of media outlets including Forbes).

Damon Lamb, PhD
Assistant Professor
Department of Psychiatry
Member, CAM Center
Health Research Scientist at the Brain Rehabilitation Research Center at the Malcom Randall VAMC

Despite the continuing challenges of the COVID-19 pandemic and the concomitant research hold, our research project investigating a putative treatment for age related memory loss, evaluated in an amnestic mild cognitive impairment cohort, is almost completed. So far, this NIH NIA R21 study has had promising results, with measure of activity in brain regions and networks important for learning memory improved with stimulation, and follow-up grants have been submitted. The large DARPA funded project investigating implanted vagus nerve stimulation for memory and learning enhancement via targeted neuroplasticity modulation is nearing completion. This project, a collaboration led by Dr. Otto in collaboration with Drs. Bizon, Setlow, Burke, has produced several interesting findings currently being prepared for publication. Follow up projects and proposals are in development or submitted, and one has already been funded.

Andrew Maurer, PhD
Assistant Professor
Department of Neuroscience
Member, CAM Center

We have advanced our research program focused on understanding how activity moves across the brain to support cognition and how this process changes with age. We completed an published a manuscript describing wave dynamics in the young rat brain (Sheremet et al., 2020) and are now conducting the experiments to extend these studies to the aged brain.

Mr. Nicholas DiCola, a shared graduate student with Dr. Sara Burke, has completed data acquisition and analysis and is preparing two manuscripts seeking to investigate how energy propagation and distribution is altered in the aging brain during sleep and behavior.

I published a manuscript presenting a novel theory of hippocampal function in *Trends In Cognitive Sciences* (*Impact Factor 15.4*).

Eric Porges, PhD
Assistant Professor
Department of Clinical Health Psychology
Member, CAM Center

In the past year, we have continued our work in cognitive aging in two primary areas. First, we are exploring both the acute and persistent impacts of non-invasive transcutaneous vagus nerve stimulation in normal aging and other populations to investigate the potential utility of the approach as a neuromodulatory cognitive intervention. The funds from the McKnight Brain Research Foundation have been used to support the collection of a normal aging cohort to complement the NIH/NIA funded study of older adults with mild cognitive impairment. Results from this ongoing project were recently presented at the 2020 Alzheimer's Association International Conference by collaborator John Williamson where we reported changes in task-free fMRI functional connectivity in the salience network as a result of vagus nerve stimulation.

Vagus nerve stimulation is also being applied by our group in normal aging to explore the potential of this neuromodulation approach to improve sleep architecture and next day cognitive function. In this ongoing study, participants are cognitively assessed at baseline, then provided with vagus nerve stimulation at the time of sleep initiation, and the following day, follow up cognitive assessments are collected. As part of a multi-cohort study, MBRF funds have allowed for the collection of normal aging adults in this protocol.

The transcutaneous vagus nerve stimulation approaches described above are now being brought into alignment with Drs. Burke and Bizon's rodent model work with the same methodology. We have begun adapting their memory tasks and our stimulation approach for use in normal aging adults.

In the second area, we are using edited magnetic resonance spectroscopy (MRS) to explore age related changes in low concentration neuro-metabolites and their functional implications. Using this approach, we have characterized the trajectory of cortical GABA (the principal inhibitory neurotransmitter in the central nervous system) concentrations across the lifespan. The McKnight Brain Aging Registry study has allowed for the integration of cognitively intact participants, 85 years of age and older into this characterization. This has revealed that our previously published, linear age-related decrease, behaves asymptoticly when this cohort is included.

We are also applying edited MRS to look at age related changes in glutathione (the most plentiful endogenous antioxidant in the brain) and its cognitive and functional applications. This investigation has been done in collaboration with Dr. Rachael Seidler at the University of Florida whose work primarily focuses on mobility. This collaboration has allowed us to document an increase in glutathione in normal aging compared to what has been seen in both younger populations and older adults with pathology. Further increasing glutathione concentrations, in a normal aging cohort, are associated with worse functional performance (pegboard and walking). These promising results are currently under review and have enabled for Dr. Seidler and I to apply for an NIA/NIH R01 extension of this work into explicitly include a memory and cognition focus.

Alexis Simpkins, MD, PhD, MSCR, FAHA
Clinical Assistant Professor
Department of Neurology
Member, CAM Center and Clinical Faculty Mentee (Woods,Cohen)

During the calendar year between December 2019 and December 2020, several projects related to aging and cerebrovascular disease were accomplished. I worked in collaboration with Dr. Adam Woods using data from patients within the ACTIVE study. This translational project investigated signatures of miRNA from exosomes isolated from serum in patient's pre-mild cognitive impairment correlates with white matter hyperintensities on MRI. An abstract with our findings was presented at the American Academy of Neurology in April 2020. We found an association between miRNA transcripts and white matter hyperintensities in aging patients pre-cognitive decline that suggests that inflammation plays a role in the early pre-symptomatic state of white matter disease.

In addition, in collaboration with the institutional Clinical Translational Science Institute (CTSI) and Sepsis Aging Research group at the University of Florida, I have presented and mentored projects on vascular cognitive impairment and effects of aging on cardiac markers of stroke. I was awarded a junior investigator award for the at the HEADS-UP pre-symposium of the International Stroke Conference on research project demonstrating health care disparities in trends in vascular dementia diagnosis in patients included in the National Inpatient Sample. Also, I mentored 2 resident projects presented at international conferences. Dr. Aisha Elfasi's abstract was accepted as a moderated poster for the In-hospital treatment & vascular cognitive impairment session of the International Stroke Conference, February 2020, and Dr. Natalie Buchwald's abstract on regional differences in hospital setting and insurance coverage for was presented as an oral poster presentation during the Vascular Cognitive Impairment session at the International Stroke Conference February 2020. These mentored-resident led projects are part of a team science collaborative working group I independently developed for residents, fellows, and trainees that incorporates conducting research through team science and career development for stroke and cerebrovascular disease. The residents have been very productive including: multiple abstract submissions, 4 manuscripts currently under review, and 2 in published, 2 clinical translational pilot grant submissions, 4 funded medical student summer research positions through the University of Florida's NIH T35 program (provides $4,653 per student and $1,200 per student per supplies), and 3 funded internal Rosalind Heilman Memorial Research Fund proposals.

John Williamson, PhD
Assistant Professor
Department of Psychiatry
Member, CAM Center
MBRF Cognitive Aging and Memory Intervention Pilot Core Awardee

Since the last reporting period, we have advanced several scientific initiatives consistent with the MBRF mission. We have joint MBRF funding (Oct 2019 start) with the University of Arizona MBI (Dr. Alexander Co-PI) to determine the effects of a non-invasive form of vagus nerve stimulation technology called transcutaneous vagus nerve stimulation (tVNS) on learning and neuroplasticity when paired with a cognitive training program. This initiative includes MRI based indicators of neuroplasticity (metabolic and functional) as well as a month follow-up assessment for retention. Slated to be carried out in 40 older adults (20 at UF and 20 at UA), we have meet with the UA team at their MBI, carried out training in the administration of the protocol and use of tVNS,

purchased the stimulators, and supplies, built custom blinding boxes for sham control (Lamb, co-investigator) and received IRB approval for the protocol. We have also piloted all methods. Due to COVID, we have delayed starting the project. UA was recently granted approval for their research re-entry plan and they anticipate resuming laboratory activities shortly. At UF, we have been recruiting participants (phone screens) for the past month and anticipate enrolling participants in January. With the year extension provided by MBRF, this puts us on course to achieve the aims of the project.

Related to the development of tVNS as a tool in older population, work continues with our NIA funded R21 project designed to determine the effects of tVNS on brain activity and cognitive performance during stimulation related to Alzheimer's disease progression in people with mild cognitive impairment. I was invited to present results from this project at the Alzheimer's Disease International Conference and presented as part of a featured symposium on the role of the locus coeruleus and nor-adrenergic interventions in AD. I presented data demonstrating tVNS caused changes in resting state derived default mode and salience network within network strength and independence, results we interpreted to be indicative of relevant target engagement for the technology. These results will be submitted for publication shortly (sample size = 40). Data acquisition now continues, after cessation due to COVID, with an anticipated completion date of mid 2021 (sample size target = 60).

Within the VA, I started a Merit Review funded project (10/2019 start) designed to assess the effects of tVNS on sleep quality in patients with post-traumatic stress disorder. PTSD is a risk factor for accelerated aging. As a supplement to this project, the Brain Rehabilitation Research Center (BRRC) funded a similar design (Williamson, PI) to determine the effects of tVNS on sleep quality in older adults with history of TBI and current subjective cognitive impairment. In that study, we will be assessing morning cognitive performance and associating it with differences in sleep architecture. Sleep is an important factor in cognitive decline in aging. And, this is a potential real-world deployable application of this technology.

Using data from the MBRF funded ACTIVE project, we recently published a paper, *Cerebral metabolite concentrations are associated with cortical and subcortical volumes and cognition in older adults,* demonstrating regionally specific relationships between metabolic indicators of neuronal integrity and inflammation and key structural volumes important in cognitive aging. Further, we reported relationships of both structural and metabolic changes and cognitive performance suggesting potentially divergent mechanisms in cognitively normal older adults.

MOST IMPORTANT SCIENTIFIC DISCOVERY IN THE PAST YEAR

Jennifer L Bizon, PhD
We completed two studies on sex differences and the influence of gonadal hormones on aspects of decision making that are very sensitive to age-associated alterations. In one study published in eLife (Impact Factor, 7.0), we showed that female rats are more impulsive than male rats and that testicular hormones are at least partially responsible for the ability to delay gratification. In the second study published in Neuropsychopharmacology (Impact Factor, 7.6), we showed that gonadal hormones, and particularly estrogen, is important for females being more risk averse than males. Both papers have implications for gender differences in decision making in aging and disease. Ongoing studies will explicitly evaluate age-associated changes in gonadal hormones as a mechanism for altered decision making in older subjects.

Sara N Burke, PhD
We made the novel discovery that in aged rats with superior performance on a test of cognitive multitasking that requires simultaneous working memory and object discrimination, there is greater activation in prelimbic neurons that project to the perirhinal cortex compared to poor performers. This contributes to a growing body of work suggesting that prefrontal cortical networks may facilitate compensation.

Adam Woods, PhD
We developed and published state of the art artificial intelligence and computational neuroscience methods for predicting tDCS treatment response and dosing requirement in older adults. In addition, we have initiated one of the few ongoing studies of the impact of COVID-19 on the cognitive, mental and brain health of older adults with measurements taken prior to the outbreak of the pandemic. Finally, we have published numerous papers that provide novel insight into the neural underpinnings of cognitive aging (working memory, executive function, episodic memory, etc.), creating new opportunities for targeted interventions to remediate the cognitive aging process and prevent dementia.

Tom Foster, PhD
A rat model study, published recently in the *Journal of Neuroscience* (Smith et al., 2020), was designed to test the hypothesis that cognitive impairments due to the aging of certain brain circuits would result in compensatory use of other brain regions to solve tasks. In a water-maze beacon discrimination task, middle-aged rats were not as consistent as young rats in discriminating between two identical beacons. The investigators hypothesized that aging of the dentate gyrus, which has a key role in discriminating between objects as stimulus features overlap, is linked to age-related variability in performance on the beacon task. The researchers found that the older, cognitively impaired rats were more likely to rely on memory for the spatial location of the goal, a strategy that the researchers associated with altered gene expression in CA1, a hippocampal region involved in spatial memory. Thus, the use of different strategies and different neural circuits in older rats could provide an animal model for examining cognitive reserve and neural compensation in aging.

Yenisel Cruz-Almeida, PhD
We have found evidence to support that hypothesis that nasal administration of oxytocin can simultaneously reduce opioid abuse liability and pain in older adults.

Natalie Ebner, PhD
Elder financial exploitation constitutes a burgeoning health crisis with dramatic negative consequences for individual lives and society at large. We published unique conceptual and empirical work on the important question of cognitive and socioemotional profiling underlying particular fraud risk susceptibility in aging towards development of effective intervention approaches. We also have formed crucial connections to the North Central Florida Senior Advocacy Network that

closely works with older adults who have experienced or are at particular risk for fraud; to increase the practical impact and outreach of our scientific work.

Joseph Gullett, PhD
We completed a 1Florida Alzheimer's Disease Research Center 2019 Pilot Grant project demonstrating the ability of a multi-modal neuroimaging machine learning pipeline to predict with over 95% accuracy and specificity whether a patient with mild cognitive impairment would progress to dementia after one year. A first-author manuscript is currently being revised for submission to the *Journal of Alzheimer's Disease*.

Rougu Fang, PhD
In collaboration with Dr. Adam Woods, we used machine learning tools to understand individuality variability and predict treatment response in tDCS using machine learning.

Damon Lamb, PhD
Our research investigating vagus nerve stimulation as a putative treatment for age related memory loss showed that measures of activity in brain regions and networks important for learning memory improved in an amnestic cohort with stimulation.

Andrew Maurer, PhD
Oscillatory communication has long been thought to be the "read out" on how activity moves across brain regions. We have completed a thorough examination of this across the temporal lobe (https://pubmed.ncbi.nlm.nih.gov/32297752/) which will serve as the premise for our upcoming aging research. In addition, working with Dr. Lynn Nadel, an affiliate faculty of the Evelyn F. McKnight Brain Institute at the University of Arizona, we have developed a theory that provides a better account of hippocampal activity in terms of cognition (In press, *Trends in Cognitive Neuroscience*, Impact Factor: 14)

Eric Porges, PhD
We have found that glutathione (the most plentiful endogenous antioxidant in the brain) is elevated in the cortex of normal aging older adults. In addition, we found that transcutaneous vagus nerve stimulation in older adults with mild cognitive impairment increased functional connectivity in brain networks where deterioration predicts cognitive decline.

Alexis Simpkins, MD, PhD
In collaboration with the institutional Clinical Translational Science Institute (CTSI) and Sepsis Aging Research group at the University of Florida, I have presented and mentored projects on vascular cognitive impairment and affects of aging on cardiac markers of stroke. I was awarded a junior investigator award for the at the HEADS-UP pre-symposium of the International Stroke Conference on research project demonstrating health care disparities in trends in vascular dementia diagnosis in patients included in the National Inpatient Sample.

John Williamson, PhD

We published work demonstrating regionally specific relationships between metabolic indicators of neuronal integrity and inflammation and key structural volumes important in cognitive aging.

PUBLICATIONS* IN PEER REVIEWED JOURNALS

***Please note that publications are listed alphabetically by first author, all McKnight-funded CAM Center faculty are highlighted, and particularly noteworthy publications are outlined.**

1. Albizu A(g), **Fang R**, Indahlastari A, O'Shea A, Stolte SE, See KB, Boutzoukas E(g), Kraft JN(g), Nissim N, **Woods AJ.** Machine learning and individual variability in electric field characteristics predict tDCS treatment response. *Brain Stimulation.* Accepted October 2020.
2. Anton SD, **Cruz-Almeida Y**, Singh A, Alpert J, Bensadon B, Cabrera M, Clark DJ, **Ebner NC**, Esser KA, Fillingim RB, Montesino Goicolea S, Min Han S, Kallas H, Johnson A, Leeuwenburgh C, Liu AC, Manini TM, Marsiske M, Moore F, Qiu P, Mankowski RT, Mardini M, McLaren C, Ranka S, Rashidi P, Saini S, Sibille KT, Someya S, Wohlgemuth S, Tucker C, Xiao R, & Pahor M (in press). Innovations in geroscience to enhance mobility in older adults. *Experimental Gerontology, 142*, https://doi.org/10.1016/j.exger.2020.111123. 2020.
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10. Caulfield K, Indahlastari A, Nissim N, Lopez J, Fleishmann H, **Woods AJ**, George M. Electric

Field Strength from Prefrontal tDCS Determines Degree of Working Memory Response: A Potential Application of Reverse-Calculation Modeling? Neuromodulation: Technology at the Neural Interface. Accepted November 2020.

11. Clark DJ, Manini TM, Ferris DP, Hass CJ, Brumback BA, **Cruz-Almeida Y**, Pahor M, Reuter-Lorenz PA, Seidler RD. Multimodal Imaging of Brain Activity to Investigate Walking and Mobility Decline in Older Adults (Mind in Motion Study): Hypothesis, Theory, and Methods. Front Aging Neurosci. 2020 Jan 8;11:358. doi: 10.3389/fnagi.2019.00358. eCollection 2019.

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PUBLICATIONS (OTHER)

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2. Hupfeld KE, Hyatt HW, Jerez PA, Mikkelsen M, Hass CJ, Edden RAE, Seidler RD, **Porges EC**. In vivo brain glutathione is higher in older age and correlates with mobility. *BioRxiv*, 2020.10.14.339507. 2020.
3. Murphy AJ, **JB Williamson**, **DG Lamb**. Neuroscience of Aging, in Encyclopedia of Gerontology and Population Aging, D. Gu and M.E. Dupre, Editors. 2020, Springer Nature Switzerland AG: Switzerland
4. Murphy AJ, **JB Williamson**, **DG Lamb**. Mild Cognitive Impairment, in Encyclopedia of Gerontology and Population Aging, D. Gu and M.E. Dupre, Editors. 2020, Springer Nature Switzerland AG: Switzerland
5. Orlando JI, Fu H, Breda JB, van Keer K, Bathula DR, Diaz-Pinto A, **Fang R**, Heng PA, Kim J, Lee J, Lee JP, Liu G, Hrvoje Bogunovic. REFUGE Challenge: A unified framework for evaluating automated methods for glaucoma assessment from fundus photographs. Medical image analysis, 59, p.101-570. 2020.
6. **Porges EC**. Autonomic Nervous System. *Encyclopedia of Gerontology and Population Aging. 2020*. New York, NY: Springer Science
7. **Porges EC**, Jensen G, Foster B, Edden R, Puts N. The trajectory of cortical GABA levels across the lifespan: An individual participant data meta-analysis of edited MRS studies. *BioRxiv,* 2020.07.23.218792. 2020.
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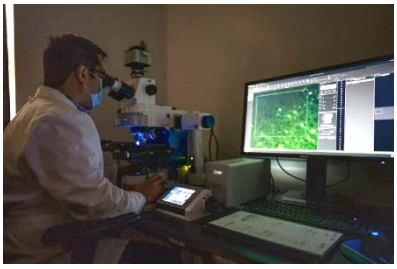
9. Robledo EA, Schutzman R, **Fang R**, Fernandez C, Kwasinski R, Leiva K, Perez-Clavijo F, Godavarty A. Physiological wound assessment from coregistered and segmented tissue hemoglobin maps. JOSA A. 2020 Aug 1;37(8):1249-56.
10. Stolte S, **Fang R**. A Survey on Medical Image Analysis in Diabetic Retinopathy. Medical Image Analysis. 2020 May 30:101742.
11. Shen Y, Sheng B, **Fang R**, Li H, Dai L, Stolte SU, Qin J, Jia W, Shen D. Domain-Invariant Interpretable Fundus Image Quality Assessment. Medical Image Analysis, 61, p.101654. 2020.
12. Tian JG, Gurley KR, Diaz MTU, Fernandez-Caban PL, Masters FJ, **Fang R.** Low-rise gable roof buildings pressure prediction using deep neural networks. Journal of Wind Engineering and Industrial Aerodynamics, 196, p.104026. 2020.





INVITED PRESENTATIONS AT SCIENTIFIC MEETINGS

Bizon JL *Seminar.* "Targeting E/I dysregulation to improve age-associated cognitive decline". 2020. University of Kansas Medical School, Department of Cell Biology Colloquium Series

Bizon JL *Discussant.* "Second workshop on research definitions for reserve and resilience in cognitive aging and dementia." 2020. 2nd workshop on reserve and resilience. Virtual.

Bizon JL *Symposium*. "Discrimination learning and spatial navigation in rat models of cognitive aging", "iNAV 2020, 3rd *Interdisciplinary* Navigation Symposium. Virtual.

Bizon JL *Symposium*. "Neural Mechanisms of cognitive aging", Winter Conference on Brain Research, Big Sky, Montana 2020.

Burke SN *Symposium*. "Perirhinal Cortical Contributions to Age-related Cognitive Decline" Ruhr-Universität Bochum IGSN – Symposium Online. 2020.

Burke SN *Seminar.* "The effects of long-term ketosis in a rodent model of cognitive aging" University of Florida Nutrition Themed '*Virtual*' Seminar Series. 2020.

Burke SN *Seminar*. "An Integrative Approach to Understanding and Treating Cognitive Aging*"* University of Texas at Austin, Behavioral Neuroscience. 2020 '*Virtual*' Seminar.

Burke SN *Symposium*. Winter Conference on Neural Plasticity. Impact of Neurometabolism on Cognitive Health. 2020. Organizer, chair, and speaker

Woods AJ *Lecture*. Remediating age-related cognitive and physical decline with transcranial direct current stimulation (tDCS). 2020 Padua Muscle Days Conference, Padova, Italy, November 20th 2020.

Woods AJ *Lecture*. The impact of Fermented Papaya Product (FPP) on cognitive and brain function in older adults: a pilot clinical trial. 2020 Padua Muscle Days Conference, Padova, Italy, November 19th 2020.

Woods AJ *Symposium*. Enhancing cognition in older adults with tDCS and cognitive training. In: Updates on Transcranial Direct Current Stimulation (tDCS): Applications and Mechanisms. NYC Neuromodulation 2020 Online, April 20th 2020.

Woods AJ *Symposium*. Neuromodulation of Cognition in Older Adults: From behavior to imaging and machine learning. NYC Neuromodulation 2020 Online, April 21st 2020.

Woods AJ *Symposium*. Remediating working memory in older adults with tDCS and cognitive training: a pathwaw to precision medicine. International Neuropsychological Society Meeting, Denver CO, February 7th 2020.

Woods AJ *Lecture*. A pathway to precision medicine for transcranial direct current stimulation. Pre-INS GATOR Conference. Beaver Creek, CO, February 4th 2020.

Foster TC *Symposium***.** Exosomes. Shock Society 2020 Annual Conference. 2020.Toronto Canada

Foster TC *Seminar***.** The senescent synapse: From membrane to nucleus. Institute on Aging, 2020. University of Florida.

Foster TC *Symposium.* Transcriptional markers of brain maintenance and cognitive reserve during aging for the 4th (Virtual) Neural Engineering Symposium, the Institute for Neural Engineering at the University of Miami.

Foster TC *Colloquium***.** The senescent synapse: From membrane to nucleus. 2020. University of Wisconsin-Milwaukee, Milwaukee Wisconsin.

Foster TC Colloquium**.** The senescent synapse: From membrane to nucleus. 2020. Augusta University, Augusta Georgia.

Ebner NC *Seminar*. Research on exploitation risk in aging. bimonthly meeting of the North Central Florida Senior Advocacy Network, zoom.

Ebner NC *Lecture.* Aging online: Rethinking adulthood and aging in an unsafe digital era*.* "Stopping Financial Exploitation: Florida On the Forefront", sponsored by The Elder Law Section of the Florida Bar Academy of Florida Elder Law Attorneys Elder Care of Alachua County Elder Options North Central Florida Senior Advocacy Network, Gainesville, FL, USA. 2019

Ebner NC *Symposium*. Other authors: *Horta, M., *Ziaei, M., *Lin, T., Porges, E. C., Fischer, H., Feifel, D., Spreng, R. N. 2020. "Oxytocin alters pattern of brain activity and amygdalar connectivity by age during dynamic facial emotion identification". North Central Florida Society for Neuroscience Conference, Gainesville, FL

Fang R *Symposium.* Transfer Generative Adversarial Net- work for Multimodal CT Image Super-Resolution, in SPIE Medical Imaging, Houston, Texas.

Maurer AP *Lecture***.** Investigating the look-ahead and oscillations in the hippocampus. 2020. Buzsaki laboratory, New York University.

Maurer AP *Seminar*. Using "Model-Result" Interactions to Understand Hippocampal LFP: Implications for Cognitive Disorders. 2020. University of California Irvine.

Maurer AP *Symposium*. Higher order theta harmonics account for slow gamma. 2020. Winter Conference on neuroplasticity, St. Kitts.

Maurer AP *Symposium*. Stability and Plasticity in Hippocampal and Cortical Networks. 2020. Winter Conference on Brain Research, Big Sky, Montana

Maurer AP *Symposium*. Rhythms on the Slope. 2020. Winter Conference on Brain Research. 2020. Big Sky, Montana

Simpkins A *Lecture*. Power to End Stroke Initiative, Student National Pharmaceutical Association-Gainesville Chapter (2020), Gainesville, Florida

Simpkins A *Symposium*. Posterior Circulation Strokes: Challenges in Recognition and Diagnosis of Acute Stroke from Vertebrobasilar Disease for the American Heart Association

Simpkins A *Presentation*. Florida Stroke Registry Stakeholders Meeting- Florida Stroke Registry, Zoom meeting presenting site Miami Florida.

Simpkins A *Lecture*. NIH Vascular Neurology Clinical Fellow Educational Lecture Series, NINDS Stroke Branch, NIH, Bethesda, Maryland

Simpkins A *Seminar*. Masters of Clinical Research Contemporary Topic Seminar Series, Medical College of South Carolina, Charleston, South Carolina

Williamson JB *Lecture.* Other authors: **Lamb DG, Porges E**, Murphy A, **Cohen R**, DeKosky S. Transcutaneous vagal nerve stimulation effects on the salience network in patients with amnestic mild cognitive impairment. 2020 Alzheimer's Association International Conference

Williamson JB *Lecture*. Other authors: **Lamb DG, Porges EC**, Murphy A, Cohen RA, DeKosky S. Transcutaneous vagal nerve stimulation effects on the salience network in patients with amnestic mild cognitive impairment. Alzheimer's Association International Conference, Amsterdam (presented virtually due to COVIS-19).

Williamson JB *Symposium*. Neuromodulation of cognition in aging and dementia (2020). American Psychological Association Annual Conference, Washington D.C.

Williamson JB *Lecture*. Visual neglect and visuospatial disorders. (2020). Annual meetings of the Florida Society of Neurology.

PRESENTATIONS AT PUBLIC (NON-SCIENTIFIC) MEETINGS OR EVENTS

1. Perez E, Frazier I, Lighthall N, & **Ebner NC.** (March, 2020). *Face forward: Age differences in decisions to trust during a social version of the Iowa Gambling Task.* Poster at the Conference of the Scientific Research Network on Decision Neuroscience and Aging, Oahu, Hawaii, USA.
2. Pehlivanoglu D, Lin T, Turner G, Spreng NR, & **Ebner NC.** (February, 2020). *Other-age effect in perceptions of facial trustworthiness.* Poster at the Annual Institute for Learning in Retirement Student Research on Aging Poster Competition and the Robert Levitt Awards at Oak Hammock, Gainesville, FL, USA.

FACULTY AWARDS AND RECOGNITIONS

Jennifer Bizon, PhD
2019 Exemplary Teaching Award, University of Florida College of Medicine
2017-2020 University of Florida Research Foundation Professorship
2020 Biomedical sciences nominee for university mentor of the year award
2020 Fellow, Hedwig van Amerigen Executive Leadership in Academic Medicine

Sara Burke, PhD
2019 Exemplary Teaching Award, University of Florida College of Medicine
2020 University of Florida Term Professorship
2020 Selected for the 2021 College of Medicine Leadership Program

Andrew Maurer, PhD
2020 Exemplary Teaching Award, University of Florida College of Medicine

Adam Woods, PhD
2020 Excellence in Research Mentorship Award, Dept. of Clinical and Health Psychology, University of Florida (2020)
2018-2020 UF Preeminence Term Professor
2020 Named Associate Editor at Frontiers in Aging Neuroscience
2020 Named to the Editorial Board of Contemporary Clinical Trials

John Williamson, PhD
2020-23 UF Preeminence Term Professor

Alexis Simpkins, MD, PhD
2020 Fellow, American Heart Association
2020 Kudos for clinical care, University of Florida
2020 HEADSUP Junior Investigator Travel Award, International Stroke Conference



TRAINEES IN MBRF-FUNDED LABORATORIES

Trainees are listed by (Mentor) Trainee Name

A. POST-DOCTORAL

(Bizon) Mojdeh Faraji, PhD
(Burke) Carly Logan, PhD
(Woods) Aprinda Indahlastari, PhD
(Woods) Stacey Alvarez-Alvarado, PhD, *NIA Diversity Supplement to REVITALIZE R01*
(Woods) Josh Crow, PhD
(Foster) Brittney Yegla, PhD
(Foster) Puja Sinha, PhD
(Foster) Linda Bean, PhD
(Cruz-Almeida) Soamy Montesino Goicolea PhD, *Advancing Minority Pain & Aging Award*
(Cruz-Almeida) Keesha Roach PhD, *NIA Pain and Aging Training Program*
(Cruz-Almeida, Ebner) Pedro Valdes-Hernandez, PhD *NIA Pain & Aging Training Program*
(Ebner) Marilyn Horta, PhD,*NIDA Substance Abuse Training Fellow Center in Public Health*
(Ebner) Tian Lin PhD
(Ebner) Didem Pehlivanoglu, PhD
(Ebner) Jill Rung, PhD, *NIDA Substance Abuse Training Center in Public Health*
(Fang) Yao Xiao, PhD
(Williamson) Erin Trifilio, PhD

B. PRE-DOCTORAL

(Bizon) Wonn Pyon, PhD student, Biomedical Sciences Program
(Bizon) Sabrina Zequeira, Master's student, Neuroscience Department
(Burke) Tara Cooper, PhD student, Biomedical Sciences Program
(Burke) Samantha Smith, PhD student, Biomedical Sciences Program
(Burke/Maurer) Nick DiCola, PhD student, Biomedical Sciences Program
(Woods) Emanuel Boutzoukas, PhD student, Clinical Health Psychology
(Woods) Hanna Hausman, PhD student, Clinical Health Psychology
(Woods) Jessica Kraft, MA, PhD student, Biomedical Sciences Program
(Woods) Nicole Evangelista, PhD student, Clinical Health Psychology
(Woods) Alejandro Albizu, PhD student, Biomedical Sciences Program
(Woods) Cheshire Hardcastle, MS, PhD student, Clinical Health Psychology
(Woods) Kailey Langer, PhD student, Clinical Health Psychology
(Woods) Furtuna Tewolde, MA, PhD student, Clinical Health Psychology
(Foster) Garrett Smith (MD/PhD program, Graduated with a PhD in Neuroscience 2020)
(Foster) Vivekananda Budamagunta, PhD student, Genetics and Genomics Program)
(Ebner) Peiwei Liu, PhD student, Department of Psychology
(Fang) Peng Liu, PhD student, Engineering
(Fang) Kyle B. See, Ph.D student, Engineering
(Fang) Skylar E. Stolte, PhD student, Engineering
(Lamb) Robert Claar, PhD student, Clinical Health Psychology
(Lamb) Binh Nguyen. PhD student, Biomedical Sciences Program (co-mentored)
(Maurer) Jack Kennedy, PhD student, Biomedical Sciences Program
(Maurer) Doug Miller, PhD student, Biomedical Sciences Program
(Maurer) Yuchen Zhou, PhD student, Engineering Program
(Maurer) Yu Qin, PhD student, Engineering Program
(Porges) Destin Shortell, PhD student, Clinical Health Psychology
(Porges) Mark Britton, PhD student, Clinical Health Psychology
(Porges) Kathleen Hupfield, PhD student, Clinical Health Psychology
(Porges) Brittany Rohl, PhD student, Clinical Health Psychology

(Porges) Jason DeFelice, PhD student, Clinical Health Psychology
(Williamson) Sarah Bottari, PhD student, Clinical Health Psychology
(Williamson) Alexandrea O'Neal, PhD student, Clinical Health Psychology

C. OTHER MENTORED LAB MEMBERS

FACULTY

(Bizon) Matt Burns, MD,PhD, Fellow, NIA K08 at council review.
(Bizon/Burke) Argyle Bumanglag, PhD., Research Assistant Professor
(Burke) Carolina Maciel, MD
(Burke/Bizon) Karina Alviña, PhD
(Foster) Ashok Kumar, PhD, Research Associate Professor
(Foster) Asha Rani, Technician in Neuroscience
(Cruz-Almeida/Ebner) Meredith Berry, Assistant Professor, K01 scored at 9th percentile

RESIDENTS

(Simpkins) Natalie Buchwald, MD
(Simpkins) Aisha Elfasi, MD
(Simpkins) Justin De Prey, MD

SELECTED UNDERGRADUATES RESEARCHERS

(Bizon) Lindsay Altidor, Undergraduate
(Bizon) Alara Guvenli, Undergraduate
(Burke) Elena Garcia, Undergraduate
(Burke) Caroline Garcia, Undergraduate
(Burke) Maya Barrett, Undergraduate
(Woods) Ayden Dunn, Undergraduate
(Cruz-Almeida/Ebner) Elisha Myers, Undergraduate
(Lamb) Cayla Fichtel-Epstein, Undergraduate
(Lamb) Pedro Tirado, Undergraduate
(Lamb) Matthew Daniel Chertok, Undergraduate
(Lamb) Chai Ryoung Park, Undergraduate
(Lamb) Noam Amozeg, Undergraduate
(Lamb) Tikahari Khanal, Undergraduate
(Lamb) Aditi Venkatesh, Undergraduate
(Porges) Alexa Heilman, Undergraduate
(Porges) Matthew Jernigan, Undergraduate
(Porges) Tommy Lee, Undergraduate
(Williamson) Sarah Olshan, Undergraduate

POST-BACCALAUREATE OR MEDICAL STUDENTS

(Bizon) Josue Deslauriers, BS
(Burke) Aleyna Ross, BS
(Burke) Jonathan Thompson, BS
(Burke) Corey Watson, BS
(Williamson) Aidan Murphy, BS
(Simpkins) Rondalyn Dickens, MS
(Simpkins) Tri M Huynh, BS
(Simpkins) Niran Vijajaraghavan, BS
(Simpkins) Esther Olasoji, MS
(Fang) Shreya Verma, MS

CLINICAL/TRANSLATIONAL PROGRAMS

A. NEW PROGRAMS

Adam Woods, PhD

Augmenting Cognitive Training in Older Adults COVID Study
Through an NIA Supplement, we are now following the ACT cohort for 9 months with monthly evaluations of cognition, mental health and a 9-month brain imaging and COVID antibody test to assess the impact of social isolation and COVID infection on older adults mental health and cognition.

Leveraging machine learning/artificial intelligence to predict treatment response to tDCS and cognitive training in older adults and design precision dosing approaches. New collaboration with junior CAM faculty member Ruogu Fang and my lab has resulted in exciting developments of algorithms for predicting treatment response in older adults and custom individualized dosing of tDCS for optimization of outcomes. A new R01 submitted by me and Dr. Fang received a fundable score and we anticipate funding in April of 2021.

Preventing Alzheimer's Disease with Cognitive Training: the PACT Trial. Dr. Woods will be leading a study site on the recently NIA funded PACT trial that will enroll over 7600 healthy older adults across the United States. This will be the largest trial of cognitive training in history with the goal of directly determining whether cognitive training can prevent the onset of Alzheimer's disease.

Tom Foster, PhD

A multi-PI proposal has been submitted to NSF AI Institute: Advancing Neurobiology of Learning across the Lifespan, which would to use artificial intelligence and machine learning to examine learning and memory across the lifespan. This will include studies to identify age-related change in strategy selection and to link cognition to brain activity and gene expression.

Natalie Ebner, PhD

We currently have one R01 pending that directly follows up on findings from our multi-institute MBRF intervention pilot study. This application investigates the specific neurocognitive and socioaffective mechanisms underlying learning to trust among older adults; and uses computational modeling of behavioral and neuroimaging data; as well as applies the novel intervention technique of real-time functional magnetic resonance imaging guided neurofeedback to promote learning to trust in older adults, with the longer-term goal to reduce fraud victimization in aging.

B. UPDATE ON EXISTING CLINICAL STUDIES

Adam Woods, PhD

Augmenting Cognitive Training in Older Adults COVID Study
Through an NIA Supplement, we are now following the ACT cohort for 9 months with monthly evaluations of cognition, mental health and a 9-month brain imaging and COVID antibody test to assess the impact of social isolation and COVID infection on older adults mental health and cognition.

Leveraging machine learning/artificial intelligence to predict treatment response to tDCS and cognitive training in older adults and design precision dosing approaches. New collaboration with junior CAM faculty member Ruogu Fang and my lab has resulted in exciting developments of algorithms for predicting treatment response in older adults and custom individualized dosing of tDCS for optimization of outcomes. A new R01 submitted by me and Dr. Fang received a fundable score and we anticipate funding in April of 2021.

Augmenting Cognitive Training in Older Adults: ACT
ACT is a multisite phase III randomized clinical trial testing the benefits of transcranial direct current stimulation for cognitive training gains in older adults (n=360). This study is a $5.8 million R01 funded across 3 McKnight sites: UF, University of Arizona, and University of Miami. The trial began 9/1/16 and is currently enrolling participants. This is the largest tDCS trial in history and the first multi-McKnight site clinical trial. 325 participants have been randomized to date.

REVITALIZE: Revitalizing Cognition in Older Adults at Risk for Alzheimer's Disease with Near-Infrared Photobiomodulation
This five-year R01 multisite Phase II randomized clinical trial will investigate the impact of near-infrared (NIR) photobiomodulation, a form of non-invasive brain stimulation, on cognition and mitochondrial function in older adults at risk for Alzheimer's disease. University of Florida (parent site) and the University of Arizona will perform a six-week intervention using NIR and assess changes in cognition, functional brain response and mitochondrial function (31P magnetic resonance spectroscopy) before, immediately post-intervention, and 3 months post-intervention in a population of 168 older adults.

EXCITE: Enhancing Cognition in Older Adults with Intermittent Hypoxia and Cognitive Training
This two-year pilot study investigates the potential impact of intermittent hypoxia, a non-invasive method shown to increase serotonin driven neuroplasticity, paired with cognitive training for remediating cognitive decline in older adults. This study is a collaborative effort between Drs. Woods, Gordon Mitchell, Steven DeKosky, and Ron Cohen. Data collection has been completed and an R01 submission is currently in preparation.

Cerebral networks of locomotor learning and retention in older adults
This four-year Merit application extends the ongoing collaborative work in R21AG053736 to investigate the impact of tDCS paired with complex walking as an intervention for mobility decline in older adults to a larger Phase II trial with increased mechanistic insight through multimodal neuroimaging. The project started in April of 2019. Enrollment is underway.

PROACT: Understanding Pain and Limitations in Osteoarthritic Disease
The goal of this project is to evaluate transcranial direct current stimulation and mindfulness-based stress reduction, alone and in combination, as treatments of chronic osteoarthritic knee pain in older adults in a two site phase II clinical trial. The project started in April of 2019, 360 participants at the University of Florida and University of Alabama at Birmingham will participate. Enrollment is underway at both sites.

Planning an adaptive clinical trial of cognitive training to improve function and delay dementia
This two-year U01 project will develop the infrastructure for a large Phase II/III clinical trial investigating the impact of various forms of cognitive training on functional abilities and dementia conversation in patients with mild cognitive impairment. I will lead the UF site on this trial and will also lead the neuroimaging and data management for the pilot trial and in the subsequent full trial submission. This grant involves sites at University of South Florida (parent site), University of California San Francisco and the University of Florida. All participants have been randomized and are currently completing training and follow-up visits. We anticipate submission of an R01 to extend the study in the next grant cycle.

Near infrared brain stimulation in older adults.
The goal of this funding is to use near infrared brain stimulation to improve cognition, 31P MRS markers of ATP, and functional neuroimaging biomarkers of cognitive and metabolic decline in healthy aging in a 2-site phase II pilot trial. Data collection in the pilot is ongoing. An R01 based on this study design is funded and underway (Revilatize)

Neuromodulation of Cognition in Older Adults: The Stimulated Brain Study
This study is a funded off of a K01 awarded to Dr. Woods and builds on the prior Stimulated Brain study funded as a CAM pilot. This study serves as a dose response study building off of the ACT study. It will enroll 80 older adults into a four arm Phase II randomized clinical trial investigating an abbreviated intervention dose of tDCS and cognitive training, as compared to ACT. 30 participants have been recruited and randomized in the study over the past 6 months. The study is currently winding down with several initial papers already published.

The UPFRONT Study
The UPFRONT study is an NIA-funded R21 phase 2 RCT investigating enhancement in mobility and executive function in older adults using combined tDCS and complex walking intervention in 60 older adults. Based on this project, we have a new VA Merit grant extending this work into a larger population. The first two papers from this study have been published this year.

Mechanism and dosimetry exploration in transcranial electrical stimulation using magnetic resonance current mapping methods
This project is an NIMH Brain Initiative funded RF1 (4 year R01) that will pioneer an objective measure of current flow in the brain using state of the art magnetic resonance imaging methods combined with in scanner application of tDCS and tACS. This project will also assess the relationship between activation in working memory related regions from an NBACK fMRI task and correspondence of change following F3-F4 in scanner tDCS. This project will provide an invaluable tool for titrating tDCS dose in our clinical interventions. This project is in its final year.

Stimulating Theta Oscillations to Enhance Working Memory
This project is a NIMH Brain Initiative funded R21 that will evaluate the impact of transcranial alternating current stimulation (tACS) on working memory network synchrony in the theta band of EEG using electrophysiology and functional magnetic resonance imaging. This study may provide a novel method for improving working memory in older adults. This study is complete and currently in a no cost extension while manuscripts and a follow up grant are prepared.

Tom Foster, PhD

We continue to employ epigenetic techniques to establish epigenetic biomarkers of cognitive function. In this case, machine learning was combined with blood measures of microRNA, brain volume, clinical (comorbid conditions), and demographic variables in older adults. We identified microRNA that predict cognition and are linked to aging and inflammation, supporting idea that microRNA can act as an epigenetic marker or a mechanism underlying differential ageing that contributes to cognitive decline (Gullett 2020). In addition, we continue to work with the MBAR to propose studies on blood based biomarkers of cognition and brain function.

We have an ongoing collaboration with Yenisel Cruz-Almeida on a project to examine chronic pain, cognition, and epigenetic markers in older adults. The interindividual variability in aging has motivated research efforts to measure aging processes using ‘aging biomarkers’ that are better predictors of disease risk and residual lifespan when compared to chronological age alone. Emerging research using the epigenetic clock as an aging biomarker supports highly reliable individualized predictions about future health and function. In 2020, we received NIH funding (Cruz-Almeida, PI) to continue this work.

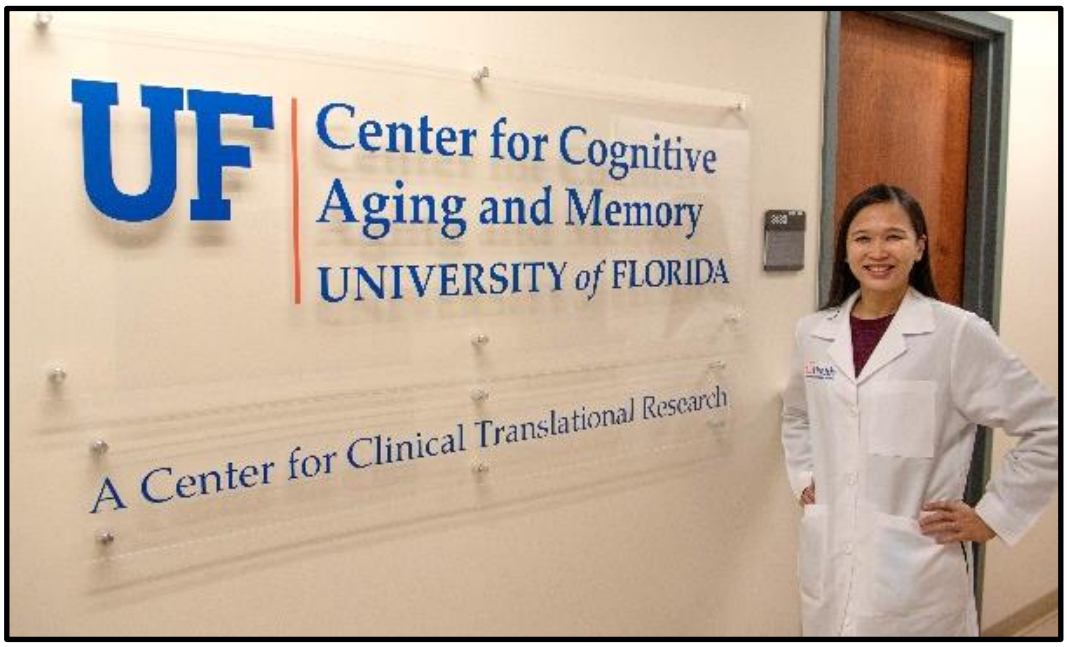
We continue ongoing collaborations Departments of Medicine, Aging and Geriatric Research, Surgery, Biostatistics and Clinical and Health Psychology, to seek support for studies examining inflammation as a mechanism for variability in cognitive decline, particularly in older sepsis survivors. A multi-PI grant was submitted to examine how persistent inflammation drives chronic critical illness in sepsis survivors. The proposal was scored, but not funded. Project 4 (Foster PI) received the best score and a revised proposal will be submitted in 2021. While we cannot address one concern regarding the need for brain imaging, if the revised proposal is funded, we will seek further funding to related cognitive function to brain imaging.

John Williamson, PhD

With Drs. DeKosky, Cohen, Porges, and Lamb via funding from the NIA, we continue work on the development of tVNS to modify brain and cognitive functions in patients with mild cognitive impairment.
Further, related to my VA work, Drs. Kevin Wang and I have submitted a grant through the DOD (currently pending) to determine biomarkers associated with cognitive decline/accelerated aging in people with history of traumatic brain injury.

In collaboration with Drs. Cohen and Porges, we continue work on aging and cognitive changes associated with microbiome differences in patients with HIV.

In collaboration with Drs. Cohen and Porges, we continue to execute the WISE study on the effects of bariatric surgery on brain health and cognition. We have several results from this study accepted for presentation at an upcoming International Neuropsychological Society conference and these will be developed as manuscripts over the next year.



a. PATENTS/APPLICATIONS

1) **Williamson, John Bonar**; **Lamb, Damon Geoffrey; and Porges, Eric S. Carter**. "System and method for monitoring and controlling nervous system behavior using autonomic features." U.S. Patent No. 10,426,956. 1 Oct. 2019. In 2020, this was licensed by Evren Technologies of Newberry Florida, a UF spinoff company received an Small Business NIH grant (SBIR) in 2020 to further develop the technology.

2) **Porges, Eric; Lamb, Damon**; Campbell Thompson, Martha; Edden, Richard. "Non-Invasive Diagnostic Biomarker for Pancreatic Islet Population." US Patent Application #16,756,489. Issued 9/24/2020.

3) Two additional focused disclosures related to brain modulation were made and the University of Florida is exercising their right to have patent submissions made. Both are currently in the process of being filed, and the content is currently embargoed.

4) **Ruogu Fang**, Yao Xiao. U.S. Provisional Patent Application Serial No. 62/983,660, filed February 29, 2020. Multimodal CT image super-resolution via transfer generative adversarial network. Ref no.: entity status: t17996us001 (222107-8690)

5) Peng Liu and **Ruogu Fang**. U.S. Provisional Patent Application Serial No. 63/001,771, filed March 30, 2020. Cfea: collaborative feature ensembling adaptation for domain adaptation in unsupervised optic disc and cup segmentation. Inventor(s): ref no.: t18094us001 (222107-8940)

6) **Ruogu Fang** and Jianqiao Tian. U.S. Provisional Patent Application Serial No. 63/032,018, filed May 29, 2020. A machine learning system and method for predicting alzheimer's disease based on retinal fundus images., T18201US001 (222107-8215).

7) **Adam J. Woods, PhD;** Aprinda Indahlastari, PhD; Alejandro Albizu; **Ruogu Fang, PhD**. U.S. Provisional Patent Application Serial No. 63/057,447 filed on July 28, 2020. System and Method of Precision Dosing for Electrical Stimulation of The Brain.

8) **Ruogu Fang** and Peng Liu. U.S. Provisional Patent Application Serial No. 63/058,008 filed on July 29, 2020 Systems and Methods For Reconstructing Realisitic Noisy Medical Images. (T18195US001 (222107-8185))

9) **Ruogu Fang**, Max Diaz. U.S. Provisional Patent Application. Nov. 30, 2020. Machine Learning For Predicting Parkinson's Disease Based On Retinal Fundus Images.

b. REVENUE GENERATED FROM TECHNOLOGY

Evren Technologies received a Small Business NIH grant (SBIR) in 2020 related to the patent awarded in 2019 to Williamson, Lamb and Porges. Otherwise, no revenue has yet been generated.

BUDGET UPDATE

1) Evelyn F. McKnight Cognitive Aging and Memory Research Fund

Budgeted Amount	$	1,083,382	
Expenditures:	$	561,990	Compensation for CAM faculty
	$	64,459	T-32 Match for student training
	$	18,377	Direct Operating Expenses
	$	49,223	Equipment
	$	140,000	Supplements for NIA- funded research
	$	200,000	Pilot funds to spur collaborative research
	$	18,647	Lab Supplies
	$	14,725	Publishing
	$	15,948	Travel
Total Expenditures	$	**1,083,369**	
Variance		12	
Carryforward from prior year	$	824,455	
Balance as of 12/31/2020	$	824,467	

2) William G. Luttge Lectureship in Neuroscience

Budgeted Amount	$	10,019	
Expenditures:			
	$	1,262	Honorariums for virtual speakers
Total Expenditures	$	**1,262**	
Variance	$	8,757	
Carryforward from prior year	$	72,534	
Balance as of 12/31/2020	$	81,290	

This variance is due to the fact that we had to cancel our planned Luttge speaker due to COVID-19. As described above, a portion of the funds have been used to support a robust virtual seminar series which can be conducted safely during the pandemic.

3) Evelyn F. McKnight Chair for Brain Research in Memory Loss

Budgeted Amount	$	145,466	
Expenditures:	$	154,388	Compensation
	$	1,500	Lab Services
Total Expenditures	$	**155,888**	
Variance	$	(10,422)	
Carryforward from prior year	$	62,147	
Balance as of 12/31/2020	$	**51,725**	

The account is on track to be balanced at the end of the fiscal year. The variance is due to fluctuations in the award date versus the receipt dated of extramural funding.

4) Evelyn F. McKnight Chair for Clinical Translational Research in Cognitive Aging

Budgeted Amount	$	145,403	
Expenditures:			
	$	211,273	Compensation
Total Expenditures	$	**211,273**	
Variance		(65,870)	
Carryforward from prior year	$	29,548	
Balance as of 12/31/2020		(36,322)	

The account is on track to be balanced at the end of the fiscal year. The variance is due to fluctuations in the award date versus the receipt dated of extramural funding.

a. MATCHING FUNDS: None

b. PROJECTED BUDGET FOR COMING YEAR

1) Evelyn F. McKnight Cognitive Aging and Memory Research Fund

Budgeted Amount	$	1,083,382	
Expected Expenditures:			
	$	575,000	Compensation
	$	65,000	T-32 Match for student training
	$	20,000	Direct Operating Expenses
	$	50,000	Equipment and Lab Supplies
	$	150,000	Matching Funds
	$	200,000	Pilot funding for collaboration
	$	15,000	Publishing
	$	5,000	Travel
	$	**1,080,000**	

The budget amount is the amount of funding received from the Endowment in calendar year 2020. The expected expenditures are estimated based on the actual expenditures for calendar year 2020.

2) William G. Luttge Lectureship in Neuroscience

Budgeted Amount	$	20,000	
Expected Expenditures:			
	$	4,000	Honorariums for virtual speakers
	$	16,000	Annual Luttge Lecture (Spring 2021)
Total Expenditures	$	**20,000**	

Variance	$	8,757
Carryforward from prior year	$	72,534
Balance as of 12/31/2020	$	81,290

The budget amount includes the projected return from the endowment and use of some of the reserves. Planned expenditures include honorariums for the eight virtual speakers outlined in the report and for the annual Luttge lecture which we are currently planning for Fall 2021, pending resumption of travel and gatherings.

3) Evelyn F. McKnight Chair for Clinical Translational Research in Cognitive Aging

Budgeted Amount:	$	145,400	
Expected Expenditures:	$	145,400	**Compensation for Dr. Cohen**

The budget is based on the amount of funding received from the Endowment in calendar year 2020. This account is used for Dr. Cohen's compensation.

4) Evelyn F. McKnight Chair for Brain Research in Memory Loss

Budgeted Amount:	$	145,466	
Expected Expenditures:	$	45,000	**Compensation for Dr. Foster**
	$	100,000	**Research Activities**

The budget is based on the amount of funding received from the Endowment in calendar year 2020. This account is used for Dr. Foster's compensation and laboratory research. It is budgeted based on his expected salary on extramural grants and planned laboratory activities.

c. EXTRAMURAL FUNDING

NIH AND VA AWARDS (CAM Center Faculty as PI)

R01 AG049711 (NIH-NIA) $461,250 09/01/15 - 04/30/20
Systemic inflammation in regulating the onset and progression of brain aging-1
PI: Tom Foster

R01AG061065-03 (NIH-NIA) $381,250 06/02/20-05/31/21
Role of Gut Microbial Dysbiosis and Aging on HIV-Associated Neurocognitive and Brain Dysfunction
PI: Ron Cohen (MPIs, Barve, Cook), Co-I: Joe Gullett, Co-I John Williamson

R01 AG049722 (NIH-NIA) $37,518 01/05/16-01/15/21
The contribution of declines in functional connectivity to cognitive aging
PI: Sara N Burke Co-I: Jennifer L Bizon

1R01AG049722 (NIH-NIA) $337,658 01/01/16-11/30/21
The Contribution of Declines in Functional Connectivity to Cognitive Aging
PI: Sara N. Burke, co-I: Andrew Maurer, Jennifer L. Bizon

R01 AG052258 (NIH-NIA) $375,000 05/05/16-04/30/21

Neuroinflammation and brain aging
PI: Tom Foster

R01AG054077 (NIH-NIA) $2,207,109 09/01/16-08/31/21
Augmenting Cognitive Training in Older Adults (ACT)
MPIs: Adam Woods (MPI: Cohen, Marsiske), co-I Eric Porges, Steve DeKosky

R01DK099334-05 (NIH-NIDDK) **$**507,382 06/25/14 - 05/31/21
Obesity and Type-2 Diabetes: Bariatric Surgery Effects on Brain Function
PI: Cohen, co-I Joseph Gullett

R01AG055544 (NIH-NIA) $380,714 09/15/17-08/30/21
Age-associated changes in hippocampal circuits and cognitive function
PI: Andrew Maurer, Co-I: Sara N Burke

U01AA026225 (NIH-NIAAA) $111,015 06/01/18-08/3/21
Alcohol associated Comorbidities and Microbiome
PI: Ron Cohen (MPI: Robert Cook)

U01AA020797 (NIH- NIAAA) $946,319 06/01/18-08/3/21
Effects of experimentally induced reductions in alcohol consumption on brain cognitive and clinical outcomes and motivation for changing drinking in older persons with HIV infection.
PI: Ron Cohen (MPI: Robert Cook)

R01MH109548 (NIH-NIMH) $437,016 04/01/17-01/31/22
Testing and forecasting hippocampal theta wave propagation in learning and memory
PI: Andrew Maurer, Co-I: Sara N Burke and Jennifer L Bizon

R01DA042069 (NIH-NIA) $547,898 05/17/21–03/31/22
Health outcomes and cognitive effects of marijuana use among persons living with HIV/AIDS
PI: Ron Cohen (MPI: Robert Cook)

R01 AG037984-11 (NIH-NIA) $375,000 09/15/18-07/31/23
Estrogen signaling the cognition over the lifespan
PI: Tom Foster

1R01AG057764-01A1 (NIH-NIA) $322,824 09/01/18-06/30/23
Uncovering and Surveilling Financial Deception Risk in Aging
PI: Natalie Ebner (MPI: Spreng)

R01 AG059809 (NIH-NIA) $327,875 08/01/18-04/30/23
Mechanisms of Oxytocin's Analgesia in Older Adults
MPIs: Yenisel Cruz-Almeida, Natalie Ebner

RF1AG060778 (NIH-NIA) $600,932 09/01/18-08/31/23
Decision making and basolateral amygdala dysfunction in aging
PI: Jennifer L Bizon (Setlow, Frazier MPIs, co-I Burke)

RF1AG064942 (NIH-NIA) $366,000 08/15/19-03/31/24
Immunotherapy targeting the HPA axis in Alzheimer's disease
PI: Jennifer L. Bizon (Golde, Lewis MPI)

RF1AG060977 (NIH-NIA) $383,294 02/01/19-01/31/24
Metabolic Interventions for Enhancing Cognitive Resilience in Aging and Alzheimer's Disease
PI: Sara N. Burke, co-I: Jennifer L. Bizon

R01AG064587 (NIH-NIA) $764,848 08/01/19-04/31/24
Revitalizing Cognition in Older Adults at Risk for Alzheimer's Disease with Near-Infrared Photobiomodulation
PI: Adam Woods (MPIs: Bowers, Alexander)

R01 AG067757 (NIH-NIA) $566,184 07/01/20-06/30/25
Biobehavioral basis of knee osteoarthritis pain
PI: Yenisel Cruz-Almeida

P01AA019072-11 (NIH/NIAAA) $332,608 07/01/20-05/31/21
Alcohol and HIV-Associated Brain Dysfunction
Site PI: Ron Cohen Co-I: Joseph Gullett (PI: Kahler)

R21AG058240 (NIH-NIA) NCE
Interactions of perirhinal tau pathology and aging in cognitive dysfunction
MPIs: Jennifer L Bizon and Sara N Burke

R21AG054876 (NIH-NIA) NCE
Treatment of mild cognitive impairment with transcutaneous vagal nerve stimulation
PI: John Williamson, co-I Damon Lamb, Eric Porges

R21MH112206 (NIH-NIMH) NCE
Stimulating Theta Oscillations to Enhance Working Memory
PI: Adam Woods (MPI: Ding)

R21AG057200 (NIH/NIA) NCE
Determining Plasticity of Brain-Regulatory Mechanisms Related to Emotion Processing: A Neurofeedback Approach in Aging and Parkinson Disease
MPIs: Natalie Ebner and Dawn Bowers

R21AG068205 (NIH-NIA) $190,625 08/01/20-05/31/22
Age-associated impaired executive function: Rescue by NMDA receptor upregulation
PI: Ashok Kumar

VHA- Brain Rehabilitation Research Center $20,000 1/01/2020-1/01/2021
Transcutaneous vagal nerve stimulation modulation of sleep quality and cognition in older veterans with subjective cognitive impairment.
PI: John Williamson

VHA – Merit Award I01RX003140 $300,000 10/01/19-09/30/23
Transcutaneous vagal nerve stimulation improvement of sleep quality in veterans with PTSD with or without history of mild TBI
PI: John Williamson, co-I: Damon Lamb

VHA – Rehabilitation R & D I50RX003000 10/01/19-09/03/24

Developmental Funds- Brain Rehabilitation Research Center
PI: Damon Lamb (Director: Bauer)

COLLABORATIVE NIH and VA AWARDS (CAM Center Faculty as co-I)

U01AG062368 (NIH- NIA) NCE
Planning an adaptive clinical trial of cognitive training to improve function and delay dementia
Site PI: Adam Woods (PI: Edwards), Co-I: Steve DeKosky, Joseph Gullett

R01 DA036534 (NIH-NIDA) NCE
Risk taking and cocaine use: interactions, mechanisms, and therapeutic targets
Co-I: Jennifer L Bizon (PI: Setlow)

RF1MH114290-01 (NIH-NIMH) $40,658 07/19/17-07/18/21
Mechanism and dosimetry exploration in transcranial electrical stimulation
using magnetic resonance current mapping methods
Co-I: Adam Woods (PI: Seidler)

P30AG028740 (NIH-NIA) $204,026 07/01/06-03/31/22
University of Florida Claude D. Pepper Older Americans Independence Center
Leader, Pilot Core: Yenisel Cruz-Almeida; Consultant: Tom Foster (PI: Pahor)

R01NS071122 (NIH-NIDA) $417,037 09/01/18-07/01/23
Alpha-synuclein Regulates Dopamine Transporter Functions
Co-Investigator: Andrew Maurer (PI: Khoshbouei)

NIH/NIA U01 AG061389 $15,557 09/01/18-08/31/23
Multimodal imaging of brain activity to investigate walking and mobility decline in older adults
Co-I Yenisel Cruz-Almeida (MPIs: Manini, Clark, Seidler)

VA Merit Award $18,296 08/01/19-07/31/23
Cerebral networks of locomotor learning and retention in older adults
Co-I: Adam Woods (PI: Clark)

R37AG033906 (NIH-NIA) $1,292,576 06/01/19-04/31/24
Understanding Pain and Limitations in Osteoarthritic Disease
Co-I: Adam Woods (PI: Fillingim)

1R01DK123329 (NIH-NIDDK) $654,318 08/01/20-07/31/24
Understanding pancreatic endocrine and exocrine loss in pre-type 1 Diabetes
Co-Is: Damon Lamb, Eric Porges (PI: Campbell-Thompson)

INSTITUTIONAL NIH TRAINING AWARDS (CAM Center Faculty, PI)

T32 AG061892 (NIH-NIA) $176,058 9/01/18-08/31/23
Clinical and Translational Pre-doctoral Training in Alzheimer's and Related Dementias
PI: Jennifer L Bizon (Lewis, MPI)

T32AG020499 (NIH-NIA) $276,370 05/01/20-04/30/25
Research Training in Non-Pharmacological Interventions for Cognition in Aging,
MCI, and Alzheimer's Disease

PI: Adam Woods (MPIs: Marsiske, Smith)

MENTORED NIH and VA AWARDS (CAM Center Faculty, PI)

K01AG050707-A1 (NIH-NIA) $123,417 09/30/16-05/31/21
Neuromodulation of Cognition in Older Adults
PI: Adam Woods

K01 AA025306-01A1 (NIH/NIAAA) $160,729 01/01/17-01/01/22
Cognitive and functional deficits associated with reduced cortical GABA in HIV-infected heavy drinkers.
PI: Eric Porges, Mentors: Ron Cohen, Jennifer Bizon

KL2 Pepper Scholars award $60,000 11/01/20–11/01/22
Mesocorticolimbic dysfunction and modulation of cognitive and behavioral impairment in a rat model of aging and synucleinopathy.
PI: Matt Burns, Mentor: Jennifer Bizon

VHA-Rehabilitation R&D IK2RX002490 $165,000 03/01/18-02/28/23
Brain changed underlying emotional and executive alterations in TBI
PI: Damon Lamb

MENTORED AWARDS- CAM Center FACULTY SERVING AS MENTORS

K99AG058786 (NIH-NIA) $86,073 04/01/18-04/31/20
Hippocampal and dopaminergic mechanisms of novelty detection underlying cognitive resilience in aging
Mentors: Sara N Burke, Jennifer L Bizon (PI: Johnson)

NIH UF CTSI TL1 $50,000 09/01/19-08/30/21
Predicting short-term and long-term effects of spinal cord stimulation: implications for clinical practice
Mentor: Rougu Fang (Student PI: See)

KL2 TR001429 (NIH-NCATS) $24,300 04/01/19-03/31/21
Carpometacarpal Osteoarthritis: Towards Identification of Biomechanical, Neuromuscular, and Somatosensory Mechanisms
Mentor: Cruz-Almeida (Candidate PI: J. Nichols)

K22 NS102334 (NIH-NINDS) $212,065 04/01/18-03/31/23
Neural mechanisms underlying psychosocial contributions to ethnic group differences in pain
Mentor: Cruz-Almeida, (PI: E. Terry)

K01 HL153210 (NIH-NHLBI) $135,108 07/15/20-06/30/24
Contributions of biopsychosocial factors in Sickle Cell Disease pain
Mentor: Cruz-Ameida (PI: K. Roach)

F31AG071264 (NIH-NIA) $41,677 07/11/20-06/30/23
Cognitive correlates of mitochondrial function in older adults

PI: Francesca Lopez, Mentors: Adam Woods, Dawn Bowers

R01AG064587-02S1 (NIH-NIA) $66,652 06/01/20-05/30/22
Revitalizing cognition in older adults at risk for Alzheimer's Disease with near-infrared photobiomodulation: Diversity Supplement
PI: Stacey Alvarez-Alvarado, Mentors: Adam Woods, Dawn Bowers, Gene Alexander

OTHER FEDERAL FUNDING

DARPA Targeted Neuroplasticity Training $1,366,326 01/01/17-12/31/20
Cognitive Augmentation through Neuroplasticity
Project leaders: Jennifer L Bizon, Sara N Burke, Co-Is Damon Lamb & Barry Setlow (PI: Otto)

DOD DN180041 $130,000 05/01/19-04/31/22
Biomarker based precision medicine approach to traumatic brain injury subphenotypes.
Site-PI: John Williamson

NSF CISE Core Program Small $266,000 10/01/19 – 9/30/22
III: Small: Modeling Multi-level Connectivity of Brain Dynamics
PI: Ruogu Fang

NSF IUCRC Phase I $150,000 01/01/18 – 12/31/22
University of Florida: Center for Big Learning
Co-Investigator: Ruogu Fang (PI: Li)

FLORIDA DEPARTMENT OF HEALTH AWARDS

Ed and Ethel Moore Alzheimer's Disease Research Program $250,000 09/1/19-08/31/21
Effects of cannabis on Alzheimer's disease-related pathology and cognitive decline
PI: Jennifer Bizon (MPI Setlow)

Ed and Ethel Moore Alzheimer's Disease Research Program $16,000 05/29/20-06/30/21
A feasibility study of real-time monitoring of Posttraumatic Stress Disorder related sleep disturbances and other symptoms among patients on medical marijuana.
Co-Investigator: John Williamson

Ed and Ethel Moore Alzheimer's Disease Research Program $124,965 05/29/20 - 06/30/22
Determining Plasticity of Brain-Regulatory Mechanisms Related to Emotion Processing: A Neurofeedback Approach in Older Adults with Amnestic Mild Cognitive Impairment
PI: Natalie Ebner

Ed and Ethel Moore Alzheimer's Disease Research Program $125,000 04/13/20-03/31/23
Cyclic Kelogenic therapy as treatment for Alzheimer's disease.
PI: Sara Burke

EDUCATIONAL PROGRAMS FOCUSING ON AGE-RELATED MEMORY LOSS

a. SCIENTIFIC

Jennifer L. Bizon, PhD

I serve as a co- Director for an NIA-funded T32 training program for PhD students whose areas of specialization fall within brain aging and Alzheimer's disease. Currently, our specialized training program funds stipend, tuition and fees for eight students across Biomedical Sciences and Clinical Health Psychology PhD programs. Approximately half of these students are working on topics relevant to cognitive aging.

Sara N. Burke, PhD

I continue to give lectures on mechanisms of brain aging to graduate students across the UF Health Science Center.

Adam Woods, PhD

I was awarded as MPI, along with Michael Marsiske and Glenn Smith, a T32 predoc training grant titled *Research Training in Non-Pharmacological Interventions for Cognition in Aging, MCI, and Alzheimer's Disease.* This training grant will afford 6 PhD students with dedicated training in non-invasive intervention methods (behavioral, lifestyle, brain stimulation) for remediating cognitive aging and improving function in patients with MCI or AD.

I was co-Organizer of the NYC Neuromodulation Online Conference 2020. Over 1500 attendees to the conference from around the world with over 50 organized symposia across 4 days.

Eric Porges, PhD

Instructed undergraduate student class "Survey of Cognitive Science Methods". Significant focus of the class was age related functional changes. Research on cognitive aging presented by Dr. Porges, Dr. Woods, Dr. Ebner, and postdoc in Dr. Burke Lab.

Alexis Simpkins, MD, PhD

Medical Clinical Research 736 Clinical Epidemiology course; Medical College of South Carolina, 11/24/2020: Translating CYP2C19 Polymorphisms for Stroke and the Role of Team Science Building Medical Clinical Research 736 Clinical Epidemiology course; Medical College of South Carolina, December 6, 2019

c. PUBLIC

Sara N Burke, PhD

I have on two occasions worked with the MBI communications team to share my science with the lay public. The first occurred at the beginning of the year following a collaborative publication between my and Dr. Marcelo Febo's laboratories (https://mbi.ufl.edu/2020/01/06/new-imaging-study-shows-key-brain-changes-in-aging-alzheimers/). More recently, I worked with the communications team to make a video about brain aging and diet that will be available to the public in early 2021.

COLLABORATIVE PROGRAMS WITH OTHER MCKNIGHT INSTITUTES, INSTITUTIONS AND RESEARCH PROGRAMS

Jennifer Bizon, PhD

Neuro- and Geo-sciences working group (UF and UAB). Specifically, our working group includes Drs. Christy Carter, Tom Buford, Abbi Hernandez, Sara Burke and myself. While somewhat surprisingly, the fields of neuro- and gero-sciences have been somewhat parallel with little interaction. The goal of our work is to integrate mechanisms that increase longevity with approaches that can promote cognitive health. Our short-term goal is to write several reviews to outline potential opportunities across fields. Further, we have submitted a pilot project to the MBRF through the intervention core to support our collaboration and collection of pilot data for an NIH grant submission.

Sara Burke, PhD

Dr. Carol A. Barnes (UArizona) and I continue to collaborate on writing the chapter on "The Aging Hippocampus" for the next edition of the *Hippocampus* Book. Other contributors to this book include 2 Nobel Laureates (E. Moser and J. O'Keefe). When completed, this chapter will be a comprehensive summary on what is currently known about age-related changes in the cellular anatomy and function, plasticity, neuromodulation, ensemble dynamics, and gene expression of the hippocampus and how this relates to memory loss and other behavioral impairments in old age. This will be a resource for clinicians, as well as current and next generation researchers interested in age-related memory loss. Dr. Jennifer Bizon and I also have a new collaboration with researchers and UA-Birmingham to investigate the gut brain axis in aging and how this is modulated by diet and vagus nerve stimulation. In support of this endeavor, we submitted a collaborative intervention grant to the MBRF and are currently working on 2 review papers focused on the importance of bridging geroscience with neuroscience to improve cognitive outcomes in older adults.

Tom Foster, PhD

A paper, Cognitive reserve in model systems for mechanistic discovery: importance of longitudinal studies (in press) included Carol Barnes from the University of Arizona.

We continue to work with the MBAR to obtain blood biomarkers: This working group involves all four McKnight Institutions and is investigating the possibility of using blood samples from the MBAR subjects to obtain genetic and epigenetic markers of successful aging and neuroimaging data. We have had phone conversations with the MBAR group, proposed several studies, and delivered estimated costs for proposed studies.

Adam Woods, PhD

ACT study. Dr. Woods is leading the ACT Phase III multisite cognitive aging and tDCS clinical trial with sites at the University of Florida and University of Arizona. This large study is ongoing.

REVITALIZE study. Dr. Woods, along with Drs. Alexander and Bowers are leading the newly funded Phase II multisite trial for near-infrared photobiomodulation at the University of Florida and University of Arizona

The PROACT R37 NIA funded study investigating the effects of tDCS on chronic knee pain in older adults is ongoing across UF and UAB.

Two funded MBRF pilots across University of Florida and University of Arizona are currently underway.

John Williamson, PhD

Gene Alexander, Ron Cohen, Adam Woods, Eric Porges, Damon Lamb and I are working on an MBRF funded collaborative project to determine the effects of tVNS paired with cognitive training in older adults on learning and neuroplasticity.

Damon Lamb, PhD

Co-investigator on MBRF funded investigation of non-invasive Vagus Nerve Stimulation for age-related memory loss.

Natalie Ebner, PhD

This project is a collaboration with Dr. Bonnie Levin (Miami), Dr. Sarah Getz (Miami), Dr. Matt Grilli (Arizona), and Dr. Bob Wilson (Arizona).

Eric Porges, PhD

McKnight Brain Research Foundation funded McKnight Brain Aging Registry (MBAR) study of neurocognitive function in those 85 and older. (University of Florida, University of Alabama – Birmingham, University of Arizona & University of Miami).

Continued collaboration with Dr. Burke of the Age-related Memory Loss (ARML) Program, Dr. Febo at the University of Florida, and Dr. Near at McGill University. Funding was acquired from the National High Magnetic Field Laboratory and data collection is ongoing applying high field (11 tesla) magnetic resonance spectroscopy measures on a cognitive aging rodent model fed a ketogenic diet. We are exploring alterations in metabolites associated with neuroinflammation as well as inhibitory neurotransmitters in vivo.

Drs. Burke and Porges are currently aligning methods between human and rodent aging models for a paired associates learning task (memory). This will generate pilot data for a translational patent application planned for the fall.

MBI NEWS

UF neuroscientists study impact of COVID-19, social isolation on cognitive, mental health of seniors

June 29, 2020

How COVID-19 and social isolation are affecting the cognitive and mental wellbeing of older adults is the subject of a new study by UF neuroscientists.

UF postdoc to present to international audience during cognitive aging workshop

September 10, 2020

Dr. Brittney Yegla to speak at Workshop on Research Definitions for Reserve and Resilience in Cognitive Aging and Dementia.

COLLABORATIVE PROGRAMS WITH NON-MCKNIGHT INSTITUTES, INSTITUTIONS AND RESEARCH PROGRAMS

Jennifer Bizon, PhD

Dr. Barry Setlow and I have a long-standing collaboration that involves investigating neural mechanisms of cognitive decline in rodent models of age-associated cognitive decline. We currently share supervisory responsibilities of two students and one post-doctoral fellow, all of whom are primarily conducting research investigating neural mechanisms of age-related cognitive decline. We share one MPI grant to investigate decision making in aging, with a second MPI R01 scored within funding range (currently pending council review). This latter grant will investigate vagus nerve stimulation and cannabis as potential interventions for promoting cognitive resilience. A third grant was recently re-submitted for review and is focused on understanding the effects of cannabis in older adults. The latter grant also includes an expert in tau related pathology and AD, Dr. Jada Lewis and individuals from College of Pharmacy, including Dr. Jason Frazier and Dr. Chris McCurdy. Independent of Dr. Setlow, I also share an MPI R01 with Drs. Todd Golde and Jada Lewis to test whether blockade of excess corticotropin releasing hormone via a novel antibody therapy can reverse or prevent cognitive decline in aged rats.

In addition to these other collaborations, Dr. Sara Burke and I continue to advance our long-standing collaboration, and currently share 7 grants. I similarly collaborate with Dr. Andrew Maurer and am co-I on his R01 funded from NIA. As described above, Dr. Burke and I are both involved in program development with investigators at UAB as part of the Neuro- and Geo-sciences working group that is focused on understanding gut-brain axis in relation to cognition in aging.

Finally, I am working with Drs. Burke, Cohen, Woods, Porges and others to develop a cross-species programmatic grant focused on non-invasive approaches to modulate neuroplasticity and improve cognitive outcomes in aging. We are meeting weekly to discuss this large proposal and are currently in the process of generating the foundational preliminary data.

Sara N Burke, PhD

I hold a collaborative R01 (NIA) with Drs. Maurer, Bizon, Lamb, Febo and McIntyre (UF), and Dr. Brattain (MIT) to examine cellular mechanisms of functional connectivity changes in advanced age. Collaborative RF1 (NIA) and FL Department of Health grants with Dominic ‘DAgostino (University of South Florida), Drs. Jennifer Bizon, Paramita Chakrabary and Ben Giasson on modulation metabolism to improve cognitive function in old age.

I hold a collaborative NIA R01 with Drew Maurer (UF), and Dr. Kamran Diba (University of Michigan) on age-related changes hippocampal circuit dynamics.

I hold a collaborative NIA R01 with Drs. Jennifer Bizon and Barry Setlow on age-related changes in amygdala circuits.

Adam Woods, PhD

Dr. Woods has ongoing collaborations in his areas of expertise in tDCS and other non-invasive brain stimulation methods as well as neuroimaging and cognitive aging at University of Arkansas for Medical Sciences, (UAMS); University of California-San Diego, University of New Mexico, University of Miami, University of Arizona, Arizona State University, City College of New York, University of Michigan, Brown University, University of South Florida, University of California San Francisco, Imperial College London, Istanbul University, and Catholic University of Korea. In addition, Dr. Woods continues to collaborate with a large number of investigators at the University of Florida

outside the MBI, including David Clark (VA Merit grant), Mingzhou Ding (BME, R21), Christiaan Leeuwenburgh (IOA), Roger Fillingim (Dentistry), etc.

Tom Foster, PhD

This collaboration between several UF faculty (Leeuwenburgh, Esser, Febo, Foster) received funding from the Pepper Center Metabolism & Translational Sciences Core is designed to: **1)** assist junior faculty interested in aging research and **2)** promote longitudinal studies on age-related cognitive decline in order to address recommendations by the Cognitive Aging Summit III. An animal colony was established to provide for on-site aging of animals, which has contributed to investigation by junior faculty interested in aging research. For the longitudinal studies, protocols are in place to assess healthspan domains by non-invasive physical/cognitive performance tests and non-invasive technologies (fMRI). A manuscript has been published (Febo et al., 2020). The results indicate that cognitive decline varies according to sex and can be predicted by psychological measures (anxiety, response to novelty), the plasticity of circadian rhythms (similar to jet-lag), and brain functional connectivity measured using fMRI. The results mirror findings in humans and form the basis for future studies examining molecular mechanisms and testing of treatments.

Collaborations between UF faculty from the Departments of Medicine (Segal, Bihorac), Aging and Geriatric Research (Leeuwenburgh, Wohlgemuth), Surgery (Efron, Brakenridege, Moore, Mohr, Moldawer) Biostatistics (Wang) and Clinical and Health Psychology (Price) to examine how persistent inflammation drives cognitive decline in older sepsis survivors and the role of cognitive reserve in protecting cognition.

Member of the Reserve and Resilience: Animal studies working group, formed as a result of the MBRF sponsored Cognitive Aging Summit III. This groups works to operationally define cognitive reserve and resilience.

Member of the international Brain Ageing Classification Working Group, to better classify and stage brain ageing itself and any related syndromes. The aim is to gain global officiation via the WHO International Classification of Diseases (ICD) for new disease and disorder classifications which are more accurate and clinically useful, and address gaps in disease classification and staging. The current ICD constitute mainly late stage and extrinsically caused processes, or those considered in some way separate to 'normal ageing', which may not be accurate or ideal for preventative, reversal and earliest detection approaches. The goal is to form consensus for the range of brain ageing classifications that are required, and to write this up as a 'brain ageing classification consensus paper' from which detailed and specific papers and ICD submissions should follow.

Eric Porges, PhD

Dr. John Williams (UF) has presented our preliminary results from our NIH/NIA R21 applying transcutaneous vagal nerve stimulation in older adults (with and without MCI). This approach is impacting the salience network functional connectivity in task free fMRI.

With Dr. Rachael Seidler (UF), we have explored in-vivo brain glutathione using MRS. We have found that cortical concentrations are higher in normal aging than in younger adults and that these results related to a number of physical function domains. A manuscript reporting these results is under review and an NIH/NIA R01 has been submitted. The proposed grant will extend this work more thoroughly to explore the relationship between brain antioxidant concentrations, memory, and cognition in normal aging.

The aforementioned project with Dr. Burke involves Dr. Jamie Near at McGill University (Canada) who will provide high field magnetic resonance spectroscopy support (11 tesla).

Dr. Porges is in a collaborative multisite study with the Dept. of Radiology at Johns Hopkins University to establish site to site variation in MRS. The results of this collaboration are under review

and have generated normative values in an adult population; this will immediately facilitate use of this measure as a possible clinical tool/biomarker in our aging research. A 3rd publication related to this project was accepted in 2019.

A collaborative project with Drs. Puts and Edden at the Dept. of Radiology at Johns Hopkins University and Dr. Jensen at Reed College to characterize the life course of cortical GABA has generated an individual data, meta-analysis currently under review at eLIFE and a preprint has been posted to BioRxiv ("The trajectory of cortical GABA levels across the lifespan: An individual participant data meta-analysis of edited MRS studies").

A collaborative project with Drs. Saleh and Edden at the Dept. of Radiology at Johns Hopkins University has yielded a recently accepted publication simultaneously measuring in-vivo GABA, Glutathione, and Ethanol in the brain after oral administration. This method is currently being applied in older adults.

A life course characterization of cortical GABA by brain region using primary data (non-metanalytic) that was initiated last year is ongoing. Data has been committed by researchers at the University of Florida, Dartmouth, Children's Hospital of Philadelphia, Stanford University, Purdue University, Emory, University of Calgary, The Johns Hopkins University, University of Oregon, McGill University, Harvard Medical School, and the University of California, San Francisco.

Damon Lamb, PhD

Co-investigator on DARPA, and NIH funded investigation of non-invasive Vagus Nerve Stimulation in humans for age-related memory loss and in implanted Vagus Nerve Stimulation in animals to enhance learning and memory.

Natalie Ebner, PhD

Various, including a close collaboration with Dr. Cruz-Almeida in the context of a joint MPI NIH R01 (see separate report for that project).

John Williamson, PhD

With Drs. DeKosky, Cohen, Porges, and Lamb via funding from the NIA, we continue work on the development of tVNS to modify brain and cognitive functions in patients with mild cognitive impairment.

Further, related to my VA work, Drs. Kevin Wang and I have submitted a grant through the DOD (currently pending) to determine biomarkers associated with cognitive decline/accelerated aging in people with history of traumatic brain injury.

In collaboration with Drs. Cohen and Porges, we continue work on aging and cognitive changes associated with microbiome differences in patients with HIV.

In collaboration with Drs. Cohen and Porges, we continue to execute the WISE study on the effects of bariatric surgery on brain health and cognition. We have several results from this study accepted for presentation at an upcoming International Neuropsychological Society conference and these will be developed as manuscripts over the next year.

FUTURE PLANS FOR RESEARCH PROGRAMS AND CLINICAL INITIATIVES

Jennifer Bizon, PhD

Our plans for the future include several exciting preclinical intervention and mechanistic studies.

Vagus nerve stimulation. The first includes the use of vagus nerve stimulation to improve cognition in aging. We have an R01 proposal that is currently pending (scored under the funding line at NIA) to support this work. In addition, these data are foundational for a large animal-human subjects Program Project proposal that is current under development with CAM center faculty. Specifically, this larger grant is focused on investigating the efficacy and mechanisms of using non-invasive approaches to enhancing neuroplasticity in older adults and will take advantage of the cross-species and diverse scientific expertise within the CAM center.

Cannabis and cognitive aging. In addition to these non-invasive approaches, we are working with Dr. Barry Setlow to develop a preclinical research program evaluating effects of cannabis use on cognition in aged rats. To date, MBRF funding has been essential for obtaining preliminary data for this line of research.

Sara N Burke, PhD

In this next year, a primary focus for new research initiatives within my laboratory will be to work with other CAM leadership (Drs. Bizon, Cohen and Woods) to develop and submit a program project grant related to "*Modulating Neuroplasticity with Stimulation to Promote Cognitive Resilience in Old Age*." To support this endeavor, we will be developing transcranial direct current stimulation (tDCS) in rats in order to examine the precise mechanisms by which this treatment improves cognitive performance in older adults. While tDCS has shown promise for improving cognitive outcomes in older adults, the specific mechanisms by which this treatment works remain elusive. To optimize the implementation of tDCS in humans, it is critical to understand the mechanisms of action at the cellular level so that this treatment can be precisely tuned to augment cognitive function. As such, invasive studies in animal models are critical for determining the cellular basis of how tDCS modulates neuroplasticity and neural network function. We also plan to directly compare tDCS to vagus nerve stimulation (VNS) to elucidate the extent to which these two different stimulation-based treatments may have overlapping, complementary, or independent mechanisms of action.

My research program will also continue to focus bridging levels of analysis (from single cells, to networks, to behavior) to examine the mechanisms of cognitive aging. We are excited to be developing new technology to do this. Specifically, leveraging the two lightsheet microscopes that are now at UF, we will be obtaining 3-dimensioal images from intact rat brains in which cellular activity is labeled with single-cell resolution. These brains will be co-registered with MRI images obtained from the same animals so that cellular activity can be directly related to resting state functional connectivity in the context of cognitive function across the lifespan. We have developed a new collaboration with researchers at MIT that will implement machine learning in order to co-register the different imaging datasets and analyze for neural activity. This approach will offer an unprecedented ability to bridge levels of analysis and forge a new path for translating data from animal models to neural network organization in humans.

Finally, we will continue to focus on the interactions of peripheral metabolism and brain function in old age. We have multiple ongoing experiments that are directly measuring how improving

metabolism function with diet or diet-based supplements can reverse age-related biochemical alterations and improve cognitive function.

Adam Woods, PhD

In the next year, Dr. Woods will continue to administer his numerous NIH funded clinical trials using novel non-invasive neuromodulation methods to remediate age-related cognitive decline in older adults.

PACT trial Dr. Woods will administer a clinical trial site at the University of Florida for the recently funded largest clinical trial testing cognitive training in healthy older adults to prevent dementia (the PACT trial).

tDCS to prevent dementia. Dr. Woods' team anticipates initiation of a new R01 receiving a fundable score to investigate personalized dosing strategies for the application of cognitive training and tDCS to prevent dementia.

ACTIVE MIND Dr. Woods' team intends to submit a new R01 to continue the ACTIVE MIND trial that is nearing completion. The ACT trial is expected to complete all randomization in early 2021 and a majority of participants will complete long-term follow up in the next year.

PROMOTING JUNIOR FACULTY In the coming year, Dr. Woods will continue to facilitate his junior faculty and post-doctoral fellows toward success in some of these funding endeavors and new independent endeavors relevant to cognitive aging, with the hope of expanding the overall bandwidth of the CAM for cognitive aging interventions and grooming a new cadre of interventional cognitive aging scientists. Dr. Woods is hopeful that his post-doctoral fellow Dr. Aprinda Indahlastari will be elevated to the Assistant Professor level in the next year - adding a critical set of expertise in computational neuroscience methods to the CAM.

CHALLENGES In addition, due to the size of his lab, Dr. Woods continues to struggle to find space solutions that will allow his large dynamic lab group to work in a unified space. The lab continues to be spread across 3 locations on campus, which undermines efficiency and limits overall potential for productivity. With continued acquisition of multi-million dollar grants, it is Dr. Woods hope that UF will afford appropriate space for his team in the coming year. Regardless, Dr. Woods will continue to make strides in the development of novel interventions to remediate cognitive aging and prevent dementia, taking novel methods from bench to bedside.

Collectively, the CAM is currently in the planning phase of an NIH program project that will leverage the numerous strengths of our faculty and research programs and will serve as a key example of the world-class program of research in cognitive aging at the Center and MBI.

Dawn Bowers, PhD

Currently we have one funded R01 from NIH/NIA that directly builds on the support provided by the MBRF. This funding is directed towards individuals with subtle cognitive complaints who are at risk for Alzheimer's disease. One diversity post-doctoral supplement and another diversity F31 are associated with this R01. Future initiatives include an R01, under development, that builds on an 8-week telehealth intervention for treatment of apathy (i.e., the PAL program), which has devastating effects on cognition and well-being in older adults.

Steven T DeKosky, MD

In addition to the studies above, which will continue into the coming years, I will work with several studies in doing the neurological assessment of volunteers prior to their entering the studies and will continue to sit on adjudication committees to determine a consensus agreement on diagnosis. Having worked with age-related memory impairment in patients and elderly volunteers, I look

forward to continuing to aid the studies in this way. We are also initiated several studies looking at information derived from MRI scans, including diffusion tensor imaging (DTI) as a marker of stability or disruption of regional connectivity, analysis of free water content in normal aging versus pathological aging, and MR spectroscopy to assess biochemical alterations in energy metabolism and neurotransmitter status in our subjects.

Tom Foster, PhD

Peripheral inflammation/neuroinflammation and brain aging. We have plans for a longitudinal study to determine if inflammation during adulthood influences the trajectory of cognitive decline. Another study will test whether senescent microglia are a cause of cognitive decline.

Investigation of senolytics in cognitive aging. Research is ongoing to determine if senolytics, a class of small molecules that selectively induce death of senescent cells can improve cognition.

Role of sex steroids on mechanisms of brain aging including oxidative stress, synaptic function, and epigenetic regulation of transcription. These studies combine behavior, electrophysiology, and epigenetics to determine if DNA methylation regulates the therapeutic window for beneficial effects of hormone replacement treatments on cognition. In addition, we address the question of whether estrogen regulates mitochondrial function and oxidative stress to influence synaptic plasticity mechanisms that underlie episodic memory.

Epigenetic Biomarkers. Studies are ongoing to characterize the epigenetic markers (DNA methylation, microRNA) in the blood of humans. In particular, we examine the epigenetic clock in humans and determine if this marker of aging predicts functional impairments. DNA methylation and microRNA are employed to examine the signaling pathways that are altered with age.

Natalie Ebner, PhD

We currently have one R01 pending that directly follows up on the study findings from our MBRF-funded intervention grant. This application investigates the specific neurocognitive and socioaffective mechanisms underlying learning to trust among older adults; and uses computational modeling of behavioral and neuroimaging data; as well as applies the novel intervention technique of real-time functional magnetic resonance imaging guided neurofeedback to promote learning to trust in older adults, with the longer term goal to reduce fraud victimization in aging.

Ruogo Fang, PhD

NIH R01 on understanding the mechanism of Cerebral Blood Flow and BBBP in Cognitive Aging and Alzheimer's Disease (collaborate with Adam Woods).

NIH R01 Secondary data analysis using machine learning for understanding mechanism and individual variability in tDCS for chronic pain.

Joseph Gullett, PhD

I will be resubmitting a K23 Clinical Trial project to the National Institute of Aging, Neuroscience in February 2021. This project utilizes a multi-modal neuroimaging pipeline which was generated from my recently completed 1Florida ADRC Pilot Grant project. The pipeline takes baseline T1 structural and resting-state fMRI scans and combines them in a predictive model of whether or not that patient with mild cognitive impairment will progress to dementia by the following year. We achieved over 95% accuracy in our longitudinal pilot data, which is being drafted for submission to a high-tier journal at this time. Further, this project generated physical brain regions which were responsible for maintenance of MCI diagnosis or improvement to a less-severe diagnosis at one year. These brain regions can potentially serve as the target for neuromodulatory interventions in future work combined with cognitive training to slow the progression of MCI. To do so, we are integrating pilot data from

an ongoing MCI intervention study in which older adults engage in 3 months of take-home cognitive training (multi-site pilot study titled *ActiveMind;* MPIs: Edwards, J., Woods, A., Kramer, J.). These data will also be processed through the machine learning pipeline described above to determine the utility of baseline MRI to predict whether a patient with MCI will benefit from cognitive training.

Damon Lamb, PhD

Several projects are currently underway or being developed to develop both our understanding of the underlying neurobiology or develop treatments for age-related memory loss. One core domain is the use of cranial nerve stimulation to modulate autonomic function and brain neuroplasticity. To better understand how these stimulation methods, particular transcutaneous vagus nerve stimulation and implanted vagus nerve stimulation, may modulate brain and autonomic function, and in particular improve memory, we are studying this at a cellular through human behavior scale across multiple collaborative projects. The animal efforts, led by Drs. Bizon and Burke, fellow MBRF-funded aging researchers, have led to two areas nascent projects that build off of our ongoing behavior-focused work: a high-throughput computational approach to processing and interpreting the massive datasets that result from our use of light sheet microscopy and the potential use of stimulation to increase clearance of amyloid beta and tau protein. On the human side, in projects led by Drs. Williamson, Porges and myself, we plan to extend and expand our study of vagus nerve stimulation on cognitive and memory functions.

Andrew Maurer, PhD

Working from our premise that cognition is supported by the movement of activity across brain regions, in collaboration with Dr. Sara Burke, we are crafting a novel research trajectory into how the “fuel” (glucose) can alter the movement activity for potential therapeutic interventions. Specifically, the Burke laboratory has a therapeutic research focus into the use of the ketogenic diet for aging, switching the metabolic fuel source from glucose to ketone bodies. We hope to investigate how glucose homeostasis relates to hippocampal physiology and cognitive performance in young and aged rats as well as investigate the ketogenic diet as a therapeutic intervention.

Eric Porges, PhD

In the coming year, we will continue our work in two primary areas: (1) we will continue to explore the relationship of age-related changes in memory and cognition and low concentration neurometabolites using edited Magnetic Resonance Spectroscopy (MRS) and (2) we will continue to explore and develop methods impacting cognition and memory, both acutely and persistently, using non-invasive vagus nerve stimulation.

Our work with low concentration neurometabolites, such as GABA (the principal inhibitory neurotransmitter) and glutathione (most plentiful endogenous antioxidant), will include the analysis of GABA MRS data collected as part of the McKnight Brain Aging Registry at the University of Florida, the University of Miami, the University of Alabama, and the University of Arizona in adults 85 years of age and older. In addition to the dissemination of the results, we will employ NIH funding to continue this investigation of longitudinal changes across multiple cortical and subcortical regions. Our work, currently under review, demonstrating an increase in glutathione in normal aging and an association with physical function will be extended to include memory and cognition. A multisite NIA/NIH grant application has been submitted and we are eager to continue to explore the role of oxidative stress and endogenous responses as they relate to brain health, memory, and cognition.

Our application of transcutaneous vagus nerve stimulation in older adults will continue over the coming year and we expect enrollment in both acute and sustained consequences studies to reach sufficient levels to facilitate the publication of results, including data supporting delayed recall after vagus nerve stimulation facilitated sleep. In addition, we will work to synchronize memory paradigms

between human and rodent models. This will allow for our non-invasive transcutaneous vagus nerve stimulation approach to parallel the invasive vagus nerve stimulation approach used in rodent models by Drs. Burke and Bizon. This synchronization of vagus nerve stimulation work between aging rodent and human models will allow for data collection in the spring to facilitate grant application in the fall. Finally, we are actively working on the refinement of self-application of transcutaneous vagus nerve stimulation approaches in older adults. Presently, we have IRB approval and will begin collecting multi-week self-application studies over the next year.

Lastly, we have been conducting an ongoing longitudinal assessment of cognitive function in the context of COVID related stress and social isolation. We have utilized the CANTAB Connect battery for home administration in an older adult cohort. We will be beginning preliminary analysis of longitudinal consequences of this context on older adult's memory and cognitive function over the next year.

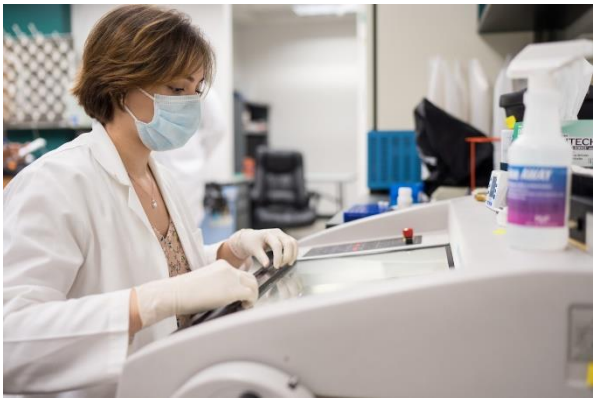
Alexis Simpkins, MD, PhD

I will be continuing my research projects and collaborations with Dr. Woods on the miRNA and white matter hyperintensities in aging Floridians. I plan to conduct a case match comparative analysis of the mRNA sequences using Partek genomic suite to select significantly differentially expressed miRNA. Those miRNA will be used for IPA ingenuity pathway analysis. Also, I will be look at the miRNA genes selected in an aged population of stroke patients with white matter hyperintensities to determine if the predicted pathways are similarly upregulated in patients that express the disease state (white matter hyperintensities on MRI) using a separate case matched co-hort of samples from an outside collaborator.

John Williamson, PhD

I intend to use the BRRC funding (target sample size 10 participants who will complete a cross over sham controlled evaluation of tVNS effects on sleep quality) to develop a line of intervention work on sleep quality aimed at improving cognitive performance and brain health in older adults. This work is occurring in conjunction with active tVNS projects in sleep in younger adults with PTSD (VA Merit Review funded), paired cognitive training in older adults (MBRF funded), and during cognitive performance in people with mild cognitive impairment (NIA funded).

Further, in collaboration with Drs. Eric Porges, Adam Woods, and Damon Lamb we will propose longitudinal projects in cognitively normal aging. Cerebrovascular disease is a major risk for older adults. Within the BRRC, Dr. Cohen and I are collaborating with neurorehabilitation therapists to understand mechanisms of response to rehabilitation approaches post-stroke to optimize return to more normal function. Further, we are developing collaborations with the VA on mechanism of accelerated aging associated with traumatic brain injury (DOD funding currently pending).



ENDOWMENT REPORT

McKnight Brain Institute Endowment's at The University of Florida
As of December 31, 2020

1) Evelyn F. McKnight Cognitive Aging and Memory Research Fund

Date of Gift and Match: 04/28/2000 & 11/07/2002

MBRF Contribution:	$	0.00
No Match in Calendar Year 2020	$	0.00
Transfers from other University Funds	$	0.00
Investment Return	$	1,684,706
Distributions for Spending	$	1,083,382
12/31/2020 Balance*	$	32,148,231
Unmatched Balance (if applicable)	$	N/A

*FY21 Q2 financials have not yet closed and are projected financial amounts. Final booked amounts will be available 1/25/2021.

2) William G. Luttge Lectureship in Neuroscience

Date of Gift and Match 06/01/2012 – No Match

MBRF Contribution:	$	0.00
No Match in Calendar Year 2020	$	0.00
Transfers from other University Funds	$	0.00
Investment Return	$	15,581
Distributions for Spending	$	10,019
12/31/2020 Balance*	$	297,280
Unmatched Balance (if applicable)	$	N/A

*FY21 Q2 financials have not yet closed and are projected financial amounts. Final booked amounts will be available 1/25/2021.

3) Evelyn F. McKnight Chair for Brain Research in Memory Loss

Date of Gift and Match	04/28/2000 & 11/07/2002	
MBRF Contribution:	$	0.00
No Match in Calendar Year 2020	$	0.00
Transfers from other University Funds	$	0.00
Investment Return	$	226,205
Distributions for Spending	$	145,466
12/31/2020 Balance*	$	4,316,542
Unmatched Balance (if applicable)	$	N/A

*FY21 Q2 financials have not yet closed and are projected financial amounts. Final booked amounts will be available 1/25/2021.

4) Evelyn F. McKnight Chair for Clinical Translational Research in Cognitive Aging

Date of Gift and Match	07/01/2015 – No Match	
MBRF Contribution:	$	0.00
No Match in Calendar Year 2020	$	0.00
Transfers from other University Funds	$	0.00
Investment Return	$	226,108
Distributions for Spending	$	145,403
12/31/2020 Balance*	$	4,314,677
Unmatched Balance (if applicable)	$	N/A

*FY21 Q2 financials have not yet closed and are projected financial amounts. Final booked amounts will be available 1/25/2021.

No funds were used for a prohibited purposed during the reporting period and all activities furthered the Purpose. No modifications are recommended to the Gift Agreement

COMMUNICATIONS (Website, News Coverage, Social Media)

WEBSITE

https://cam.mbi.ufl.edu/

The number of visits on the CAM website in past 30 days: 135

SOCIAL MEDIA

The CAM Center now has a recently approved University of Florida sanctioned twitter account (@UF_CAMcenter) which currently has 81 followers. A major goal for this year is to generate regular content to build followers to this account. In addition to this UF account, we have listed below those faculty who have personal accounts.

Jennifer L Bizon, PhD
Twitter: @JenBizon, 656 Followers, **LinkedIn**: 160 followers

Sara N Burke, PhD
Twitter: @saranburke24, 917 followers, **LinkedIn**: 73 followers

Adam Woods, PhD
Twitter: @adamjwoods, 479 followers, **Facebook**: 412 followers, **LinkedIn**: 425 followers

Natalie Ebner, PhD
Twitter: @natalie_ebner, 500 followers

Joseph Gullett, PhD
Twitter: 21 followers, **Instagram**: 100 followers

NEWS COVERAGE

- **(Bizon)** MBI and University coverage of papers showing regulation of decision making by gonadal hormones: https://mbi.ufl.edu/2020/09/28/uf-neuroscientists-find-sex-hormones-may-influence-risk-taking-impulsivity-in-rats/.
- **(Burke)** MBI and University coverage of paper showing activity based connectivity maps associated with learning are altered in aging, https://mbi.ufl.edu/2020/01/06/new-imaging-study-shows-key-brain-changes-in-aging-alzheimers/)
- **(Cruz-Almeida)** IHMC, https://youtu.be/G9vcnP8vWMc, November 2019
- **(Foster)** Published work (Smith et al., 2020) highlighted in the *JNeurosci* Featured Research page. https://mbi.ufl.edu/2020/07/07/research-snapshot-drs-garrett-smith-thomas-c-foster/
- **(Foster)** Brittney Yegla, PhD was among featured speakers from across the world who presented at the 2nd Workshop on Research Definitions for Reserve and Resilience in

Cognitive Aging and Dementia https://neuroscience.ufl.edu/2020/09/13/uf-postdoc-to-present-to-international-audience-during-cognitive-aging-workshop/

- **(Ebner)** Senior Living Executive, January, 2020 http://content.yudu.com/web/406u7/0A40767/SLEJan.Feb2020/html/index.html?page=39&origin=reader
- **(Woods)** https://mbi.ufl.edu/2020/11/16/study-examines-how-brain-structure-and-brain-function-impact-aging/
- **(Woods and Gullett)** https://mbi.ufl.edu/2020/06/16/research-snapshot-drs-adam-woods-joseph-Gullett/
- **(Woods)** https://mbi.ufl.edu/2020/05/26/guidelines-for-non-invasive-brain-stimulation-during-covid-19-pandemic/
- **(Woods)** https://mbi.ufl.edu/2020/09/02/study-identifies-a-potential-biomarker-for-decreased-brain-processing-speed-in-aging/
- **(Woods)** https://mbi.ufl.edu/2020/06/29/uf-neuroscientists-study-impact-of-covid-19-social-isolation-on-cognitive-mental-health-of-seniors/
- **(Woods)** https://mbi.ufl.edu/2020/06/23/specific-brain-network-may-be-key-to-successful-aging-study-suggests/

NEW PODCASTS, BLOGS, WEBINARS, YOUTUBE VIDEOS

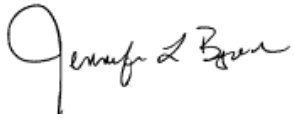
- **(Woods)** Podcasts on transcranial direct current stimulation. https://www.stitcher.com/show/evolving-past-alzheimers/episode/using-electricity-to-improve-cognition-with-adam-woods-65881190
- **(Woods)** Non-Invasive Brain Stimulation. https://www.navneuro.com/54-non-invasive-brain-stimulation-with-dr-adam-woods/
- **(Fang)** HWCOE: https://www.eng.ufl.edu/ https://www.eng.ufl.edu/newengineer/in-the-headlines/scientists-are-looking-into-the-eyes-of-patients-to-diagnose-parkinsons-disease/
- **(Fang)** “Eye Exam Could Lead to Early Parkinson’s Disease Diagnosis” Radiological Society of North America – original press release – 11/23/2020 https://press.rsna.org/timssnet/media/pressreleases/14_pr_target.cfm?ID=2229
- **(Fang)** “Blood Vessels in the Eye May Diagnose Parkinson's Disease” Medscape Medical News – online publication – 11/29/2020 https://www.medscape.com/viewarticle/941700
- **(Fang)** “How an Eye Exam May Improve Early Diagnosis of Parkinson Disease” American Journal of Managed Care – 11/2/2020 https://www.ajmc.com/view/how-an-eye-exam-may-improve-early-diagnosis-of-parkinson-disease
- **(Fang)** “Eye exam possible test to determine Parkinson's disease” Big News Network (.com) – specialist online news service – 11/29/2020 https://www.bignewsnetwork.com/news/267109611/eye-exam-possible-test-to-determine-parkinson-disease

- **(Fang)** “Scientists Are Looking Into The Eyes Of Patients To Diagnose Parkinson’s Disease” Forbes – 11/25/2020 https://www.forbes.com/sites/jackierocheleau/2020/11/25/scientists-are-looking-into-the-eyes-of-patients-to-diagnose-parkinsons-disease/?sh=59fd1f442faa
- **(Fang)** “The Eyes Offer a ‘Promising Window’ Into Brain Pathology” Diagnostics World News – covering emerging technologies in diagnostics – 12/1/2020 https://www.diagnosticsworldnews.com/news/2020/12/01/the-eyes-offer-a-promising-window-into-brain-pathology
- **(Fang)** “Simple Eye Exam with Powerful Artificial Intelligence Could Lead to Early Parkinson’s Disease Diagnosis” SciTech Daily – online daily news about science and technology – 11/23/2020 https://scitechdaily.com/simple-eye-exam-with-powerful-artificial-intelligence-could-lead-to-early-parkinsons-disease-diagnosis/
- **(Fang)** “RSNA 20: AI-Based Eye Exam Could Aid Early Parkinson’s Disease Diagnosis” Applied Radiology – The Journal of Practical Medical Imaging and Management – 11/23/2020 https://www.appliedradiology.com/communities/Artificial-Intelligence/rsna-20-ai-based-eye-exam-could-aid-early-parkinson-s-disease-diagnosis
- **(Simpkins)** I co-created a webinar for the American Heart Association to educate the public on Posterior Circulation Strokes: Challenges in Recognition and Diagnosis of Acute Ischemic Stroke from Vertebrobasilar Disease. https://learn.heart.org/lms/activity?@curriculum.id=1&@activity.id=7206197&@activity.bundleActivityId=-1

Report Submitted by:

 **1/13/2021**

Todd E. Golde, M.D., Ph.D.
Director, Evelyn F. and William L. McKnight Brain Institute
Director, 1Florida Alzheimer’s Disease Research Center
Member, Center for Translational Research in Neurodegenerative Disease
Professor, Department of Neuroscience, College of Medicine



Jennifer L Bizon, PhD
Co-Director, CAM Center
Professor and Interim Chair
Department of Neuroscience

Ron Cohen, PhD
Co-Director, CAM Center
Professor and Evelyn McKnight Chair of Clinical Translation in Cognitive Aging and Memory
Department of Clinical and Health Psychology

BIOSKETCHES LISTED ALPHABETICALLY BELOW

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Karina Alviña

eRA COMMONS USERNAME (credential, e.g., agency login): kalvina

POSITION TITLE: Research Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Pontifical Catholic University of Chile	B.S.	2002	Biological Sciences
Pontifical Catholic University of Chile *(Thesis conducted at the Albert Einstein College of Medicine)*	Ph.D.	2008	Biological Sciences, Physiology
Columbia University	Postdoc	8/2009-12/2011	Neuroscience
Albert Einstein College of Medicine	Postdoc	2/2012-6/2016	Neuroscience

A. Personal Statement

My long-term research goal is to understand how cells in the nervous system communicate with each other in normal and pathological conditions, such as those observed during aging and/or neurodegenerative disorders. Throughout my Ph.D., post-doctoral training, and junior faculty experience I have led several projects that range from studying intrinsic properties of single brain cells to in vivo studies of behavior and mechanisms underlying neurological disorders. I have extensive training in neurophysiology, specifically in the use of acute brain slices to study electrophysiological properties of cells and neural circuits, using rodents as animal models (a and b). My research focuses specifically on two main fronts: first, understanding neural mechanisms that lead to aberrant responses caused by stress (a) and aging-associated processes of neurodegeneration, and second, how environmental manipulations such as diet and exercise can be used as resilience agents. During my career, I have also done in vivo recordings in other animal models (electric fish, see below) of neural computation, and collaborated extensively on different studies related to understanding mechanisms of disease (c).

a. Hippocampal Injection of the Exercise-Induced Myokine Irisin Suppresses Acute Stress-Induced Neurobehavioral Impairment in a Sex-Dependent Manner. Jodeiri Farshbaf M, Garasia S, Moussoki DPK, Mondal AK, Cherkowsky D, Manal N, and **Alviña K**. Behav Neurosci. 2020 Jun;134(3):233-247. doi: 10.1037/bne0000367. PMID: 32437197
b. Ben-Simon Y, Rodenas-Ruano A, **Alviña K**, Lam AD, Stuenkel EL, Castillo PE, and Ashery U. A combined optogenetic-knockdown strategy reveals a major role of Tomosyn in mossy fiber synaptic plasticity. Cell Rep. 2015; 12 (3):396-404. doi:10.1016/j.celrep.2015.06.037 PMID: 26166572 PMCID: PMC4525481
c. Ashraf-Uz-Zaman M, Shahi S, Akwii R, Sajib MS, Farshbaf MJ, Kallem RR, Putnam W, Wang W, Zhang R, **Alviña K,** Trippier PC, Mikelis CM, German NA. Design, synthesis and structure-activity relationship study of novel urea compounds as FGFR1 inhibitors to treat metastatic triple-negative breast cancer. Eur J Med Chem. 2020 Sep 24;209:112866. doi: 10.1016/j.ejmech.2020.112866. PMID: 33039722

B. Positions and Honors

Employment

03/2001 – 12/2003	Teaching Assistant, Neurobiology for Biological Sciences undergraduate students Pontifical Catholic University of Chile
03/2002 – 12/2002	Biology teacher High School students
03/2003 – 12/2004	Teaching Assistant, Physiology for Medical students Pontifical Catholic University of Chile
06/2004	Teaching Assistant, Neurobiology course Marine Biological Laboratory
09/2013 – 12/2013	Teaching Assistant Neuroanatomy course Albert Einstein College of Medicine
09/2015 – 05/2016	Adjunct Assistant Professor Department of Natural Sciences, Hostos Community College, CUNY, New York, NY
01/2016 – 05/2016	Adjunct Assistant Professor Department of Psychology, Queens College, City College of New York, New York, NY
09/2016 – 12/2019	Assistant Professor Department of Biological Sciences, Texas Tech University, Lubbock, TX
01/2020 – Present	Research Assistant Professor Department of Neuroscience, University of Florida, Gainesville, FL

Honors

2008	Pontifical Catholic University of Chile. Best Doctoral Thesis in Biological Sciences
2012-2015	NIH Training grant for Postdoctoral Fellows. Grant #5T32NS007439-14
2012-2015	Society for Neuroscience Scholar
2017	Grass Fellowship, Grass Foundation, Marine Biological Laboratory, Woods Hole, MA.
2020	AlzSTAR Fellow for the 1Florida Alzheimer's Disease Research Center (1F LADRC)

C. Contributions to Science

1. As an Assistant Professor, I am fully dedicated to establishing a productive research program that studies mechanisms underlying synaptic function, from cellular level to behavior. I am particularly interested in processes that are triggered by stress and that result in the onset and exacerbation of several neuropsychiatric disorders, including anxiety, depression, and post-traumatic stress disorder. We have started several projects that focus on pathways altered by stress, including: acute-stress induced neurobehaviors and exercise as resilience tool (a); Neuropeptide Y (NPY) and resilience to stress (b); alterations to gut microbiome that can be detrimental to brain function (c); environmental factors that increase the risk for neurodevelopmental disorders (d) such as elevated dietary salt consumption that is associated with autism-like behavior in mice (e).
    a. Hippocampal Injection of the Exercise-Induced Myokine Irisin Suppresses Acute Stress-Induced Neurobehavioral Impairment in a Sex-Dependent Manner. Jodeiri Farshbaf M, Garasia S, Moussoki DPK, Mondal AK, Cherkowsky D, Manal N, and **Alviña K**. Behav Neurosci. 2020 Jun;134(3):233-247. doi: 10.1037/bne0000367. PMID: 32437197
    b. Long Term Effects of Stress on Hippocampal Function: Emphasis on Early Life Stress Paradigms and Potential Involvement of Neuropeptide Y. **Alviña, K**, Jodeiri Farshbaf M, and Mondal AK. J Neurosci Res 2020 doi: 10.1002/jnr.24614. PMID: 32162350
    c. Peirce JM, **Alviña K**. The role of inflammation and the gut microbiome in depression and anxiety. J Neurosci Res. 2019 Oct;97(10):1223-1241. doi: 10.1002/jnr.24476. PMID: 31144383
    d. Maternal elevated salt consumption and the development of autism spectrum disorder in the offspring. Afroz KF and **Alviña K**. J Neuroinflammation 2019. 16(1):265. doi: 10.1186/s12974-019-1666-2. PMID: 31837704 PMCID: PMC6911292
    e. Altered gut microbiome and autism-like behavior are associated with parental high salt diet in male mice. Afroz FF, Reyes N, Young K, Parikh K, Misra V, and **Alviña K**. In review.

2. As a Postdoctoral I focused on how the hippocampus orchestrates its functions through its circuit and physiology. I studied in detail the "detonator synapse", the mossy fiber to CA3 pyramidal cell synapse, which is unique in the CNS due to its neurotransmitter release properties and role in memory function.

Amongst others, my main project was to study calcium signals associated with bidirectional activity-dependent synaptic plasticity in the CA3 region of the hippocampus. My results showed that post-synaptic calcium levels at the mossy fiber synapse correlate precisely with the sign of synaptic plasticity mediated by NMDA-type glutamate receptors (NMDARs). This is relevant considering the very limited knowledge currently exists regarding how NMDARs are dynamically regulated by activity in a long-term manner, even though NMDARs plasticity (e.g. NMDAR-LTP/LTD) has been described at several key brain areas where it strongly impacts spike transfer and could contribute significantly to learning and memory (**Alviña K**, Lutzu S. and Castillo PE. *Postsynaptic calcium dynamics associated with bidirectional plasticity of NMDA receptor-mediated transmission*, in preparation). I was also involved in several other projects that shed light on the role of transcription factors that modulate the number of synapses in the area CA3 of the hippocampus, and thus impact contextual memory formation (b); the function of growth factor receptors (c) in synaptic activity, and the previously unknown function of presynaptic proteins (d).

a. Weng FJ, Garcia RI, Lutzu S, **Alviña K**, Zhang Y, Dushko M, Ku T, Zemoura K, Rich D, Garcia-Dominguez D, Hung M, Yelhekar TD, Sørensen AT, Xu W, Chung K, Castillo PE, Lin Y. Npas4 Is a Critical Regulator of Learning-Induced Plasticity at Mossy Fiber-CA3 Synapses during Contextual Memory Formation. Neuron. 2018 Jan 29. pii: S0896-6273(18)30051-5. doi: 10.1016/j.neuron.2018.01.026. PMID: 2942993
b. Nandi S, **Alviña K**, Lituma PJ, Castillo PE, Hébert JM. Neurotrophin and FGF Signaling Adapter Proteins, FRS2 and FRS3, Regulate Dentate Granule Cell Maturation and Excitatory Synaptogenesis. Neuroscience. 2018; 369: 192-201. doi: 0.1016/j.neuroscience.2017.11.017 PMID: 29155277
c. Ben-Simon Y, Rodenas-Ruano A, **Alviña K**, Lam AD, Stuenkel EL, Castillo PE, and Ashery U. A combined optogenetic-knockdown strategy reveals a major role of Tomosyn in mossy fiber synaptic plasticity. *Cell Rep*. 2015; 12 (3):396-404. doi:10.1016/j.celrep.2015.06.037 PMID: 26166572 PMCID: PMC4525481

3. The focus of my first postdoctoral experience was to discern how the cerebellum and cerebellum-like structures (i.e. dorsal cochlear nuclei in the mammalian brain) encode information. Here I performed in vivo recordings from cerebellar cells in awake weakly electric fish, a great model to study the role of the cerebellum (and cerebellum-like structures) in the generation of predictions based on previous knowledge, which is essential for adaptive learning, and cancellation of self-generated motor signals that could interfere with sensory and motor information from the outside world. My work concentrated on obtaining physiological data of cerebellar granule cells while encoding different sensory and motor modalities of synaptic inputs in vivo, thus providing the base for an extensive subsequent modeling study published in Nat Neuroscience (a). This publication has been extensively cited and even featured in a New York Times article regarding how the brain works. In addition, I studied Purkinje cells from the electric fish's cerebellum, their responses to sensory and motor stimulation and the rules for the development of synaptic plasticity. This work provided novel information that confirmed the existence of 2 different types of Purkinje cells in the fish's cerebellum and allowed for comparison with cerebellum-like structures (better characterized in the electric fish) and with cerebelli across different species. These findings were later published in J Neurophysiology (b).
    a. Kennedy A, Wayne G, Kaifosh P, **Alviña K**, Abbott LF, and Sawtell NB. A temporal basis for predicting the sensory consequences of motor commands in an electric fish. *Nat Neurosci.* 2014 Mar; 17(3):416-22. doi: 10.1038/nn.3650. PMID: 24531306
    b. **Alviña K** and Sawtell NB. Sensory processing and corollary discharge effects in posterior caudal lobe Purkinje cells in a weakly electric mormyrid fish. J Neurophysiol. 2014 Jul 15; 112(2):328-39. doi: 10.1152/jn.00016.2014. PMID: 2479016

4. For my doctoral studies, I concentrated on ionic mechanisms that regulate the spontaneous activity of cerebellar neurons, and thus impact motor behavior. Specifically, I studied how mutations in the P/Q-type Ca2+ channel affect the spontaneous activity of the principal cells in the cerebellar cortex (Purkinje cells). P/Q channel mutant mice are a perfect animal model for the human disease Episodic Ataxia type 2. We discovered that Purkinje cells in these mice show an abnormally erratic spontaneous activity, which results in a significant impairment of their ability to integrate synaptic inputs and ultimately in motor behavior deficits. My work contributed to dissect the precise cellular mechanism (which involved

2 different ion channels) that resulted in cerebellar malfunction, and provided clear avenues for possible therapeutic alternatives in humans after we used an FDA-approved drug that could rescue the phenotype in ataxic mice. This project resulted in several publications in highly regarded journals, including one in Nat Neuroscience (a) and 2 first author back to back papers in J Neuroscience (b and c).

a. Walter JT, **Alviña K**, Womack MD, Chevez C and Khodakhah K. Decreases in the precision of Purkinje cell pacemaking cause cerebellar dysfunction and ataxia. Nat Neurosci. 2006 Mar; 9(3):389-97. PMID: 16474392
b. **Alviña K** and Khodakhah K. The therapeutic mode of action of 4-aminopyridine in cerebellar ataxia. J Neurosci. 2010, 30 (21): 7258-68 doi: 10.1523/JNEUROSCI.3582-09.2010. PMID: 20505092
c. **Alviña K** and Khodakhah K. KCa channels as therapeutic targets in episodic ataxia type 2. J Neurosci. 2010, 30 (21): 7249-57 doi: 10.1523/JNEUROSCI.6341-09.2010 PMID: 20505091

5. During my Ph.D. thesis, I also studied the intrinsic electrical properties of DCN cells and uncovered specific Ca2+ channels that regulate their spontaneous activity; I also focused on how these cells integrate synaptic inputs from Purkinje cells. My results challenged a long-standing hypothesis of how these cells respond to inputs (i.e. with a rebound depolarization in response to inhibition). I found that only a minority of DCN cells does show this response, even in vivo, thus prompting the reevaluation of traditional views on how the cerebellum works. My work not only resulted in a first-author publication in Nat Neuroscience (a) and two other publications in Neuroscience and J Physiology (b), but also established a new line of research in the Khodakhah laboratory.
    a. **Alviña K**, Walter JT, Kohn A, Ellis-Davies G and Khodakhah K. Questioning the role of rebound firing in the cerebellum. Nat Neurosci. 2008 Nov;11(11):1256-8. doi: 10.1038/nn.2195. PMID: 18820695
    b. **Alviña K** and Khodakhah K. Selective regulation of spontaneous activity of neurons of the deep cerebellar nuclei by N-type calcium channels in juvenile rats. J Physiol. 2008, 586 (10): 2523-38 PMID: 18372310

For a complete list of publications: https://www.ncbi.nlm.nih.gov/pubmed/?term=alvina+k

D. Additional Information: Research Support and/or Scholastic Performance

Completed Support

5T32NS007439-14 NIH Training grant for Postdoctoral Fellows, Albert Einstein College of Medicine, Dominik Purpura Department of Neuroscience 2012-2015

Current Support

Florida Department of Health Ed and Ethel Moore Alzheimer's Disease Research Program — Alviña, K (role: PI, effort 25%) — Awarded $99,000
Role of Irisin as mediator of exercise-related cognitive improvement in Alzheimer's Disease

Pending Support

R01 PRO00033265 — Alviña, K (role: Co-PI, effort 10%) — Requested $1,877,127
Centrifugal regulation of olfactory function by melanin-concentrating hormone

BrightFocus Foundation Standard Award Program in Alzheimer's Disease Research — Alviña, K (role: PI, effort 10%) — Requested $300,000
The myokine Irisin as mediator of exercise-induced improvement of cognitive function in Alzheimer's Disease

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Bizon, Jennifer Lynn

eRA COMMONS USER NAME (credential, e.g., agency login): jbizon

POSITION TITLE: Professor and Interim Chair, Department of Neuroscience

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of North Carolina at Chapel Hill, Chapel Hill, North Carolina	BS	05/1993	Psychology
University of California, Irvine, Irvine, California	PhD	08/1998	Neurobiology and Behavior
John Hopkins University, Baltimore, MD	Postdoctoral Fellow	09/2002	Neuroscience and Psychological Sciences

A. Personal Statement

My NIH-funded research program is broadly focused on determining the neural processes that support cognitive and behavioral changes in aging and age-related neurodegenerative disease. Using rodent models, my laboratory employs an integrative approach that combines sensitive behavioral assessments with cellular, molecular, optogenetic and pharmacological methodologies (a-d). We have uncovered disruptions in both glutamatergic and GABAergic signaling in the aged brain that contribute to impairments in memory, cognitive flexibility, and decision making (a-c). Our long-term goal is to identify the circuit and cellular alterations associated with brain aging and disease that are most relevant to cognitive dysfunction, and to design strategies that target these mechanisms to improve cognitive health and life quality in older adults.

Despite the significant challenges in 2020, the Bizon lab continued to make progress in advancing our understanding of the neural mechanisms that contribute to decline of cognition in aging. As part of one of our funded R01s from National Institute on Aging (NIA) focused on understanding drivers of age-associated changes in decision making, we published two new studies showing that male and female sex hormones play differing roles in risk-taking inclinations and the ability to delay gratification. The findings from these rodent-model studies were reported in the journals Neuropsychopharmacology (Impact Factor 7.9) and eLife (Impact Factor 7.4). Our data could provide useful insight for why decision making is altered in aging and for development of approaches to optimize decisions in older adults.

I now serve as co-Director of the Center for Cognitive Aging and Memory Clinical Translational Research (the "CAM Center"). With the co-Director, Dr. Ron Cohen and Associate Directors, Drs. Adam Woods and Sara Burke, we have made great strides in the past year integrating the structure and operations of the Age-Related Memory Loss Core Program ("ARML Core Program") and the Cognitive Aging and Memory Clinical Translational Research Program ("CAM-CTRP") into a unified CAM Center that encompasses complementary and collaborative research and educational programs on cognitive aging. Accomplishments of the CAM Center faculty are detailed in the associated report.

a. Bañuelos C, Beas BS, McQuail JA, Gilbert RJ, Frazier CJ, Setlow B, **Bizon JL**. (2014) Prefrontal cortical GABAergic dysfunction contributes to age-related working memory impairment. *The Journal of Neuroscience.* 34(10):3457-66. PMCID: 3942567

b. McQuail JA, Frazier CJ, **Bizon JL**. (2015) Molecular aspects of age-related cognitive decline: Role of GABA signaling. *Trends in Molecular Medicine* 2015 Jul;21(7):450-60.

c. McQuail JA, Beas BS, Simpson K, Kelly K, Frazier CJ, Setlow B, **Bizon JL** (2016) NR2A-containing NMDA receptors in the prefrontal cortex are required for working memory and predict age-related cognitive decline. *The Journal of Neuroscience.* 36(50):12537-12548. PMCID: 5157101.

d. Hernandez CM, Orsini CA, Wheeler A-R, Ten Eyck TW, Betzhold SM, Labiste CC, Setlow B, & **Bizon JL.** Testicular hormones mediate robust sex differences in intertemporal choice. *eLife*. 28;9:e58604.

B. Positions and Honors

Positions and Employment

1993-1998	Graduate Student Assistant, University of California, Irvine
1998-2003	Postdoctoral Fellow, Johns Hopkins University
2002-2004	Assistant Research Scientist, Dept. of Psychology, Johns Hopkins University
2004-2010	Assistant Professor of Psychology, Texas A&M University
2004-2010	Faculty of Neuroscience, Texas A&M University
2010-2016	Associate Professor of Neuroscience and Psychiatry, University of Florida College of Medicine
2016-present	Professor, Department of Neuroscience, University of Florida College of Medicine
2017-2020	Associate Chair, Department of Neuroscience, University of Florida
2020-present	Interim Chair, Department of Neuroscience, University of Florida College of Medicine

Other Experience and Professional Memberships

2009	Member, NIA Special Emphasis Panel (ZAG1 ZIJ-5), Mechanisms of Cognitive Aging
2010 -	Advisory Board, Alzheimer's Drug Discovery Foundation
2010-11, 2015	*Ad hoc* member, NIH Clinical Neuroscience and Neurodegeneration Study Section
2011-2015	Director, Neuroscience Graduate Program, University of Florida College of Medicine
2012	*Ad hoc* member, NIH Chronic Dysfunction and Integrative Neurodegeneration
2013 -	Member, NIH Neurodevelopment, Synaptic Plasticity, Neurodegeneration Fellowship Study Section
2014	Member, NIEHS Special Emphasis Panel (ZES1 LWJ-K), Environmental Contributors to Neurodegeneration
2015-2016	*Ad hoc* member, NIH National Institute on Aging Neuroscience Study Section (NIA-N)
2016 -	Section Editor, Cognition, Behavior and Physiology Section, Neurobiology of Aging
2016 - 2018	Chair, NIH Neurodevelopment, Synaptic Plasticity, Neurodegeneration Fellowship Study Section
2019	Member, NIAID, Special Emphasis Scientific Review Panel- Program Project
2019	Member, NIMHD, Research Centers in Minority Institution (U54) Scientific Review Panel, (ZMD1 MLS M1)

Honors

1994	UC Regents Graduate Fellowship, UC Regents
1995	Individual NRSA, F31 pre-doctoral award, National Institute of Mental Health
2001	Individual NRSA, F32 post-doctoral award, National Institute on Aging
2008	Montague Center for Teaching Excellence Award, Texas A&M University
2009	Leadership and Service Award, Faculty of Neuroscience, Texas A&M University
2011-16, 2019	Exemplary Teaching Award, College of Medicine, University of Florida
2017-2019	Term Professor, University of Florida
2018-2020	Research Foundation Professor, University of Florida

C. Contributions to Science

URL for full list of published work: https://www.ncbi.nlm.nih.gov/pubmed/?term=bizon+jl

1. A primary focus of my laboratory is to understand how alterations in excitatory/inhibitory (E/I) signaling dynamics in the prefrontal cortex contribute to age-related cognitive decline. To date, much of our work has

focused on GABA(B) receptors (refs a,b), which contribute to GABA signaling via both pre- and postsynaptic mechanisms. In PFC, we have documented a number of biochemical (refs a,c) and electrophysiological (ref b) changes in GABA(B)R signaling, which together suggest that pyramidal neurons in this brain region are subject to age-related increases in tonic inhibition (refs a, c). Potentially in response to this increased inhibition, GABA(B)R subunit expression is significantly reduced in the aged PFC (refs b, c). We have found that lower PFC GABA(B)R subunit expression strongly predicts better working memory abilities among aged rats (ref a). We have further identified specific excitatory signaling alterations that contribute to working memory impairments in aging, including reductions in presumptive synaptic NR2A-NMDARs (ref d). Based on these findings, my laboratory has provided preclinical validation of GABA(B)R antagonists and positive allosteric modulators of synaptic NMDARs for improving age-related cognitive decline.

a. Bañuelos C, Beas BS, McQuail JA, Gilbert RJ, Frazier CJ, Setlow B, **Bizon JL**. (2014) Prefrontal cortical GABAergic dysfunction contributes to age-related working memory impairment. *The Journal of Neuroscience.* 34(10):3457-66. PMCID: 3942567.

b. Carpenter HE, Kelly KB, **Bizon JL**, Frazier CJ. (2016) Age related changes in tonic activation of pre- and post-synaptic GABA(B) receptors in medial prefrontal cortex. *Neurobiology of Aging*. 45:88-97. PMCID: 523522.

c. Beas BS, McQuail JA, Bañuelos C, Setlow B, **Bizon JL**. (2017) Prefrontal cortical GABAergic signaling and impaired behavioral flexibility. *Neuroscience.* 345:274-286. PMCID: 5333995.

d. McQuail JA, Beas BS, Simpson K, Kyle K, Frazier CJ, Setlow B, **Bizon JL.** (2016) NR2A-containing NMDA receptors in the prefrontal cortex are required for working memory and predict age-related cognitive decline. *The Journal of Neuroscience.* 36(50):12537-12548. PMCID: 5157101.

2. My laboratory has developed sensitive behavioral methods to model hippocampal/medial temporal lobe-mediated deficits in aged rodents (refs a, b, c) and has used these behavioral models to investigate underlying neural mechanisms of cognitive decline in aging. Specifically, in the past several years, we have established sensitive behavioral tools for investigating how the perception and encoding of sensory stimuli is altered in aging and how such alterations contribute to mnemonic decline (refs a, c, d*).* We are now employing these same rigorous psychophysical methods (ref d) to better understand cognitive decline associated with Alzheimer's disease, using viral mediated delivery of wildtype and mutant tau to middle-aged and aged rat perirhinal cortex. Using this model, we are exploring whether perceptual discrimination learning assessments have utility as a behavioral biomarker for disease pathology.

   a. LaSarge CL, Montgomery KS, Tucker C, Slaton GS, Griffith WH, Setlow B, **Bizon JL**. (2007) Deficits across multiple cognitive domains in a subset of aged Fischer 344 rats. *Neurobiology of Aging*. Jun;28(6):928-36.

   b. **Bizon JL**, LaSarge CL, Montgomery KS, McDermott AN, Setlow B, Griffith WH. (2009) Spatial reference and working memory across the lifespan of male Fischer 344 rats. *Neurobiology of Aging*. 30(4):646-55. PMCID: 2703480.

   c. Montgomery, KS, Edwards, G, Kumar, A, Levites, Y, Meyers CA, Gluck M, Setlow, B and **Bizon, JL.** (2016) Deficits in hippocampal-dependent transfer generalization learning and synaptic function in mouse models of amyloidosis. *Hippocampus*. 26(4):455-71.PMCID: 4803574.

   d. Yoder WM, Gaynor, L, Burke SN, Setlow B, Smith DW, **Bizon JL.** (2017) Interaction between age and perceptual similarity in olfactory discrimination learning: relationship with spatial learning impairment. *Neurobiology of Aging.* 53:122-137. PMCID: 5393344.

3. Deciding among options that include both benefits and risks of adverse outcomes is fundamental to our ability to effectively navigate everyday life. As part of a long-standing collaboration with Dr. Barry Setlow, my laboratory has a strong interest in using animal models to understand the neural processes that support decision making. One element of this work involves elucidation of the neural circuits and signaling mechanisms that mediate how individuals weigh rewards against putative costs such as punishment or delay to reward delivery (refs c, d). A second element of this work is to determine how cost-benefit decision making changes across the lifespan (refs a, b). Our work was the first to show that aged rats have a strong preference for delayed over immediate rewards relative to young adult rats. These data are consistent with observations showing that aged humans are better at delaying gratification, and suggest that age-related neurobiological alterations are not universally detrimental but can support some beneficial cognitive outcomes (ref a).

a. Simon NW, LaSarge CL, Montgomery KS, Williams MT, Mendez IA, Setlow, B, **Bizon, JL.** (2010) Good things come to those who wait: attenuated discounting of delayed rewards in aged Fischer 344 rats. *Neurobiology of Aging*. 31(5):853-62. PMCID: 2866647.

b. Hernandez CM, Vetere LM, Orsini CA, McQuail JA, Maurer AP, Burke SA, Setlow B, **Bizon JL** (2017) Decline of prefrontal cortical-mediated executive functions but attenuated delay discounting in aged Fischer 344X brown Norway hybrid rats. *Neurobiology of Aging*. 60: 141-152. PMCID: 5669385.

c. Orsini CA, Hernandez CM, Kelly KB, Sarthak S, Frazier CJ, **Bizon JL**, Setlow B. (2017) Optogenetic inhibition reveals distinct roles for basolateral amygdala activation during discrete timepoints in risky decision making. *The Journal of Neuroscience.* 37, 11537-11548. PMCID: 5707761

d. Hernandez CM, Orsini CA, Labiste CC, Wheeler A-R, Ten Eyck TW, Bruner MM, Frazier CJ, Setlow B, **Bizon JL** (2019). Optogenetic dissection of basolateral amygdala contributions to intertemporal choice in young and aged rats. ***eLife.*** Apr 24;8. pii: e46174. PMCID 6530979

4. My early research showed that memory loss is associated with impaired HPA axis function and protracted glucocorticoid release following a stressor, and that such changes occur in the absence of frank hippocampal neural loss. Instead, we found that these changes are likely attributable to attenuated GR/MR expression within both aged hippocampus and prefrontal cortex (ref a). Other findings in neuroscience at the time highlighted the remarkable neurogenic capacity of the adult hippocampus (Kempermann and Gage, 1998; Gould and McEwen, 1993), and led to questions about whether age-related changes in this phenomenon could contribute to decline of mnemonic abilities associated with aging. My postdoctoral studies examined hippocampal neurogenesis in relation to age-related memory loss and showed that while there is a marked attenuation of new neurons born in the aged hippocampus (>-90%), new neuron production and differentiation did not predict the memory abilities of aged rats (refs b-d). Indeed, many aged rats were able to maintain spatial learning performance on par with young adults despite dramatic reductions in hippocampal neurogenesis. While these studies did not specifically address the role of hippocampal neurogenesis in normal learning and memory, they do indicate that reduced neurogenesis in normal aging is not sufficient to account for spatial memory dysfunction.

a. **Bizon JL**, Helm KA, Han JS, Chun HJ, Pucilowska J, Lund, PK, Gallagher, M (2001) Hypothalamic-pituitary-adrenal axis function and corticosterone receptor expression in behaviourally characterized young and aged Long-Evans rats. *European Journal of Neurosci*ence 14(10):1739-51.

b. **Bizon JL**, Gallagher M. (2003) Production of new cells in the rat dentate gyrus over the lifespan: relation to cognitive decline. *European Journal of Neuroscience*. 18(1):215-9.

c. **Bizon JL**, Lee HJ, Gallagher M. (2004) Neurogenesis in a rat model of age-related cognitive decline. *Aging Cell*. 3(4):227-34.

d. **Bizon JL**, Gallagher M. (2005) More is less: neurogenesis and age-related cognitive decline in Long-Evans rats. *Science Aging Knowledge Environment*. 2005(7):re2.

5. I have had a long-standing interest in the role of basal forebrain and cholinergic signaling in the modulation of cortical circuits and memory function. Highlights of this work include several studies from my pre-doctoral training in the laboratory of Dr. Christine Gall, in which we identified sources of local trophic support for basal forebrain and striatal cholinergic neurons (ref a, Bizon et al., 1996, Lauterborn et al., 1995). Subsequently, I used the selective neurotoxin 192-IgG saporin to show that removal of cholinergic neurons alters spatial learning strategies (ref b) and HPA function (Han et al., 2002) in young rats. More recently, we investigated both the number (ref d) and electrophysiological properties (ref c, Dubois et al., 2014) of cholinergic neurons in relation to age-related hippocampal-dependent spatial memory impairment. Our findings show that while there is modest cholinergic neuron loss with advanced aging, such changes cannot fully account for spatial learning deficits. Notably, our studies highlight a role for co-distributed basal forebrain GABAergic neurons in both cholinergic dysfunction (Dubois et al. 2014) and impaired memory (ref d).

a. **Bizon JL**, Lauterborn JC, Gall CM. (1999) Subpopulations of striatal interneurons can be distinguished on the basis of neurotrophic factor expression. *Journal of Comparative Neurology*. 408(2):283-298.

b. **Bizon JL**, Han JS, Hudon C, Gallagher M. (2003) Effects of hippocampal cholinergic deafferentation on learning strategy selection in a visible platform version of the water maze. *Hippocampus*. 13(6):676-84.

c. Murchison D, McDermott AN, LaSarge CL, Peebles KA, **Bizon JL**, Griffith, WH (2009) Enhanced calcium buffering in F344 rat cholinergic basal forebrain neurons is associated with age-related cognitive impairment. *Journal of Neurophysiology*. 102(4):2194-207 PMCID: 2775378.

d. Bañuelos C, LaSarge CL, McQuail JA, Hartman JJ, Gilbert RJ, Ormerod, B, **Bizon, JL**. Age-related changes in rostral basal forebrain cholinergic and GABAergic projection neurons: relationship with spatial impairment. *Neurobiology of Aging*. 2013 Mar;34(3):845-62. PMCID: 3632262.

D. CURRENT RESEARCH SUPPORT

RF1AG060778 (NIH-NIA) 2018/09/01-2023/08/31
Decision making and basolateral amygdala dysfunction in aging
Role: MPI (Setlow, Frazier MPIs)
The goal of this project is to determine the contributions of basolateral amygdala and related circuitry to age- and tau pathology-associated alterations in cost-benefit decision making

RF1AG064942 (NIH-NIA) 2019/08/15-2024/03/31
Immunotherapy targeting the HPA axis in Alzheimer's disease
Role: MPI (Golde, Lewis MPI)
The goal of this project is to determine the efficacy of an antibody against CRF at blocking neuropathology and cognitive deficits associated with Alzheimer's disease pathology

R21AG058240 (NIH-NIA) NCE
Interactions of perirhinal tau pathology and aging in cognitive dysfunction
Role:MPI (Burke MPI)
The goal of this project is to determine the contributions of perirhinal cortical tau pathology to perceptual and cognitive dysfunction in an aged rat model

R01 DA036534 (NIH-NIDA) NCE
Risk taking and cocaine use: interactions, mechanisms, and therapeutic targets
Role: co-I (Setlow PI)
The goal of this project is to determine neural mechanisms underlying relationships between risk taking behavior and cocaine self-administration.

R01 AG049722 (NIH-NIA) 2016/01/05-2021/01/15
The contribution of declines in functional connectivity to cognitive aging
Role: co-I (Burke PI)
The goal of this project is to investigate how disrupted communication between the prefrontal cortex and hippocampus contributes to age-associated cognitive decline.

R01 MH109548 (NIH-NIMH) 2016/01/01-2021/10/01
Testing and forecasting hippocampal theta wave propagation in learning and memory
Role: co-I (Maurer PI)
The goal of this project is to investigate how basal forebrain and entorhinal input to hippocampus regulate brain rhythms in behaving animals.

T32 AG061892 (NIH-NIA) 2018/09/01-2023/08/31
Clinical and Translational Pre-doctoral Training in Alzheimer's and Related Dementias
Role: MPI (Lewis, MPI)
The goal of this project is to support graduate training in Alzheimer's disease and related dementias

R01 AG060977 (NIH-NIA) 2019/02/01-2024/1/31
Metabolic interventions for enhancing cognitive resilience in aging and AD
Role: co-Investigator (Burke PI)
Agency: National Institute on Aging

Ed and Ethel Moore Alzheimer's Disease Research Program 2021/01/01-2023/01/01
Effects of cannabis on Alzheimer's disease-related pathology and cognitive decline.
Role: MPI, (MPI Setlow)

Pending

R01AG067429R1 (NIH-NIA) 2021/4/1-2026/3/31
Mechanisms and therapeutic potential of vagus nerve stimulation in aging and Alzheimer's Disease
Role: MPI (Setlow MPI)
Requested: $400,000 direct/yr (Requested)
Agency: National Institute on Aging
Pending Council Review- Impact Score in Funding Range

R01AG072714R1 (NIH-NIA) 2020/12/10-3/31/26
Effects of cannabis on age-related cognitive decline and Alzheimer's disease pathology
Role: MPI (Setlow MPI)
Requested: $400,000 direct/yr (Requested)
Agency: National Institute on Aging
Pending Scientific Review

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Dawn Bowers, Ph.D.

eRA COMMONS USER NAME (credential, e.g., agency login): dbowers

POSITION TITLE: Professor of Clinical & Health Psychology and Neurology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	END Date MM/YYYY	FIELD OF STUDY
Emory University	--	1968-1970	Chemistry
University of Florida	B.S.	1972	Psychology
University of Florida	M.S.	1974	Clinical Psychology
Boston University	internship	1977	Neuropsychology
University of Florida	Ph.D.	1978	Clinical & Health Psychology
University of Florida	Post-Doc	1979	Behavioral Neurology

Personal Statement

I am a university professor, a cognitive neuroscientist, and a board certified clinical neuropsychologist with longstanding research and clinical expertise in neurocognitive and emotional changes associated with age-related neurologic disease. I have been research funded for over 35 years. I am strongly committed to research training and currently serve as the MPI and Program Director for an NINDS-funded T32 predoctoral program focused on Interdisciplinary Training in Movement Disorders and Neurorestoration. I have a keen understanding of the mentoring process for aspiring clinical scientists and have been the primary sponsor for numerous pre-doctoral and post-doctoral NRSA recipients, post-doctoral minority supplements as well as multiple CDA-2 and K-23 applicants. I have been the recipient of various mentoring awards, both international, national, and local and have mentored over 26 doctoral students who have gone one to be successful clinician scientists in their own right. Within my home department, I direct a post-doctoral program focused on clinical training in neuropsychology. My current research focuses on novel interventions for cognitive decline, real time fMRI for modulating emotional responsivity, psychophysiologic signatures of apathy and depression, and interactive effects of novel therapies on cognition and mood.

Recent Publications with Trainees *(in italics)*

Scott, B., Eisinger, R., Burns, M., Lopes, J., Okun, M.S., Gunduz, A., Bowers, D. (2020). Co-occurrence of apathy and impulse control disorders in Parkinson's disease. . *Neurology*. 2020 Nov 17;95(20):e2769-e2780. doi: 10.1212/WNL.0000000000010965. Epub 2020 Oct 1. PMID: 33004605.

Kenney, L.E., Rohl, B., Lopez, F.V., *Lafo, J.A.*, Jacobson, C., Okun, M.S., Foote, K.D., Bowers, D. (2020). The UF Deep Brain Stimulation Cognitive Rating Scale (DBS-CRS): Clinical decision making, validity, and outcomes. *Frontiers Neuroscience, 14, p 1-10; doi 10.3389/ fnhum .2020.678216.*

Marra, D., Hamlett, K., Bauer, R.M., Bowers, D. (2020). Validity of teleneuropsychology for older adults in response to Covid-19: A systematic and critical review. *The Clinical Neuropsychologist,* Jun 10;1-42. doi: 10.1080/13854046.2020.1769192

Trifilio, E., Tanner JJ, *Butterfield L*, *Mangal P, Maye JE*, Marsiske M, Price CC, Bowers D. (2019). A tale of two stories: validity of an alternative story memory test in a sample of older adults. *The Clinical Neuropsychologist,* Jan 12, 1-16.

Positions and Honors

Positions and Employment

1976-1977	Teaching Fellow in Neurology, Boston University College of Medicine
1976-1977	Internship in Clinical Psychology/Neuropsychology, Boston VAMC
1976-1977	Externship in Geriatric Neuropsychology, Framingham Heart Study, MA
1979	Post-doctoral Fellowship, Behavioral Neurology, UF College of Medicine
1980- 1998	Associate Professor in Neurology [Assistant 1980-85], UF College of Medicine
1984-1998	Neuropsychologist, State of Florida Memory Disorders Clinic
1998-	Professor of Clinical & Health Psychology [Associate 1998-2002]
2006-2018	Area head, Neuropsychology Area, Dept. Clinical & Health Psychology
2006-	Director, Neuropsychology Post-doctoral Program

Other Positions and Professional Memberships

1995-1998	Member, Merit Review Committee, Mental Health &d Behavioral Science, Dept. Veterans Affairs
1999-2003	Special Review Panel, Minority Research Infrastructure Support Program (MRISP), NIMH
2000-	Editorial Boards, The Clinical Neuropsychologist, JINS
2004-05	Ad hoc Member, NIH Biobehavioral Mechanisms of Emotion, Stress, and Health Study Section
2011-12	Ad hoc Member, Special Emphasis Panel, Clinical and Imaging Translations Study Section (ZRG1 DTCS Y(81).
2012	Panel Member, NIH Review of LRP proposals
2012-15	Board of Governors, International Neuropsychological Society
2012-14	Chair & Vice Chair, Faculty Council, College of PHHP
2013-	Fellows Committee, Division 40, APA (Member 2013-16; Chair 2016-17)
2013-17	Merit Review Panel for Mental Health and Behavioral Sciences-B, BLRD and SCR&D; Department of Veterans Affairs
2017-2018	Member, NINDS T32 review committee, NIH
2020	Member, NINDS T32 review committee, NIH
2020-2022	Member, NINDS R15 Review Committee
Membership	American Psychological Association (Divisions 12, 20, & 40), International Neuropsychology Society, American Academy of Clinical Neuropsychology, Society for Neuroscience

Honors

2006-	UF Foundation Research Professor
2012	Fellow, American Psychological Association, Division 40
2013	Board Certification in Clinical Neuropsychology (ABBP/cn)
2014	Paul Satz Career Mentoring Award, International Neuropsychology Society
2014	Edith Kaplan Neuropsychology Award, Massachusetts Psychological Society
2015	Doctoral Mentoring Award, College of Public Health and Health Professions, UF
2015	Audrey Shumacher Teaching Award, Department of Clinical & Health Psychology
2015	Research Award, Department of Clinical & Health Psychology
2016	University of Florida Doctoral Mentoring Award
2017	UF Term Professor Award, University of Florida

Contributions to Science

Motivational Disturbance in Older Adults including Parkinson Disease. This line of research focuses on apathy, a motivational disturbance which we believe is the primary neuropsychiatric signature in Parkinson disease. In an initial study published over a decade ago Brain, we reported that Parkinson patients had muted emotional reactivity, as indexed by blunted startle eyeblink responses, which was presumed to reflect aberrant amygdala gating related to dopamine. Since that time, my team has examined psychometric properties of different apathy scales and shown how depression and apathy differentially predict cognitive, electrophysiologic, and trajectory of motor decline in Parkinson disease. The importance of this dissociation

relates to diagnosis and treatment, as pharmacologic therapy for depression with SSRI's actually worsening apathy. Current efforts relate to non-pharmacologic treatment approaches for apathy, ranging from motivational telehealth interventions to emotion regulation strategies.

- Bowers, D., Miller, K., Mikos, A., Kirsch-Darrow, L., Springer, S., Fernandez, H., Foote, K., Okun, M.S. (2006). Startling facts about emotion in Parkinson disease: Blunted reactivity to aversive stimuli. *Brain, 129,* 3345-3365.
- Kirsch-Darrow, L., Fernandez, H., Okun, M., Bowers, D. (2006). Dissociating apathy and depression in Parkinsons's disease. *Neurology.* 67(1), 20-27.
- Zahodne, L, Marsiske, M., Okun, M.S., Rodriguez, R., Malaty, I, Bowers, D. (2012). Mood and motor symptoms in Parkinson's Disease: a multivariate latent growth curve modeling. N*europsychology*, 26, 71-80. PMID: 22142359
- Renfroe, J.B., Bradley, M.M., Okun, M.S., Bowers, D. (2016). Motivational engagement in Parkinson disease: perception and preparation for action. *International Journal of Psychophysiology, 99,* 24-32. PMID:26659013

Vascular Comorbidities and Cognition in Parkinson Disease. Despite clinical lore that patients with Parkinson Disease are impervious to effects of hypertension due to the blood pressure lowering effects of various dopamine medications, we have shown that those with hypertension and other vascular comorbidities 'take a hit' in terms of executive function, similar to that of non-Parkinson Disease older adults.

- Jones, J., Malaty, I., Price C.C., Okun, M.S., Bowers, D. (2012). Health comorbidities and cognition in 1948 patients with idiopathic Parkinson disease. *Parkinsonism and Related Disorders.* 18 (10), 1073-1078 PMID: 22776043
- Jones, J., Jacobson, C., Murphy, M.C., Price, C.E., Okun, M.S., Bowers, D. (2014). Influence of hypertension on neurocognitive domains in non-demented Parkinson's disease patients. *Parkinson's Disease, 2014, Article ID 507529,* [http://dx.doi.org/10.1144/2014/507529]. PMID: 24587937 PMCID: PMC3920751.
- Scott, B.M., Maye, J., Jones, J., Thomas, K., Mangal, P., Trifilio, E., Hass, C., Marsiske, M., Bowers, D. (2016). Post-exercise pulse pressure is a better predictor of executive function than pre-exercise pulse pressure in cognitively normal older adults. *Aging, Neuropsychology, and Cognition.* 23 (4), 464-476. PMID: 26629911
- Jones, J., Price, CE, Tanner, J., Okun, M.S., Bowers, D. (2017). Is cognition more vulnerable to the effects of cardiovascular risk in Parkinson patients versus controls: A neuroimaging andneuropsychological study. *J. International Neuropsychology Society.* 23, 1-10 PMID: 28162137

Retrosplenial Amnesia. This body of work described the first human case of a pure amnestic syndrome due to an isolated lesion of the retrosplenial (RS) region. This region, located beneath the posterior cingulum, receives direct input from the fornix of the hippocampus, projects forward via the cingulum and serves as way station for input from the adjacent parietal region. We conceptualized the amnesia induced by this lesion as a 'disconnection' variant, and a neuroimaging study (PET) of this patient showed hypometabolism of the thalamus and hypermetabolism of the ipsilateral frontal lobe. Since our early description, other cases of retrosplenial amnesia have been described, and **this region has been implicated as part of an information hub in classic Alzheimer's syndrome.**

- Valenstein, E., Bowers, D., Verfaellie, M., Heilman, K., Day, A., and Watson, R. (1987). Retrosplenial amnesia. *Brain, 110*, 1631-1646.
- Bowers, D., Verfaellie, M., Valenstein, E., and Heilman, K. (1988). Impaired acquisition of temporal information in retrosplenial amnesia. *Brain and Cognition, 8,* 47-66
- Heilman, K.M., Bowers, D., Watson, R., Day, A., Valenstein, E., Hammond, E., and Duara, R. (1990). Frontal hypermetabolism and thalamic hypometabolism in a patient with abnormal orienting and retrosplenial amnesia. *Neuropsychologia, 28,* 161-170.
- McDonald, C., Crosson, B., Valenstein, E., and Bowers, D. (2001). Verbal encoding deficits in a patient with retrosplenial amnesia. *Neurocase, 7*, 407-17.

Pseudoneglect. Early in my career, I described a mild asymmetry in spatial attention whereby normal individuals tend to attentional favor the left side of space. I referred to this phenomenon as 'pseduoneglect' since the spatial error was opposite in direction to that in patients with the neglect syndrome following right parietal strokes. Since the initial discovery, pseudoneglect (or spatial asymmetry) has been observed across

studies ranging from judgements of brightness, numerosity, size, and representation to neuroimaging studies. The original study initially describing this phenomenon (Bowers & Heilman, 1980) has been cited overt 1000 times, and continues to be studied today.

- Bowers D, Heilman KM. (1980). Pseudoneglect: effects of hemispace on a tactile line bisection task. Neuropsychologia 18: 491–498
- Heilman KM, Bowers D, Watson RT. (1984). Pseudoneglect in a patient with partial callosal disconnection. Brain. 107 (Pt 2):519-32.
- W atson RT, Heilman KM, Bowers D. (1985). Magnetic resonance imaging (MRI, NMR) scan in a case of caollosal apraxia and pseudoneglect. Brain, 108 (Pt 2):535-6

Research Support

Ongoing Research Support

#20A15 Florida Dept of Health PI: Ebner 01/2020-12/2023
Ed & Ethel Moore Alzheimer's Program
Determining Plasticity of Brain-Regulatory Mechanisms Related to Emotion Processing: A Neurofeedback Approach in Older Adults with Amnestic Mild Cognitive Impairment
This project uses real time fMRI neurofeedback to examine the ability of older adults and those with amnestic MCI to self-regulate the level of brain activity in limbic regions.
Role: Co-Inv

NIH/NIA R01-AG064587 MPI: Bowers (Woods/Alexander) 08/01/2019-3/2024
Revitalizing Cognition in Older Adults at Risk for Alzheimer's disease with Near Infrared Photobiomodulation
This multi-site Phase II clinical trial tests whether NIR photobiomodulation will affect cognition and neural network connectivity in older adults with subjective cognitive complaints and family members with Alzheimer's disease.

NINDS 2T32-NS082168 MPI: Bowers, Vaillancourt 05/2015- 06/2025
Interdisciplinary Training in Movement Disorders and Neurorestoration
This grant focuses on interdisciplinary training of predoctoral trainees across cognitive/movement science.
Role: MPI

R01-AG12802177, Supplement PI: Ebner 08/2019-09/2022
Uncovering and Surveilling Financial Deception Risk in Aging, Supplement.
This supplement examines factors contributing to susceptibility to deception and scams in older adults at risk for Alzheimer's disease.
Role: Co-I

NIH/NINSA-1UH3NS109845 MPI: Oweiss/Foote 09/2019-8/31/2024
Dual Lead Thalamic DBR-DBS Interface for Closed Loop Control of Severe Essential Tremor
This study examines utility of smart DBS system for control of tremors in individuals with refractory Essential Tremor.
Role: Co-I

Parkinson Foundation PI: Bowers 06/2019-6/2021
Shining Light on the Brain: Revitalizing cognition and motor symptoms in patients with Parkinson disease
The goal of this pilot project is to test a novel therapeutic intervention for improving motor and cognitive symptoms in individuals with Parkinson disease
Role: PI

McKnight Research Foundation MPI:Bowers/Alexander 05/2018-12/2021
A Pilot Intervention with Near Infrared Stimulation: Revitalizing Cognition in Older Adults
This is a randomized sham controlled trial with community dwelling older adults that is testing whether transcranial and infranasal delivery of near infrared light (NIR) will positively influence cognition and mood.
Role: MPI

NIH/R21-AG057200 MPI: Ebner/Bowers, MPI) 04/2017-12/2020
Determining plasticity of brain-regulatory mechanisms related to emotion processing: A Neurofeedback approach in aging and Parkinson Disease
This project examines use of real time fMRI to provide neurofeedback for increasing limbic activation (anterior insula) and its influence cognitive and behavioral ratings.

NIH R01-HD091658 PI: Hegland 04/2017-03/2022
Mechanisms of Airway Protection Dysfunction in Parkinson's Disease
The major goal of this project is to further specify the sensory mechanisms associated with airway protection disorders in order to advance the clinical management of patients with Parkinson's disease and Aspiration Pneumonia (APn).
Role: Co-I

NIH R01-NS096008 MPI:Gunduz, Okun 07/2016-6/2021
The Human Thalamocortical Network in Tourette.
This proposal tests the viability of a novel 'smart' DBS system that senses the onset of the tic cascade prior overt tic behavior.
Role: Co-I

UH3-NS095553 MPI: Gunduz/Foote 2016-2021
NIH/NINDS
Closing the Loop on Tremor: A Responsive Deep Brain Stimulator for Treatment of Tremor
This project examines the thalamocortical neurophysiology of tremor.
Role: Co-I

Recently Completed Research Support
R03-MH109333 PI: Bowers 2017-2018
Dissociating Components of Anhedonia: Pilot Behavioral and fMRI Data for Effort Expenditure for Rewards Task
The goal of this study is to examine the neural correlates of anhedonia in older and younger adults.
Role: PI

ALZ67-State of Florida PI: Bowers 2016-2018
Pilot Intervention in Mild Cognitive Impairment: A Proof of Concept Study with Transcranial Near Infrared Stimulation
This pilot study will test in a randomized sham controlled trial whether a novel intervention, near infrared brain stimulation, has potential for improving cognitive symptoms in individuals with amnestic mild cognitive impairment.

ALZ-121 State of Florida PI: Wicklund 2016-2018
Consortium for Diagnostic Algorithm with Novel Markers in early Alzheimer's Disease
This project aims to validate novel neuropsychological and imaging measures and develop diagnostic algorithms for classifying early AD using clinical, neuropsychological, and neuroimaging data.
Role: Co-I

Fogarty Foundation MPI: Bowers/Sinha 12/2017-08/2018
Dose Response Relationship between Near Infrared Stimulation and Brain Activity using Neuroimaging
This project examined relationship between resting state connectivity using fMRI and sham, low dose, and high dose of NIR stimulation in healthy older adults.
Role: Mentor

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Bumanglag, Argyle V.

eRA COMMONS USER NAME (credential, e.g., agency login): abumanglag

POSITION TITLE: Research Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Hawaii, Honolulu HI	BA	05/2002	Psychology
University of Arizona, Tucson AZ	PhD	12/2010	Neuroscience
Yale University, New Haven CT	Post-doc	06/2012	Neuroscience
Morehouse School of Medicine, Atlanta GA	Post-doc	06/2019	Neuroscience

A. Personal Statement

I received my PhD in Neuroscience at the University of Arizona under the mentorship of Dr. Robert Sloviter, and my research career has focused primarily on understanding hippocampal epileptogenesis and the nature of the latent period following brain injury. Our finding that granule cell-onset epilepsy is coincident with the initial injury, and not delayed, suggested that selective neuronal injury or dysfunction could be a primary epileptogenic mechanism. Our recent experiments based on this hypothesis, in conjunction with years of meticulous epilepsy animal model development, have led to the development of a new model of temporal lobe epilepsy described in this grant application. We have recently shown that intrahippocampal injections of Stable Substance-P Saporin reliably produces hippocampal sclerosis pathology and chronic seizures in rats.

I joined the laboratories of Drs. Jennifer Bizon and Sara Burke at the University of Florida, where we are are focused on understanding and treating disruptions in excitatory/inhibitory balance in the aged brain. Relatedly, we have begun preliminary work examining behavioral comorbidities associated with temporal lobe epilepsy across the lifespan.

B. Positions and Honors

2002-2010 Graduate Research Associate, Graduate Interdisciplinary Program in Neuroscience, University of Arizona, Tucson, AZ
2010-2011 Postdoctoral Associate, Department of Neurosurgery, Yale University, New Haven, CT
2011-2012 Associate Research Scientist, Department of Neurosurgery, Yale University, New Haven, CT
2012-2019 Postdoctoral Research Fellow, Morehouse School of Medicine, Atlanta, GA
2019- Research Assistant Professor, University of Florida, Gainesville, FL

Other experience and professional memberships

2008- Member, Society for Neuroscience
2010-2012 Member, American Epilepsy Society

Selected Honors

NIH Neuroscience Training Grant Fellowship (2002-2003)

C. Contributions to Science

1. **Hippocampal epileptogenesis and the latent period following selective brain injury:** The primary focus of my research has been on understanding the nature of the “latent period” following epileptogenic brain injury in acquired temporal lobe epilepsy. The “latent period” between a precipitating brain injury and clinical epilepsy is often regarded as a “gestational,” seizure-free period of "epileptogenesis," during which a secondary mechanism, triggered by the initial injury, matures. This concept of an obligatory secondary mechanism that only slowly causes epilepsy to emerge, has had a significant impact on the field of epilepsy research for decades. My initial work was the first study to use continuous (24/7) *in vivo* monitoring of hippocampal activity to determine exactly when seizures first occurred after status epilepticus-induced brain injury (Bumanglag and Sloviter, 2008). We determined that animals began to have behavioral seizures 2-3 days after convulsive status epilepticus (SE) in awake rats. We hypothesized that the minimal latency to clinical epilepsy following convulsive SE was due to the extent of the initial neuron loss (Bumanglag and Sloviter, 2008). Therefore, we developed an animal model of epilepsy using prolonged perforant path stimulation under urethane sedation, which avoided convulsive SE, and produced selective hippocampal pathology and a verified 2-4 week latent period to clinical seizures. In our recently completed study using continuous depth recording directly from the granule cell layer in awake rats after prolonged non-convulsive SE, we have shown that epileptogenesis can be an immediate consequence of neuron loss, and that the latent period, when it exists, is a subtle epileptic state in transition to a more clinically obvious epileptic state (Bumanglag and Sloviter, 2018).

    a. **Bumanglag AV**, Sloviter RS. Minimal latency to hippocampal epileptogenesis and clinical epilepsy after perforant pathway stimulation-induced status epilepticus in awake rats. *J Comp Neurol* 2008; 510: 561-580.
    b. Sloviter RS, **Bumanglag AV**, Schwarcz R, Frotscher M. Abnormal dentate gyrus network circuitry in temporal lobe epilepsy. In: *Jasper’s Basic Mechanisms of the Epilepsies, 4th Edition* (Noebels J, Avoli M, Rogawski M, Olsen R, Delgado-Escueta A, Eds), Oxford University 2012.
    c. Sloviter RS, **Bumanglag AV**. Defining “epileptogenesis” and identifying “antiepileptogenic targets” in animal models of acquired temporal lobe epilepsy is not as simple as it might seem. *Neuropharmacology* 2013; 69:3-15.
    d. **Bumanglag AV**, Sloviter RS. No latency to dentate granule cell epileptogenesis in experimental temporal lobe epilepsy with hippocampal sclerosis. *Epilepsia* 2018, *in press.* DOI: 10.1111/epi.14580.

2. **Selective GABA neuron dysfunction results in hippocampal sclerosis and chronic epilepsy.** The finding that epileptogenesis can be an immediate process coincident with the initial neuron loss refocused our efforts on determining whether GABA neuron dysfunction may be immediately epileptogenic. Our work on epileptogenesis led to the development of a novel animal model of TLE using intrahippocampal injection of Stable Substance P-Saporin (SSP-Saporin) to selectively target and ablate hippocampal GABA neurons in rats. Using this method to create a longitudinally extensive hippocampal defect, we are able to produce an animal model of TLE that reliably replicates the defining features of clinical TLE-HS+. Using granule cell layer depth electrode recordings, we were able to determine that animals became epileptic and generated granule cell-onset seizures months after selective SSP-Saporin-mediated ablation of hippocampal GABA neurons.

    a. Chun E*, **Bumanglag AV***, Burke SN, Sloviter RS. 2019. Targeted hippocampal GABA neuron ablation by Stable Substance P-saporin causes hippocampal sclerosis and chronic epilepsy in rats. Epilepsia 60(5):e52-e57. doi:10.1111/epi.14723. **Both authors contributed equally to this work*

Complete List of Published Work in My Bibliography

https://www.ncbi.nlm.nih.gov/sites/myncbi/argyle.bumanglag.1/bibliography/56560282/public/?sort=date&direction=descending

D. Additional Information: Research Support and/or Scholastic Performance

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.

Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: BURKE, SARA

eRA COMMONS USER NAME (agency login): sburke

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Oregon, Eugene, OR	BS	08/1999	Psychology, Chemistry
University of Oregon, Eugene, OR	MS	12/2000	Psychology
University of Arizona, Tucson, AZ	PHD	05/2009	Neuroscience, pharmacology
University of Arizona, Tucson, AZ	Postdoctoral Fellow	09/2013	Non-human primate and rodent models of cognitive aging

A. PERSONAL STATEMENT

Although a majority of the 44 million Americans over the age of 65 will experience cognitive decline that interferes with their quality of life, understanding the loss of function in the brain that produces impairments in advanced age remains elusive. A significant barrier to uncovering the neurobiology of age-related cognitive decline is that no single brain region supports complex behavior in isolation, and old age affects different brain regions in distinct ways. Thus, attempts to correct impairments in one brain area may actually exacerbate dysfunction in other regions, blocking the restoration of normal behavior. Furthermore, a fundamental gap exists in our understanding of how these brain structures interact over the lifespan, and how this relates to cognitive and physical abilities. Thus, in order to design therapeutic strategies for maintaining function in the elderly, it is imperative that we understand how different brain regions communicate with each other in support of behavior, and how this is altered by old age. The *long-term goals* of my NIH-funded research program are to 1) pinpoint alterations in how different brain regions communicate over the lifespan and how this contributes to loss of function in advanced age, and 2) to design therapeutic strategies for alleviating cognitive dysfunction in order to promote positive health outcomes in the elderly (e.g. ref a). To do this, my laboratory uses multiple levels of analysis, including designing and validating novel behavioral paradigms (b), gene expression in defined neural circuits (c), and small animal resting state fMRI (d). Using a cross-disciplinary and integrative approach, current projects in my laboratory are focused on uncovering mechanisms of age-related impairments in hippocampal-dependent sensory discrimination across modalities in normal aging and in a novel model of tau pathology, identifying age-associated changes in medial temporal lobe-prefrontal functional connectivity that contribute to memory deficits using *in vivo* neurophysiology, cellular imaging as well as resting state fMRI, and testing whether diet-based therapies that improve neurometabolism can globally improve neural network function in old animals. Our rationale is that by elucidating how aging influences systems-level dynamics, we will be better positioned to develop interventions that broadly improve cognition and everyday living.

a. Hernandez AR, Campos KT, Truckenbrod LM, Hernandez CM, Sakarya Y, McQuail JA, Carter CS, Bizon JL, Maurer AP, **Burke SN** (2018). The anti-epileptic ketogenic diet reduces adiposity and alters hippocampal transporter levels in aged rats. *Journal of Gerontology, Series A.*

b. Hernandez AR, Truckenbrod LM, Campos KT, Williams SA, **Burke SN** (2019). Sex Differences in age-related impairments vary across cognitive and physical assessments in rats. *Behavioral Neuroscience, in press.* DOI: 10.1037/bne0000352.

c. Hernandez AR, Reasor JE, Truckenbrod LM, Campos KT, Federico QP, Fertal KE, Lubke KN, Johnson SA, Clark BJ, Maurer AP, **Burke SN** (2018). Dissociable effects of advanced age on prefrontal cortical and medial temporal lobe ensemble activity. *Neurobiology of Aging,* 70:217-232.

d. Colon-Perez LM, Turner SM, Lubke KN, Febo M*, **Buke SN*** (2019). Multi-scale Imaging Reveals Aberrant Functional Connectome Organization and Elevated Dorsal Striatal Arc Expression in Advanced Age. *eNeuro*, Dec 26;6(6).

B. POSITIONS AND HONORS

Positions and Employment

1997 - 1999	Undergraduate Research Assistant, Dr. Richard Marrocco's Visual-Attention laboratory, University of Oregon, Eugene, OR
1999 - 2000	Graduate Research Associate, Dr. Richard Marrocco's Visual-Attention laboratory, University of Oregon, Eugene, OR
2000 - 2002	Research Associate, Dr. Alvin Eisner's Visual Adaptation laboratory, Oregon Health & Science University, Portland, OR
2003 - 2004	Graduate Teaching Assistant for MSB407: Cellular, Molecular Neuroscience, University of Arizona, Tucson, AZ
2006 – 2011	Teaching Assistant for NRSC4/524: Gerontology, University of Arizona, Tucson, AZ
2013 – 2019	Assistant Professor, Department of Neuroscience, University of Florida, Gainesville, FL
2019 – *present*	Associate Professor, Department of Neuroscience, University of Florida, Gainesville, FL

Other Experience and Professional Memberships

2008 - 2009	Mentor and small group leader, Undergraduate Biology Research Program, Univ. of Arizona
2010 - 2011	Membership Survey Advisory Group, Society for Neuroscience
2010 - 2011	Mentor, University of Arizona Assurance Program
2015 - 2016	Member of Council for Undergraduate Research
2016 - 2019	Director of the UF Summer Neuroscience Internship Program
2017 - 2019	President of Florida Consortium on the Neurobiology of Cognition (http://fcneurocog.org/)
2002- *present*	Member, Society for Neuroscience
2014 - *present*	Member, North Central Florida Chapter of the Society for Neuroscience
2014 - *present*	Mentor, University of Florida Scholar Award
2015 - *present*	Member Faculty for Undergraduate Neuroscience

Honors

1999	Departmental Honor's in Psychology, University of Oregon
1999	Magna Cum Laude, University of Oregon
1999	Inducted, Phi Beta Kappa
2002	National Institute of Health Training Grant Recipient, University of Arizona
2006	Recipient of the Ruth L. Kirschstein National Research Service Award, National Institute of Health
2008	D.G. Marquis Behavioral Neuroscience Award, American Psychology Association
2009	Mentor of the Year Award, Undergraduate Biology Research Program, University of Arizona
2010	D.G. Marquis Behavioral Neuroscience Award, American Psychology Association
2012	Honorable Mention, Mentor of the Year, Undergraduate Biology Research Program, University of Arizona
2014	Best Talk, Department Data Blitz, Department of Neuroscience, University of Florida
2014-2015	Exemplary Teaching Award, University of Florida College of Medicine
2015	Claude D. Pepper Older Americans Independence Junior Scholar
2014-2015	Exemplary Teaching Award, University of Florida College of Medicine
2016	Excellence Awards for Assistant Professors
2017	American Psychological Association Early Career Award for Distinguished Contribution in Cognitive and Behavioral Neuroscience
2018	McKnight Brain Institute Leadership Award
2020	University Term Professorship Award

C. Contribution to Science

1. A majority of research regarding mechanisms of cognitive aging in animal models has primarily examined one brain region within a single study, with many focusing on the hippocampus or prefrontal cortex in

isolation. While this work has been foundational, it cannot uncover mechanisms of distributed network dysfunction. Thus, one aspect of my current research program is to examine the alterations in network-level interactions across multiple brain structures that underlie cognitive dysfunction in aging and the early stages of Alzheimer's disease. In support of this objective, we have published a series of experiments that examine the role of prefrontal cortical-medial temporal communication in higher cognition. Specifically, we have shown that performance on the working memory/bi-conditional task (WM/BAT), which assesses multitasking abilities is highly sensitive to detecting deficits in old age compared to more traditional cognitive tests used to quantify age-related impairments, such as the Morris watermaze (Hernandez et al., 2015). This task (formerly called the object-place paired association task) detects behavior deficits in both aged male and female rats, and performance is not affected by sex or estrus phase (a). Moreover, we have linked age-associated impairments on the WM/BAT to disrupted communication between the medial prefrontal cortex and the perirhinal cortex (b,c). Finally, we have recently shown that cognitive training on WM/BAT alters the functional connectome of aged rats, and elevated resting state connectivity between the prefrontal cortex and dorsal striatum is correlated with suboptimal response-based strategies during training on this task (d). My expertise in using behavioral assays to assay circuit engagement is directly relevant to the current proposal.

a. Hernandez AR, Truckenbrod LM, Campos KT, Williams SA, **Burke SN** (2019). Sex Differences in age-related impairments vary across cognitive and physical assessments in rats. *Behavioral Neuroscience, in press.* DOI: 10.1037/bne0000352.
b. Hernandez AR, Reasor JE, Truckenbrod LM, Lubke, K, Johnson SA, Bizon JL, Maurer AP, **Burke SN** (2016). Medial Prefrontal-Perirhinal Cortical Communication is Necessary for Flexible Response Selection. *Neurobiology of Learning and Memory,* 137:36-47.
c. Hernandez AR, Reasor JE, Truckenbrod LM, Campos KT, Federico QP, Fertal KE, Lubke KN, Johnson SA, Clark BJ, Maurer AP, **Burke SN** (2018). Dissociable effects of advanced age on prefrontal cortical and medial temporal lobe ensemble activity. *Neurobiology of Aging,* 70:217-232.
d. Colon-Perez LM, Turner SM, Lubke KN, Febo M*, **Buke SN*** (2019). Multi-scale Imaging Reveals Aberrant Functional Connectome Organization and Elevated Dorsal Striatal Arc Expression in Advanced Age. *eNeuro*, Dec 26;6(6).

2. A long-standing presumption in the field of cognitive aging had been that aged animals have difficulty recognizing stimuli because they "forget" items that have been previously experienced. This idea, however, was difficult to reconcile with other data showing that aged subjects have an increase in false memories. I designed a series of experiments to elucidate the origins of age-associated recognition memory impairments that led to the novel observation that old animals have recognition memory deficits because they have a reduced ability to discriminate novel stimuli from those that are familiar, which manifests as a false memory (a). This work led to foundational insights regarding age-associated declines in recognition memory, which presumably arise from perirhinal cortical dysfunction, and was later replicated in monkeys (b) and humans (Ryan et al., 2012). We have recently extended this work to show that recognition impairments are due to a reduced ability of aged rats to discriminate between similar stimuli with a LEGO©-object discrimination task (c), and this is related to hyperactivity in CA3 of the hippocampus and the lateral entorhinal cortical neurons that project to CA3 (d).
   a. **Burke SN**, Wallace JL, Nematollahi S, Uprety AR, Barnes CA (2010). Pattern separation deficits may contribute to age-associated recognition impairments. *Behav Neurosci*. 2010 Oct;124(5):559-73.
   b. **Burke SN**, Wallace JL, Hartzell AL, Nematollahi S, Plange K, Barnes CA (2011). Age-associated deficits in pattern separation functions of the perirhinal cortex: a cross-species consensus. *Behav Neurosci*. 125(6):836-47.
   c. Johnson SA, Turner SM, Santacroce LA, Carty KN, Shafiq L, Bizon JL, Maurer AP, **Burke SN** (2017). Rodent age-related impairments in discriminating perceptually similar objects parallel those observed in humans. *Hippocampus*. 27(7):759-776.
   d. Maurer AP, Johnson SA, Hernandez AR, Reasor J, Cossio DM, Fertal KE, Mizell JM, Lubke KN, Clark BJ, **Burke SN** (2017). Age-related changes in lateral entorhinal and CA3 neuron allocation predict poor performance on object discrimination. *Frontiers in Systems Neuroscience*, 30;11:49.

3. In young animals, dynamic hippocampal activity patterns support learning and memory. I have been involved in a series of papers that show how behavior-dependent modulation of hippocampal activity is compromised in aged animals to produce memory deficits (a,b). Moreover, we have shown that altering NMDA receptor currents with the Alzheimer's disease therapeutic memantine can restore experience-dependent plasticity in

aged memory-impaired rats (a). This paper, on which I was first author, received the D.G. Marquis Behavioral Neuroscience Award from the American Psychological Association for the best paper published in *Behavioral Neuroscience* in 2008. More recently, we have shown that disrupted activity deficits in the hippocampus may be linked to impaired neurometabolism. Specifically, we have observed that expression of several ATP-dependent transporters is reduced in old compared to young rats. Importantly, reduced transporter expression in old animals can be normalized by a ketogenic diet (c), which also improves WM/BAT performance (see Contribution 1, d). These papers demonstrate my expertise regarding the physiological signatures of neural dysfunction and a commitment to explore new therapeutics for treating cognitive aging.

a. **Burke SN**, Maurer AP, Yang Z, Navratilova Z, Barnes CA (2008). Glutamate receptor-mediated restoration of experience-dependent place field expansion plasticity in aged rats. *Behav Neurosci*. 122(3):535-48.
b. Gerrard JL, **Burke SN**, McNaughton BL, Barnes CA (2008). Sequence reactivation in the hippocampus is impaired in aged rats. *J Neurosci*. 28(31):7883-90.
c. Hernandez AR, Campos KT, Truckenbrod LM, Hernandez CM, Sakarya Y, McQuail JA, Carter CS, Bizon JL, Maurer AP, **Burke SN** (2018). The anti-epileptic ketogenic diet reduces adiposity and alters hippocampal transporter levels in aged rats. *Journal of Gerontology, Series A.*
d. Hernandez AR, Hernandez CM, Campos K, Truckenbrod L, Federico Q, Moon B, McQuail JA, Maurer AP, Bizon JL, **Burke SN** (2018). A ketogenic diet improves cognition and has biochemical effects in prefrontal cortex that are dissociable from hippocampus. *Frontiers in Aging Neuroscience,* 10:391.

4. My prior publications were the first to demonstrate that age-related deficits in object recognition memory are mediated by perirhinal cortical dysfunction. The perirhinal cortex is an area of the brain that receives sensory information from all modalities and is interconnected with the hippocampus to support memory. Using neurophysiological approaches (a) and activity-induced gene expression (b), my work showed that both excitatory and inhibitory perirhinal activity is blunted in aged rats (c) during an object exploration task and that this decline in perirhinal activity is tightly related to behavioral performance.
   a. **Burke SN**, Hartzell AL, Lister JP, Hoang LT, Barnes CA (2012). Layer V perirhinal cortical ensemble activity during object exploration: a comparison between young and aged rats. *Hippocampus* 22(10):2080-93.
   b. **Burke SN**, Maurer AP, Nematollahi S, Uprety A, Wallace JL, Barnes CA (2014). Advanced age dissociates dual functions of the perirhinal cortex. *J Neurosci.* 34(2):467-80.
   c. Maurer AP*, **Burke SN***, Diba K, Barnes CA (2017). Advanced Age is Associated with Attenuated Principal Cell and Interneuron Activity in the Perirhinal Cortex. *J Neurosci,* 37(37):8965-8974. *These authors contributed equally.

5. Although the spatial correlates of hippocampal firing properties have been extensively described, less was known regarding the influence on non-spatial sensory information (e.g., 3-dimensional objects) on the activity patterns of these neurons. The perirhinal cortex is extensively interconnected with the hippocampus and receives sensory input from most neocortical sensory areas. Prior to my research it was believed that this structure supported recognition memory with changes in firing rate as a stimulus goes from novel to familiar. My work produced two foundational insights regarding the perirhinal cortex and its interactions with the hippocampus. First, we showed the perirhinal cortical neurons selectively respond to objects, but that firing rates do not change as a function of novelty (a,b). This observation called for a refinement of standard models of recognition memory. Second, we found that the neurons in the hippocampal subregion receiving direct perirhinal input are robustly modulated by objects (c).
   a. **Burke SN**, Maurer AP, Hartzell AL, Nematollahi S, Uprety A, Wallace JL, Barnes CA (2012). Representation of three-dimensional objects by the rat perirhinal cortex. *Hippocampus* 22(10):2032-44.
   b. **Burke SN**, Hartzell AL, Lister JP, Hoang LT, Barnes CA (2012). Layer V perirhinal cortical ensemble activity during object exploration: a comparison between young and aged rats. *Hippocampus* 22(10):2080-93.
   b. **Burke SN**, Maurer AP, Nematollahi S, Uprety AR, Wallace JL and Barnes CA (2011). The influence of objects on place field expression and size in distal hippocampal CA1. *Hippocampus*, 21(7):783-801.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/sara.burke.1/bibliography/47433007/public/?sortby=pubDate&sdirection=descending

D. RESEARCH SUPPORT

Ongoing Research Support

NIH/NIA RF1AG060977, Role: PI 02/01/2019-01/31/2024
Title: Metabolic Interventions for Enhancing Cognitive Resilience in Aging and Alzheimer's Disease
The goal of this award is to determine the mechanisms by which dietary ketosis improves cognition in aged animals.

NIH/NIA 1R01AG049722, Role: PI 2016/01/01-2021/11/30
Title: The Contribution of Declines in Functional Connectivity to Cognitive Aging
The major goal of this proposal is to determine how alterations in systems-level neural coordination in old animals produce cognitive impairments.
Pending renewal (percentile score: 17%)

DARPA Targeted Neuroplasticity Training**,** Role: Project leader for Task 1.1 (PI: Otto) 2017/01/01-2020/12/31
Title: Cognitive Augmentation through Neuroplasticity
The major goal of this award is to define the mechanisms by which peripheral stimulation of the vagus nerve improves behavioral performance.

NIH/NIMH R01MH109548, Role: co-I (PI: Maurer) 2017/04/01-2022/01/31
Title: Testing and forecasting hippocampal theta wave propagation in learning and memory
The goal of this award is to understand the relationship between hippocampal oscillatory dynamics and memory.

NIH/NIA R01AG055544, Role: co-I (PI: Maurer) 2017/09/15-2019/08/30
Title: Age-associated changes in hippocampal circuits and cognitive function
The goal of this award is to determine if age-related changes in hippocampal circuit dynamics is due to synaptic senescence for adaptive compensation.

NIH/NIA 1R01AG060778-01, Role: co-I (PI: Bizon) 07/01/2018-06/30/2023
Title: Decision making and basolateral amygdala dysfunction in aging
The goal of this project is to understand how basolateral amygdala dysfunction contributes to altered decision making in aging.

McKnight Brain Research Foundation, Role: PI 10/01/2013-09/30/2021
Title: Neural system dysfunction and cognitive aging
This goal of this award is to provide institutional support and seed funds for supplementing the maintenance of a rigorous research program aimed and determining the neurobiological basis of cognitive impairments in the elderly and to identify potential therapeutic strategies.

Mentored Support

NIH/NIA K99AG058786 PI: Johnson, Role: Mentor 04/01/2018-04/31/2020
Title: Hippocampal and dopaminergic mechanisms of novelty detection underlying cognitive resilience in aging
The goal of this mentored award is to provide Dr. Johnson with training in neurophysiological recording, analysis and optogenetics and she prepares to transition to research independence.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Burns, Matthew Robert

eRA COMMONS USERNAME (credential, e.g., agency login): MBURNS11

POSITION TITLE: Senior Clinical and Research Fellow

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Oberlin College, Oberlin, OH.	B.A.	1996	2001	Physics
Oberlin College, Oberlin, OH.	B.A.	1996	2001	Religion
University of Illinois-Chicago College of Medicine, Chicago, IL.	M.D.	2005	2014	Medicine
University of Illinois-Chicago College of Medicine, Chicago, IL.	Ph.D.	2007	2014	Anatomy and Cell Biology
Northshore University Health System, Evanston, IL.	n/a	2014	2015	Internship, Medicine
University of Chicago Medical Center, Chicago, IL.	n/a	2015	2018	Residency, Neurology
University of Florida, Fixel Center for Neurological Diseases, Gainesville, FL.	n/a	2018	2020	Fellowship, Movement Disorders

A. Personal Statement

I have a long-standing interest in translational research in age-related neurologic disorders, and it is my long-term career goal is to translate my previous research training in cellular and molecular biology, electrophysiology, and neurodegenerative disease as well as clinical training in neurology, movement disorders, and dementia through K and R level extramural support into therapies for patients with age-related neurodegenerative disorders and age-related cognitive and memory changes.

Over the last two years of fellowship training and now entering a tenure track faculty position, I have pursued research and support in this area. I was recently awarded a two-year Pepper foundation scholarship providing both salary and research support for work in cognitive and affective changes in an animal model of synucleinopathy. I was also awarded fist alternate for KL2 support for this work which will provide additional salary and research support over the next several years. In addition, I received a competitive score under the pay line for an Alzheimer's Disease and Related Disorders K08 first submission to the NIA for proposed work on the relationship between age and synuceinopathy in cognitive and affective dysfunction including a non-invasive and potentially disease-modifying neuromodulatory therapy for these disorders. Moreover, I have received Mangurian Foundation support for a potentially disease modifying neuromodulatory therapy in Lewy Body Dementia and am pursuing first-in-class clinical trials for this therapy as well for both synuclein-related cognitive impairment and age-related cognitive impairment.

I hope to pursue further translational research at the McKnight Brain Institute, Pepper Center at the Institute for Aging, and Centr for Cognitive Aging and Memory at The University of Florida with the ultimate goal of winning K and subsequent R level support. Sufficient protected time for research beyond the fellowship period makes support essential. I hope this support will be the foundation of a career as a physician scientist and research into better care and new treatments for patients suffering from cognitive decline due to aging and age-related neurodegenerative disease.

1. ***Burns MR**, McFarland N*. Current Management and Emerging Therapies in Multiple System Atrophy. Neurotherapeutics: the journal of the American Society for Experimental NeuroTherapeutics. Forthcoming, 2020;
2. ***Burns MR**, Chiu SY, Patel B, Mitroponopolis SG, Wong JK, Ramirez-Zamora A*. Advances and Future Directions of Neuromodulation in Neurological Disorders. Neurology Clinics. Forthcoming;
3. Scott BM, Eisinger RS, **Burns MR**, Lopes J, Okun MS, Gunduz A, Bowers D. Co-occurrence of apathy and impulse control disorders in Parkinson disease. Neurology. 2020 Nov 17;95(20):e2769-e2780. doi: 10.1212/WNL.0000000000010965. Epub 2020 Oct 1. PubMed PMID: 33004605; PubMed Central PMCID: PMC7734726.
4. **Burns MR**, Chiu SY, Patel B, Mitropanopoulos SG, Wong JK, Ramirez-Zamora A. Advances and Future Directions of Neuromodulation in Neurologic Disorders. Neurol Clin. 2021 Feb;39(1):71-85. doi: 10.1016/j.ncl.2020.09.004. Epub 2020 Nov 7. Review. PubMed PMID: 33223090

B. Positions and Honors

Positions and Employment

2001-2002	Math, physics, and music teacher, St. Gregory The Great High School, Chicago, IL.
2002-2004	Lab Technician, Laboratory of Dr. Lee Miller, Feinberg School of Medicine
2004-2005	KAPLAN test prep teacher, MCAT and GRE
2008	Neuroanatomy teaching assistant, UIC College of Medicine Dept. of Anatomy and Cell Biology
2011-2013	Adjunct Professor of Neuroscience, Liberal Arts Dept., School of the Art Institute of Chicago
2016-2018	MERITS Program Scholar, University of Chicago Pritzker School of Medicine
2018-2020	Parkinson's Foundation Institutional MDS Fellowship Award recipient.
2020-2021	MBI/Norman Fixel Institute for Neurological Diseases Clinical Fellowship Award recipient

Other positions and Professional Memberships

Honors

2005-2006	Illinois State Senate General Assembly Medical School Tuition Scholarship
2006	American Academy of Neurology Medical School Student Summer Research Fellowship
2006-2007	Elected UIC Medical School Class Secretary
2016	Outstanding PGY-II Presentation, Barry G. W. Arnason Research Symposium
2018	Outstanding PGY-IV Presentation, Barry G. W. Arnason Research Symposium
2020	Norman Fixel Institute Outstanding Research Award

Memberships in Professional Societies

2008-present	American Society for Neurochemistry
2010-present	Society for Neuroscience
2014-present	American Academy of Neurology
2018-present	International Parkinson and Movement Disorders Society

C. Contributions to Science

1. **Early Career:** My research career began with work in an undergraduate applied quantum mechanics seminar that produced a review of formulations of quantum mechanics for which I contributed the review of the Feynman Path Integral formulation. I then took the quantitative skills I developed in the electrophysiology lab of Dr. Lee Miller. I trained primates to play “center-out task” video games to assess motor cortex and cerebellum control of limb and hand movement, designed and built 2D robot arm training device for primate use, performed data acquisition for brain-machine interface optimization experiments, designed epidural electrode array for implantation and recording from motor cortex, and assisted in motor cortical electrode array implantation surgeries for primate subjects.
   a. *Styer DF, Balkin MS, Becker KM, **Burns MR**, Dudley CE, Forth ST, Gaumer JS, Kramer MA, Oertel DC, Park LH, Rinkoski MT, Smith CT, and Wotherspoon TD* (2002). 9 Formulations of Quantum Mechanics. Am. J. Phys. **70** (3).

2. **Graduate Career:** Completed doctoral research in the labs of Drs. Scott Brady and Gerardo Morfini; Designed and executed experiments to understand the role of fast axonal transport in neurodegenerative diseases including the hereditary spastic paraplegias; Developed expertise in

cellular, mouse, and squid models of neurodegenerative disease in part through work at The Marine Biology Labs in Woods Hole, MA; Optimized and regularly applied lentiviral gene therapy and antibody-based techniques; Presented laboratory data and new developments in the field at lab meetings, departmental seminars, and national and international conferences; Contributed to manuscript, RO1, and private foundation grant writing, editing, and submission.

a. *Leo Lanfranco*, Carina Weissman*,* ***Matthew Burns*,*** *Yuyu Song, Minsu Kang, Scott Brady, Peter Baas†, Gerardo Morfini†*, Mutant spastin proteins promote deficits in axonal transport through an isoform-specific mechanism involving casein kinase 2 activation, Human Molecular Genetics, (2017). *co-first-authors.
b. *Morfini GA,* ***Burns M****, Binder LI, Kanaan NM, LaPointe N, Bosco DA, Brown RH Jr, Brown H, Tiwari A, Hayward L, Edgar J, Nave KA, Garberrn J, Atagi Y, Song Y, Pigino G, Brady ST*. Axonal transport defects in neurodegenerative diseases. J. Neurosci. 2009 Oct. 14; 29(41) :12776-86.
c. *Dráberová E, Vinopal S, Morfini G, Liu PS, Sládková V, Sulimenko T,* ***Burns MR****, Solowska J, Kulandaivel K, de Chadarévian JP, Legido A, Mörk SJ, Janáček J, Baas PW, Dráber P, Katsetos CD*. Microtubule-severing ATPase spastin in glioblastoma: increased expression in human glioblastoma cell lines and inverse roles in cell motility and proliferation. J Neuropathol Exp Neurol. 2011 Sep;70(9):811-26.
d. *Morfini GA,* ***Burns MR****, Stenoien DL, Brady ST*. Axonal Transport . In: Basic Neurochemistry. Brady ST, Siegel G, Albers W, Price D, editors. Philadelphia: Lippincott-Raven; 2011. Chapter 8.

3. **Postdoctoral Career:** Since completing my graduate work, I have continued my research interest in mechanisms of neurodegeneration with a specific focus on cognitive and behavioral symptoms of aging, Parkinson's disease dementia, and other age-related cognitive disorders. I have also pursued work in the area of neuromodulation and recently received internal funding to support development of a high field MR-compatible microfluidics optrode for experimental electrophysiology, optogenetics, and imaging in rodent models of parkinsonisms and dementia. I have also received 2 years of salary and research support from the Pepper foundation to study the relationship between aging and synucleinopathy in cognitive and affective dysfunction. Finally, I am a sub-investigator on a randomized, double-blind, placebo-controlled multiple dose study to assess efficacy, safety, tolerability, and pharmacokinetics of ABBV-8E12 in Progressive Supranuclear Palsy.

a. ***Burns MR****, McFarland NR*. Current Management and Emerging Therapies in Multiple System Atrophy. Neurotherapeutics. 2020 Aug 6.
b. *Barry Setlow, Shelby L. Blaes,* ***Matthew R. Burns****, R. Joseph Dragone, & Caitlin A. Orsini*. (2020). Using rodent models to understand interactions between gambling and substance use. Current Opinion in Behavioral Sciences. 31, 37-41
c. *Scott BM, Eisinger RS,* ***Burns MR****, Lopes J, Okun MS, Gunduz A, Bowers D*. Co-occurrence of apathy and impulse control disorders in Parkinson's disease. Neurology. 2020 Oct 1
d. *Okromelidze L, Tsuboi T, Eisinger RS,* ***Burns MR****, Charbel M, Rana M, Grewal SS, Lu CQ, Almeida L, Foote KD, Okun MS, Middlebrooks EH*. Functional and Structural Connectivity Patterns Associated with Clinical Outcomes in Deep Brain Stimulation of the Globus Pallidus Internus for Generalized Dystonia. AJNR Am J Neuroradiol. 2020 Mar;41(3):508-514. doi: 10.3174/ajnr.A6429. Epub 2020 Feb 13.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/1zg5bwYlhRLkP/bibliography/40400733/public/?sort=date&direction=ascending

D. Additional Information: Research Support

Pepper Scholars award (Burns: PI) 11/1/2020 – 11/1/2022
Mesocorticolimbic dysfunction and modulation of cognitive and behavioral impairment in a rat model of aging and synucleinopathy.
Role: PI

Mangurian (Burns: PI) 01/01/2020-12/31/2020
UFF Project
Modulation of Synuclein Pathology Through Induction of Gamma Band Oscillations in a Mouse Model of DLB
We hypothesize that treatment of a synucleinopathy mouse model with multisensory gamma stimulation will slow disease progression as measured through imaging and histopathology.
Role: PI

University of Florida Opportunity Funding (Burns: Co-PI) 06/01/2019 – 06/31/2021
UFF Project
Fabrication and testing of a high density high field MRI compatible carbon nanofiber optrode for electrical and optical modulation of cognitive and affective networks in aging and synuclein animal models
Role: Co-PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Cohen, Ronald

eRA COMMONS USER NAME (credential, e.g., agency login): rcohen1

POSITION TITLE: Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Tulane University	BS	05/1976	Psychology
Louisiana State University	PHD	12/1982	Psychology
UCLA Neuropsychiatric Institute, Westwood CA	Resident	07/1982	Clin Psych Internship
University of Florida, Gainesville, FL	Post Doc	09/1983	Neuropsychology

A. PERSONAL STATEMENT

I am the Director of the Center for Cognitive Aging and Memory (CAM), which is part of the Institute on Aging of the University of Florida. The CAM, which is funded by an endowment from the McKnight Brain Research Foundation, is focused on clinical-translational studies of age-associated changes in cognitive, behavioral and brain structure and function. Specifically, the research focus of the center is on successful cognitive aging in the absence of neurodegenerative disease. More broadly, our research focuses on a variety of age-associated comorbidities including vascular disease and cerebral hemodynamic function, the effects of obesity and metabolic disturbances on the aging brain, and also various medical disorders and etiological factors that may contribute to accelerated brain aging and cognitive decline. I have had ongoing funding focusing on HIV-associated brain dysfunction over the past 20 years. In addition, to our focus on these co-morbidities, our center conducts studies involving the collection of multimodal neuroimaging data in conjunction with neurocognitive and serum laboratory measures. My NIH funded research has employed neuroimaging methods to assess and study brain structure and function. We also focus on clinical translation and development of new methods and approaches for delineating pathophysiological mechanisms related to cerebral inflammation, blood flow, and metabolic disturbances via neuroimaging. Before I came to UF three years ago to develop the CAM, I was a Professor at Brown University, where I co-directed the Memory Disorders Program for many years. I have conducted clinical and cognitive neuroscience research and directed a clinical program aimed at the assessment of neurodegenerative diseases, including Alzheimer's, and vascular dementia, and also normal aging. I have extensive background in clinical and cognitive neuroscience with specific expertise in attention-executive functioning and its relationship to learning and memory with over 320peer-reviewed articles, and numerous book chapters. Besides co-editing several books on topics related to areas of clinical neuropsychological research, I authored "Neuropsychology of Attention" in 1993, which was the first book on this topic in the field. This book was just updated in a second edition and published last year. I also have a book "Brain Imaging in Behavioral Medicine and Clinical Neuroscience", which was among the first to address the use of neuroimaging methods for studying various problems in behavioral medicine. I have decades of NIH research support (as PI as well as co-I) to study attention, executive function and the brain. In the context of the current proposed SBIR study, I have worked with Vigorous Mind on past projects and have served as a Scientific Advisor to the company. I am currently MPI on a large multi-site NIA supported clinical trial, and have considerable experience successfully running longitudinal clinical research studies in older adults. I am also PI or MPI on several NIH supported grants focusing on HIV, aging, alcohol, marijuana use, and the microbiome. We recently submitted a P01 on this topic to NIAAA on which on I am MPI with Dr. Robert Cook of the Dept of Epidemiology focusing on this topic.

B. Positions and Honors

Positions and Employment

2012 - 2019	Professor, Depts. Clinical and Health Psychology, Neurology, Psychiatry, and Aging, UF
2012 - 2019	Director, Center for Cognitive Aging and Memory, University of Florida

Honors

2012	Endowment Center for Cognitive Aging and Memory, McKnight Brain Research Foundation
2015	Evelyn McKnight Chair, Cognitive Aging and Memory in Clinical Translation
2016	UF Distinguished Professor
2019	Fellow, American Psychological Association

C. Contributions to Science

1. My research was an outgrowth of interest and expertise in neuropsychology and cognitive neuroscience. My early research focused on attentional influences on cognitive functions, including studies of the effects of particular neurological brain disorders and psychiatric disturbances on effort and attentional control. This led to a number of publications focusing on the cingulate cortex, intentional behavior and also emotional processing, with much of this work culminating in the publication of his book “Neuropsychology of Attention. These studies present major contributions to neuropsychology and cognitive neuroscience. A few examples of these studies are listed above. My early clinical research focused on neurodegenerative disease in the elderly (AD). This evolved into investigations focusing on vascular dementia, as shown in a sample of my publications below, which employed neuroimaging methods to examine white matter abnormalities (FLAIR), cortical and subcortical morphometry, and functional imaging.

a. Cohen RA, O'Donnell BF, Meadows ME, Moonis M, Stone WF, Drachman DA. ERP indices and neuropsychological performance as predictors of functional outcome in dementia. J Geriatr Psychiatry Neurol. 1995 Oct;8(4):217-25. PubMed PMID: 8561835.
b. Cohen RA, Paul RH, Zawacki TM, Sethi M, Ott BR, Moser DJ, Stone W, Noto R, Gordon N. Single photon emission computed tomography, magnetic resonance imaging hyperintensity, and cognitive impairments in patients with vascular dementia. J Neuroimaging. 2001 Jul;11(3):253-60. PubMed PMID: 11462291.
c. Cohen RA, Paul RH, Ott BR, Moser DJ, Zawacki TM, Stone W, Gordon N. The relationship of subcortical MRI hyperintensities and brain volume to cognitive function in vascular dementia. J Int Neuropsychol Soc. 2002 Sep;8(6):743-52. PubMed PMID: 12240738.
d. Sweet LH, Paul RH, Cohen RA, Moser D, Ott BR, Gordon N, Browndyke JN, Shah P, Garrett KD. Neuroimaging correlates of dementia rating scale performance at baseline and 12-month follow-up among patients with vascular dementia. J Geriatr Psychiatry Neurol. 2003 Dec;16(4):240-4. PubMed PMID: 14653434.

2. As my work on VaD progressed, it became clear that it was necessary to examine patients with vascular disease and risk factors before they developed dementia. This led to R01 funded studies focusing on cognitive and neuroimaging abnormalities associated with cardiovascular disease, including heart failure. This work incorporated systemic vascular indices in conjunction with structural and functional measures. We also began to exam vessel and blood-barrier disturbances that might linked vascular factors with AD (Stopa et al.). To address these questions my research began to employ other neuroimaging methods, including ASL to assess CBF disturbances in relationship to FMRI alterations in HF and vascular cognitive impairment. My laboratory made significant contributions to characterizing the interaction between systolic problems linked to cardiac output and microvascular disease in the brain causing hemodynamic dysregulation and vulnerability to neuronal and white matter injury.

a. Haley AP, Sweet LH, Gunstad J, Forman DE, Poppas A, Paul RH, Tate DF, Cohen RA. Verbal working memory and atherosclerosis in patients with cardiovascular disease: an fMRI study. J Neuroimaging. 2007 Jul;17(3):227-33. PubMed PMID: 17608908.
b. Jefferson AL, Tate DF, Poppas A, Brickman AM, Paul RH, Gunstad J, Cohen RA. Lower cardiac output is associated with greater white matter hyperintensities in older adults with cardiovascular disease. J

Am Geriatr Soc. 2007 Jul;55(7):1044-8. PubMed PMID: 17608877; PubMed Central PMCID: PMC2721459.

c. Stopa EG, Butala P, Salloway S, Johanson CE, Gonzalez L, Tavares R, Hovanesian V, Hulette CM, Vitek MP, Cohen RA. Cerebral cortical arteriolar angiopathy, vascular beta-amyloid, smooth muscle actin, Braak stage, and APOE genotype. Stroke. 2008 Mar;39(3):814-21. PubMed PMID: 18258839.

d. Cohen RA, Poppas A, Forman DE, Hoth KF, Haley AP, Gunstad J, Jefferson AL, Tate DF, Paul RH, Sweet LH, Ono M, Jerskey BA, Gerhard-Herman M. Vascular and cognitive functions associated with cardiovascular disease in the elderly. J Clin Exp Neuropsychol. 2009 Jan;31(1):96-110. PubMed PMID: 18608677; PubMed Central PMCID: PMC2739675.

3. My research on vascular and metabolic factors affecting the aging brain led to R01 funding focusing on HIV. I was a co-PI of HIV Neuroimaging Initiative to investigated longitudinal changes in brain function, structure and cerebral metabolite abnormalities. This work employed MRS, DTI, and more recently FMRI. Subsequent R01 grants awarded to me examined HIV and aging, and HIV in the context of alcohol and other drug use. Neuroimaging methods continue to play a major role in this area of my research, with current funded projects employing FMRI to examine functional connectivity in relationship to white matter connectivity and regional cerebral metabolite disturbance.

a. Paul RH, Ernst T, Brickman AM, Yiannoutsos CT, Tate DF, Cohen RA, Navia BA. Relative sensitivity of magnetic resonance spectroscopy and quantitative magnetic resonance imaging to cognitive function among nondemented individuals infected with HIV. J Int Neuropsychol Soc. 2008 Sep;14(5):725-33. PubMed PMID: 18764968.

b. Bunea F, She Y, Ombao H, Gongvatana A, Devlin K, Cohen R. Penalized least squares regression methods and applications to neuroimaging. Neuroimage. 2011 Apr 15;55(4):1519-27. PubMed PMID: 21167288.

c. Gongvatana A, Harezlak J, Buchthal S, Daar E, Schifitto G, Campbell T, Taylor M, Singer E, Algers J, Zhong J, Brown M, McMahon D, So YT, Mi D, Heaton R, Robertson K, Yiannoutsos C, Cohen RA, Navia B. Progressive cerebral injury in the setting of chronic HIV infection and antiretroviral therapy. J Neurovirol. 2013 Jun;19(3):209-18. PubMed PMID: 23613008; PubMed Central PMCID: PMC3740160.

d. Caldwell JZ, Gongvatana A, Navia BA, Sweet LH, Tashima K, Ding M, Cohen RA. Neural dysregulation during a working memory task in human immunodeficiency virus-seropositive and hepatitis C coinfected individuals. J Neurovirol. 2014 Aug;20(4):398-411. PubMed PMID: 24867610; PubMed Central PMCID: PMC4351737.

4. In addition, to these specific areas of clinical focus, my laboratory continues to conduct studies that address more basic cognitive and behavioral neuroscience questions using neuroimaging as a core component. Some examples are listed below. Studies with Wing, McCaffery, Sweet and me focused on the role of brain reward and inhibitory control systems in obesity. This related to other work on obesity and metabolic effects on the brain and recent R01 funding to use use neuroimaging to study bariatric surgery and weight loss effects on the brain. We continue to also conduct studies to better understand the neural bases of functional neuroimaging responses, including the temporal dynamics of the BOLD response of specific tasks (e.g., Paskavitz et al). I also continue to conduct studies that examine older adults with and without evidence of cognitive decline. For example, Ott et al. showed the relationship between ventricular volume increases and CSF biomarkers in AD, MCI and healthy controls. This represents a small sample of the areas of research that my center continues to explore.

a. McCaffery JM, Haley AP, Sweet LH, Phelan S, Raynor HA, Del Parigi A, Cohen R, Wing RR. Differential functional magnetic resonance imaging response to food pictures in successful weight-loss maintainers relative to normal-weight and obese controls. Am J Clin Nutr. 2009 Oct;90(4):928-34. PubMed PMID: 19675107; PubMed Central PMCID: PMC2744621.

b. Ott BR, Cohen RA, Gongvatana A, Okonkwo OC, Johanson CE, Stopa EG, Donahue JE, Silverberg GD, Alzheimer's Disease Neuroimaging Initiative. Brain ventricular volume and cerebrospinal fluid biomarkers of Alzheimer's disease. J Alzheimers Dis. 2010;20(2):647-57. PubMed PMID: 20182051; PubMed Central PMCID: PMC3078034.

c. Paskavitz JF, Sweet LH, Wellen J, Helmer KG, Rao SM, Cohen RA. Recruitment and stabilization of brain activation within a working memory task; an FMRI study. Brain Imaging Behav. 2010 Mar;4(1):5-21. PubMed PMID: 20503110.

d. Daiello LA, Gongvatana A, Dunsiger S, Cohen RA, Ott BR. Association of fish oil supplement use with preservation of brain volume and cognitive function. Alzheimers Dement. 2015 Feb;11(2):226-35. PubMed PMID: 24954371.

5. A major emphasis on my work over the past decade has been clinical translational research focused at factors that affect the brain and cognition in in the context of normal aging. We have been conducting studies within the CAM-CTRP of the UF Institute on Aging directed at the influence of systemic and neuroinflammation, endocrine changes, and other factors occurring with aging that may accelerate cognitive decline as people reach advance age. Examples of this research, including several published this year are provided blow
   a. Woods AJ, Cohen RA, Pahor M. Cognitive frailty: frontiers and challenges. J Nutr Health Aging. 2013 Sep;17(9):741-3. PubMed PMID: 24154645; PubMed Central PMCID: PMC4471842.
   b. Gullett JM, Chen Z, O'Shea A, et al. MicroRNA predicts cognitive performance in healthy older adults. *Neurobiol Aging.* 2020;95:186-194.
   c. Gullett JM, O'Shea A, Lamb DG, et al. The association of white matter free water with cognition in older adults. *Neuroimage.* 2020;219:117040.
   d. Seider TR, Porges EC, Woods AJ, Cohen RA. An fMRI study of age-associated changes in basic visual discrimination. *Brain Imaging Behav.* 2020.
   e. Williamson JB, Lamb DG, Porges EC, **Woods AJ**, Langer K, Cohen R. Cerebral metabolite concentrations are associated with cortical and subcortical volumes and cognition in older adults. Frontiers in Aging Neuroscience, Accepted December 2020.

Link to bibliography:https://www.ncbi.nlm.nih.gov/myncbi/1j9ug8sDyhtQU/bibliography/public/

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

NIH/NIA 1R01AG054077-01 (Woods/Cohen, Multiple PIs) 09/1/2016-4/30/2021
Augmenting Cognitive Training in Older Adults – The ACT Grant

1R01DK09933401A1 (Cohen, PI) 09/30/2014-8/30/2020
NIDDK
"Obesity and Type-2 Diabetes: Bariatric Surgery Effects on Brain Function"

2 P01 AA019072 (Monti, PI) 09/1/2015-5/31/2020
Alcohol and HIV: Biobehavioral Interactions and Intervention
Role: Co-I; PI: Research Component 1

R01DA042069 (Cook, PI) 08/15/2017-03/31/2022
Health Outcomes and Cognitive Effects of Marijuana Use among Persons Living with HIV/AIDS
Role: Cohen, Co-I
Examining the relationship between the microbiome and cognitive function in HIV infected, cannabis users.

U01AA020797 (Cook, Cohen, MPIs) 09/1/2016-06/30/2021
Effects of Experimentally-Induced Reductions in Alcohol Consumption on Brain Cognitive and Clinical Outcomes and Motivation for Changing Drinking in Older Persons with HIV Infection

U01AA020797 (Cook, Cohen, MPIs) 09/01/2016 – 06/30/2021
National Institute of Health NIAAA
Effects of experimentally-induced reduction alcohol use on cognitive and brain function in HIV-infected adults. This project examines the effects of reduced alcohol consumption on cognition and brain functioning among HIV infected people who are heavy drinkers. A contingency management approach is employed by which participants are given financial incentive in an escalating fashion the longer they go without drinking.

P1R211HL140492-01 (Salmoirago-Blotcher, PI) 5/25/2018 – 04/30/2020
NHLBI
Exploring the Role of Mindfulness Training In the Promotion of Medication Adherence In Heart Failure Outpatients. The goal of this project is to study the feasibility and possible mechanism of mindfulness training for the promotion of medication adherence in heart failure outpatients.

R011AG061065 (Barve, Cohen,Cook PI's) 10/01/2018 – 09/30/2023
NIA: Microbiome study of HIV and aging
The Role of Gut Microbial Dysbiosis and Aging on HIV- associated neurcogitive and brain dysfunction
The project examines of the microbiome on the interaction of age and HIV infection. The methods are similar to those employed in the 30-80 day study (longitudinal neuroimaging, cognitive assessment, biospecimens), but with a different cohort in which ETOH is not the basis for recruitment.

R21NR017749 (Kelly, PI) 09/27/2018 – 07/31/2020
National Institute of Health NINR
Developing the Biobehavioral Foundation for Self-Management of Psychoneurological Symptoms in Hematopoietic Cell Transplant (HCT) Survivors
This research will study biobehavioral factors associated with PN symptoms to gain knowledge needed to provide a foundation for considering the development of a targeted dietary self-management interventions to mitigate PN symptoms of HCT and provide a basis for obtaining and maintaining optimal quality of life for HCT recipients.
articipants undergo cognitive and neuroimaging assessments at baseline (Pre-CM) and then at 30 days of CM and after completion of CM at 90 days. Follow up assessments are conducted one year post baseline.

Completed - related R01 projects.

2R01NS036524-11A1 (Cohen, Co-I) 04/01/1997 – 08/31/2016
Imaging Biomarkers for HIV-associated Cognitive Impairment

5R01MH074368-05 (Cohen, PI) 09/01/2010 – 02/28/2013

A1U54EB020403-01 Thompson (PI) 09/29/ 2014-09/30/2018
ENIGMA: Center for Worldwide Medicine, Imaging and Genomics
Enigma creates novel computational algorithms and a new model for Consortium Science to revolutionize Big Data applications to (1) Imaging Genomics, (2) Connectomics, and (3) Machine Learning & Clinical Prediction.
Role: Co-I; Director of HIV Data Initiative

R21AG053736-01A1 (Clark; PI) 06/01/2017-05/31/2019
Combining tDCS and Neurorehabilitation To Treat Age-Related Deficits of Mobility and Cognition
This study examines whether brain stimulation is effective in increasing neural plasticity, thereby enhancing motor functions and mobility in older adults. In my role as co-I, I provide support for the neuroimaging conducted as part of the protocol.
Role: Co-I

R56 HL127175-01 (Williamson, PI) 09/08/2015-08/31/2018
NHLBI
Brain and Cognition Effects of Cardio Resynchronization Therapy in Heart Failure
The goal of this study is to determine the influence of increased blood flow through cardiac resynchronization on the brain and cognition.
Role: Co-I

R21AG054876 – (Williamson, PI) 09/01/2017-05/31/2019
Treatment of Mild Cognitive Impairment with Transcutaneous Vagal Nerve Stimulation
Role: Co-I

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Cruz-Almeida, Yenisel

eRA COMMONS USER NAME (credential, e.g., agency login): ycruzalmeida

POSITION TITLE: Assistant Professor & Director

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Florida, Gainesville, FL	BS	05/2001	Microbiology/Cell Science, Immunology
University of Miami, Miami, FL	MSPH	08/2004	Pain, Epidemiology, Biostatistics
University of Miami, Miami, FL	PhD	12/2011	Pain, Neuroscience, Somatosensation
University of Florida, Gainesville, FL	Postdoctoral	12/2012	Pain, Immunology, Neuroepidemiology

A. Personal Statement

Research: I have a longstanding interest in understanding the observed inter-individual variability of the complex, multidimensional pain experience. My **PAIN** (**P**henotyping & **A**ssessment **I**n **N**euroscience) laboratory at UF applies multiple clinical and translational research methods including quantitative sensory testing, multi-modal neuroimaging and blood biomarkers related to endocrine and immune function as well as epigenetics. This focus stems from my previous multi-disciplinary research training across the fields of Epidemiology and Systems Neuroscience within the context of translational pain research. I am currently PI of 2 NIH funded R01 awards focused on knee osteoarthritis pain and my body of work is documented in 75 peer-reviewed publications across the translational research continuum.

Mentoring: My strong commitment to training the next generation of scientists is evidenced by my role as the Pain Research and Intervention Center of Excellence Director of Training and Career Development where I oversee the educational training of our T32 (Pain and Aging) and P30 (Resource Center for Minority Aging Research) post-doctoral trainees. In addition, I serve on the UF CTSI KL2 Scholars and KL2 Workforce Development Programs as well as serving as Leader of the UF OAIC Pilot & Exploratory Studies Core. I am a certified “Master Mentor” after completing the semester long CTSI Mentor Academy program that promotes a culture of support for mentoring and training while optimizing mentoring relationships for mentors and mentees at all levels of career development. I also currently serve as a permanent member of NIH study section on the Neurobiology of Pain and Itch (NPI) at CSR. Thus, my track record of scholarly achievement performing clinical translational research and my long-standing commitment to supporting trainees in science, qualify me to lead the proposed research.

B. Positions and Honors

Employment

1997 - 1999	Clinical Research Coordinator, Florida Ophthalmic Institute, Gainesville, FL
1999 - 2001	Medical Laboratory Assistant, Shands Hospital, Gainesville, FL
2002 - 2006	Research Associate, University of Miami, Miami Project to Cure Paralysis, Miami, FL
2004 - 2006	Senior Research Associate, University of Miami, Miami Project to Cure Paralysis, Miami, FL
2006 - 2011	PhD Student, University of Miami, Neuroscience Graduate Program, Miami, FL
2011 - 2012	Post-doctoral Fellow, University of Florida, College of Dentistry, Gainesville, FL

2012 - 2014 Research Assistant Professor, University of Florida, College of Dentistry, Gainesville, FL
2014 - Assistant Professor, University of Florida, College of Medicine, and Dentistry Gainesville, FL
2019 - Director, Training & Career Development, Pain Research & Intervention CoE, Gainesville, FL

Other Experience and Professional Memberships

2003 - Member, American Pain Society
2004 - Member, International Association for the Study of Pain
2004 - 2012 Member, National Neurotrauma Society
2006 - Member, Society for Neuroscience
2009 - Ad-hoc Reviewer, Pain Medicine
2012 - Ad-hoc Reviewer, Journal of Pain
2013 - Member, Gerontological Society of America
2013 - Ad-hoc Reviewer, Clinical Journal of Pain
2013 - Editorial Board, Journal of Geriatrics & Palliative Care
2014 - Ad-hoc Reviewer, Experimental Gerontology
2014 - Chapter Faculty Advisor, Gamma Eta Sorority, Multicultural Greek Council
2014 - 2016 Elected Member, American Pain Society, Early Career Forum Planning Committee
2014 - 2016 Elected Chair, American Pain Society, SIG: Measurement of Pain and its Impact
2015 - Executive Board Member, ElderCare of Alachua County UFHealth
2015 - Appointed Member, American Pain Society, Membership Committee
2015 - 2016 Appointed Member, American Pain Society, Early Career Advisory Group
2016 - 2018 Elected Co-Chair, American Pain Society, SIG: Geriatrics
2016 - 2019 Elected Senator, University of Florida, Faculty Senate
2017 - Member, UF CTSI KL2 Advisory Committee
2017 - 2020 Temporary Member, NIH-CSR: Somatosensory and Pain Systems (SPS) Study Section
2018 - Member, UF CTSI KL2 Workforce Development
2018 - Editorial Board, Frontiers in Neurology: Applied Neuroimaging Section
2018 - Mentor, UF Summer Neuroscience Internship Program
2018 - Member, NIA: Special Emphasis Panel Study Section
2018 - Co-Chair, American Pain Society, METER Working Group
2019 - Member, NIH-CSR: Special Emphasis Panel Study Section (ZAG1 ZIJ-4)
2019 - Editorial Board, Journal of Pain
2019 - 2022 Elected Secretary, American Pain Society, Executive Board of Directors
2020 - 2026 Permanent member, Somatosensory and Pain Systems, Neurobiology of Pain and Itch NIH/CSR Study Section

Honors

1998 Leadership Award, University of Florida Hispanic Student Association
1999 Outstanding Student Award in Community Service, University of Florida
2004 Award for Academic Merit, University of Miami
2004 Young Investigator Travel Award, American Pain Society
2006 Lois Pope LIFE Fellow, University of Miami Neuroscience Program
2006 T-32 Predoctoral Training Fellow, NINDS/NIH
2006 Young Investigator Travel Award, American Pain Society
2007 Florida Graduate Academic Scholar Award, University of Miami
2008 Congress Scholarship, Congress of Spinal Cord Medicine and Rehabilitation
2010 Inductee, Alpha Epsilon Lambda Graduate Honor Society
2010 RR&D Predoctoral Fellowship Award, Department of Veteran Affairs
2011 Top Student Competition Finalist, National Neurotrauma Symposium
2011 Young Investigator Best Clinical Poster Presentation Award, Miami VA Medical Center
2011 Young Investigator Travel Award, American Pain Society

2011 Margaret Whelan Student Scholarship Award, University of Miami Medical Faculty Association
2012 T-90 Postdoctoral Training Fellow, NIDCR/NIH
2013 Junior Pepper Scholar, OAIC, University of Florida
2013 Young Investigator Travel Award, American Pain Society
2013 GSA Junior Investigator Award Finalist: Aging, the CNS and Mobility in Older Adults
2014 Cognitive Aging & Memory Junior Scholar, University of Florida
2014 Scientific Annual Meeting Faculty, Tampa, Florida, American Pain Society
2015 Annual Meeting Faculty, Palm Springs California, American Pain Society
2015 Annual Meeting Faculty, Orlando Florida, Gerontological Society of America
2015 Annual Meeting Best Poster Presentation Award, Washington, DC, OAIC Meeting
2015 McKnight Brain Institute (MBI) Travel Award
2017 Faculty Enhancement Award, University of Florida
2018 UTMB Pepper OAIC, Team Science Leadership Scholarship Award
2019 McKnight Brain Institute (MBI) Faculty Leadership Award
2019 University of Florida Term Professorship Award

C. Contributions to Science (Selected from 75 peer-reviewed publications)

1. My early research focused on chronic pain after spinal cord injury (SCI). My publications during my training revolved around measuring pain from a biopsychosocial perspective. Specifically, we characterized the psychosocial profiles associated with clinical pain after SCI both cross-sectionally as well as longitudinally. My work has also included the characterization of somatosensory function after SCI and for the first time, how these various phenotypes are associated with brain metabolites.
   a. **Cruz-Almeida Y**, Felix ER, Martinez-Arizala A, Widerström-Noga EG. Decreased spinothalamic and dorsal column medial lemniscus-mediated function is associated with neuropathic pain after spinal cord injury. J Neurotrauma. 2012 Nov 20;29(17):2706-15. PubMed PMID: 22845918; PubMed Central PMCID: PMC3510448.
   b. **Cruz-Almeida Y**, Felix ER, Martinez-Arizala A, Widerström-Noga EG. Pain symptom profiles in persons with spinal cord injury. Pain Med. 2009 Oct;10(7):1246-59. PubMed PMID: 19818035.
   c. **Cruz-Almeida Y**, Alameda G, Widerström-Noga EG. Differentiation between pain-related interference and interference caused by the functional impairments of spinal cord injury. Spinal Cord. 2009 May;47(5):390-5. PubMed PMID: 19030010.
   d. **Cruz-Almeida Y**, Martinez-Arizala A, Widerström-Noga EG. Chronicity of pain associated with spinal cord injury: A longitudinal analysis. J Rehabil Res Dev. 2005 Sep-Oct;42(5):585-94. PubMed PMID: 16586184.

2. In another line of research, we have investigated factors contributing to individual differences in pain related to knee osteoarthritis. In collaboration with other researchers, we have used sophisticated psychophysical protocols to investigate age-related changes in pain modulation profiles, which may contribute to increased clinical pain among older adults. We have also examined the extent to which demographic factors contribute to individual differences in pain responses, including their interactions with psychosocial variables.
   a. **Cruz-Almeida Y**, Cardoso JS, Riley JL 3rd, Goodin B, King CD, Petrov M, Bartley EJ, Sibille KT, Glover TL, Herbert MS, Bulls HW, Addison A, Staud R, Redden D, Bradley LA, Fillingim RB. Physical performance and movement-evoked pain profiles in community-dwelling individuals at risk for knee osteoarthritis. Exp Gerontol. 2017 Nov;98:186-191. PubMed PMID: 28842222; PubMed Central PMCID: PMC5652068.
   b. Cardoso JS, Riley JL 3rd, Glover T, Sibille KT, Bartley EJ, Goodin BR, Bulls HW, Herbert M, Addison AS, Staud R, Redden DT, Bradley LA, Fillingim RB, **Cruz-Almeida Y***. Experimental pain phenotyping in community-dwelling individuals with knee osteoarthritis. Pain. 2016 Sep;157(9):2104-14. PubMed PMID: 27340911; PubMed Central PMCID: PMC4988907. ***Senior Author**
   c. **Cruz-Almeida Y**, Sibille KT, Goodin BR, Petrov ME, Bartley EJ, Riley JL 3rd, King CD, Glover TL, Sotolongo A, Herbert MS, Schmidt JK, Fessler BJ, Staud R, Redden D, Bradley LA, Fillingim RB. Racial and ethnic differences in older adults with knee osteoarthritis. Arthritis Rheumatol. 2014 Jul;66(7):1800-10. PubMed PMID: 24729357; PubMed Central PMCID: PMC4077911.

d. **Cruz-Almeida Y**, King CD, Goodin BR, Sibille KT, Glover TL, Riley JL, Sotolongo A, Herbert MS, Schmidt J, Fessler BJ, Redden DT, Staud R, Bradley LA, Fillingim RB. Psychological profiles and pain characteristics of older adults with knee osteoarthritis. Arthritis Care Res (Hoboken). 2013 Nov;65(11):1786-94. PubMed PMID: 23861288; PubMed Central PMCID: PMC3922880.

3. Ongoing research efforts address the utility of various methodology in measuring pain mechanisms across the lifespan.
   a. **Cruz-Almeida Y**, Aguirre M, Sorenson H, Tighe P, Wallet SM, Riley JL 3rd. Age differences in salivary markers of inflammation in response to experimental pain: does venipuncture matter? J Pain Res. 2017 Oct 3;10:2365-2372. doi: 10.2147/JPR.S138460. eCollection 2017.
   b. **Cruz-Almeida Y**, Fillingim RB. Can quantitative sensory testing move us closer to mechanism-based pain management? *Pain Med.* 2014 Jan;15(1):61-72. PubMed PMID: 24010588; PubMed Central PMCID: PMC3947088.
   c. **Cruz-Almeida Y**, Aguirre M, Sorenson HL, Tighe P, Wallet SM, Riley JL 3rd. Age differences in cytokine expression under conditions of health using experimental pain models. Exp Gerontol. 2015 Dec;72:150-6. PubMed PMID: 26456458; PubMed Central PMCID: PMC4664177.
   d. **Cruz-Almeida Y**, King CD, Wallet SM, Riley JL 3rd. Immune biomarker response depends on choice of experimental pain stimulus in healthy adults: a preliminary study. Pain Res Treat. 2012;2012:538739. PubMed PMID: 23213513; PubMed Central PMCID: PMC3508574.

4. More recent efforts are focused in understanding the neurobiology of pain in older versus younger individuals that may account for increased prevalence of chronic pain in this population using multimodal neuroimaging and neurocognitive measures.
   a. **Cruz-Almeida Y**, Fillingim RB, Riley III JL, Woods AJ, Porges E, Cohen R & Cole JH (2019). Chronic Pain is Associated with a Brain Aging Biomarker in Community-Dwelling Older Individuals. Pain. *2019 May;160(5):1119-1130.* Pubmed PMID:31009418; PubMed Central PMCID: *In Process*
   b. **Cruz-Almeida Y**, Sinha P, Rani A, Huo Z, Fillingim RB, Foster TC. Epigenetic Aging is Associated with Clinical and Experimental Pain in Community-Dwelling Older Adults. Mol Pain. 2019 Jan-Dec; 15:1744806919871819.
   c. Lysne P, Cohen R, Hoyos L, Fillingim RB, Riley III JL, **Cruz-Almeida Y**. Age and Pain Differences in Non-Verbal Fluency: Associations with Cortical Thickness and Subcortical Volumes. Exp Gerontol. 2019 Oct 15;126:110708.
   d. **Cruz-Almeida Y** & Cole J. Pain, aging, and the brain: new pieces to a complex puzzle. Pain. 2020 Mar; 161(3):461-463.

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

K01 HL153210, NIH/NHLBI K. Roach (PI) 07/15/20-06/30/24
Contributions of biopsychosocial factors in Sickle Cell Disease pain
The goal of this study is to understand the role of the AVPR1A gene and its effect on stress and pain in patients with sickle cell disease pain.
Role: Mentor

R01 AG067757, NIH/NIA Y. Cruz-Almeida (PI) 07/01/20-06/30/25
Biobehavioral basis of knee osteoarthritis pain
The goal of the proposed project is to understand the brain, cellular and epigenetic mechanisms whereby pain prospectively impacts function in knee osteoarthritis pain.
Role: PI

KL2 TR001429, NIH/NCATS J. Nichols (Candidate PI**)** 04/01/19-03/31/21
Carpometacarpal Osteoarthritis: Towards Identification of Biomechanical, Neuromuscular, and Somatosensory Mechanisms
The goal of the proposed project is to understand the mechanisms underlying carpometacarpal osteoarthritis
Role: Mentor

R01 AG059809, NIH/NIA Y. Cruz-Almeida, N. Ebner (MPI) 08/01/18-04/30/23
Mechanisms of Oxytocin's Analgesia in Older Adults
The goal of the proposed project is to determine the systemic and brain inflammatory mechanisms underlying oxytocin's analgesia in older individuals with knee osteoarthritis.
Role: Contact PI

U01 AG061389, NIH/NIA T. Manini, D. Clark, R. Seidler (MPI) 09/01/18-08/31/23
Multimodal imaging of brain activity to investigate walking and mobility decline in older adults
The goal of the proposed project is to determine the central neural control of mobility in older adults by collecting EEG during walking and correlating these findings with a comprehensive set of diverse mobility outcomes (clinic-based walking, complex walking and community mobility measures).
Role: Co-Investigator

K22 NS102334, NIH/NINDS E. Terry (PI) 04/01/18-03/31/23
Neural mechanisms underlying psychosocial contributions to ethnic group differences in pain
The goal for this mentored career development proposal is to elucidate the brain mechanisms involved in pain catastrophizing and its influence on pain processing in different ethnic groups.
Role: Mentor

P30 AG028740, NIH/NIA M. Pahor (PI) 04/01/18-03/31/22
University of Florida Claude D. Pepper Older Americans Independence Center
The mission of the University of Florida Older Americans Independence Center (OAIC) is to assess the risk factors of physical disability in older adults, develop and test effective prevention therapies, and train new investigators in research on aging and disability, while developing their leadership qualities.
Role: Leader, Pilot & Exploratory Studies Core

Selected Past Research Support

K01 AG048259, NIH/NIA Y. Cruz-Almeida (PI) 05/15/15-08/14/20
Neuroimaging age-related changes in pain modulation
The goal of the proposed project is to understand the neurobiological mechanisms underlying age-related differences in conditioned pain modulation.
Role: PI

K01 AG048259-S1, NIH/NIA Y. Cruz-Almeida (PI) 08/01/18 – 04/30/19
Neuroimaging Age-Related Changes in Pain Modulation in Alzheimer's Disease
The goal of the proposed project is to evaluate conditioned pain modulation in individuals with Alzheimer's
Role: PI

R01 DE019456, NIH/NIDCR L. Shaddox (PI) 06/01/14-05/31/18
Mechanisms and treatment response of aggressive periodontitis in children
The goal of the proposed project is to phenotype children with periodontitis derived from inflammatory phenotypes and sensitivity profiles.
Role: Co-Investigator

R01 AG039659, NIH/NIA J. Riley (PI) 08/01/12-05/31/17
The effects of aging on experimental models of pain inhibition and facilitation
The goal of the proposed project is to evaluate the effects of aging on multiple experimental models of pain modulation.
Role: Co-Investigator

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: DeKosky, Steven T.

eRA COMMONS USER NAME (credential, e.g., agency login): DeKoskyST

POSITION TITLE: Professor of Neurology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Bucknell University, Lewisburg, PA	A.B.	1968	Psychology
University of Florida, Gainesville, FL	Graduate School	1968-70	Psychology/Neuroscience
University of Florida, College of Medicine	M.D.	1974	Medicine
The Johns Hopkins Hospital, Baltimore, MD	Internship	1974-75	Internal Medicine
University of Florida College of Medicine	Residency	1975-78	Neurology
University of Virginia, Charlottesville, VA	Post Doc	1978-79	Neurochemistry

A. Personal Statement

For the CAM studies, I will continue to serve as Co-Investigator. The CAM workl investigates transcranial DC stimulation and transcranial magnitic stimulation attempting to stabilize or improve age-related memory impairment, among persons with mild cognitive impairment (MCI) I am particularly well-suited for my role as I have worked in age-related memory impairment and Alzheimer's disease (AD) and related disorders for over 30 years, studying behavioral, neurochemical, neuroanatomical, genetic, and pathological changes (amyloid, neurofibrillary tangles) in AD, MCI, and normal elderly. I have also been involved with epidemiological studies of dementia in several populations, including in western Pennsylvania and rural India. My neurochemistry and molecular neuroscience lab was funded extramurally for over 30 years; to translate my bench research studies, I began clinical studies in cognitive, behavioral, neuroimaging and therapeutic interventions correlating imaging and cognition, trials of new medications including First in Man studies in the Pitt Alzheimer's Disease Research Center (ADRC), and NIH-funded large scale (>3,000 Ss), long term (>6 years), multicenter dementia prevention trials using Gingko biloba; I was PI of the GEM trial. I was founding co-director of the University of Kentucky ADRC (1985-1990;) then director of the Pittsburgh ADRC, (1994-2008) and serve as chair of several Drug Safety Monitoring Boards. I have served as consultant/advisor for multiple pharma and biotech companies, ADRCs, and chaired the Alzheimer's Association Med-Sci Advisory Council, and the Med-Sci Advisory Panel of Alzheimer's Disease International. I chaired the American Academy of Neurology's Practice Parameter Workgroup on Early Detection, Diagnosis, and Treatment of Dementia, and served on or chaired multiple committees or review committees for the NIA regarding aging and dementia. I also served on the NCCAM (now NCCIH) Council and was a member of the NIH Council of Councils (overseeing the Common Fund). I chaired the University of Pittsburgh department of neurology for 8 years. In these capacities I have supervised undergraduates, PhDs, post docs, and both basic and clinical research faculty. Then, as Vice President and Dean of the University of Virginia School of Medicine (2008-2013) I developed further skills in management of large research and academic projects, My return to research via a sabbatical year at Penn (bioethics) and Pitt (in the PET labs) facilitated my re-entry into research and research administration. I now am Deputy Director of the McKnight Brain Institute, the center of neuroscience research and teaching at UF,

Associate Director of the NIA-funded 1Florida ADRC, and involved in several research grants focused on human and animal models of age-related memory loss and therapeutic interventions.

B. Positions and Honors

1979-1990	Asst.to Assoc. Prof, Depts. Neurology & Anatomy/Neurobiology, Univ. Kentucky, Lexington, KY and Staff Neurologist, Lexington VA Medical Center
1985-1990	Co-Director/Co-PI, Alzheimer's Disease Research Center, Univ. of Kentucky, Lexington, KY
1985-1987	Interim Chair, Department of Neurology, University of Kentucky, Lexington, KY
1985-1987	Director, Neurology Residency Training Program, University of Kentucky, Lexington, KY
1990-2002	Professor of Psychiatry, Neurology, and Neurobiology, University of Pittsburgh School of Medicine and Western Psychiatric Institute and Clinic (WPIC), Pittsburgh, PA
1990-1994	Co-Director, Alzheimer's Disease Research Center, University of Pittsburgh, Pittsburgh, PA
1992-2001	Director, Div. of Geriatrics & Neuropsychiatry, Dept. of Psychiatry/WPIC, Univ. of Pittsburgh
1994-2008	Director, ADRC, University of Pittsburgh Medical Center, Pittsburgh, PA
1997-2008	Professor, Dept. of Human Genetics, Graduate School of Public Health, University of Pittsburgh
2000-2008	Chair, Department of Neurology, University of Pittsburgh, Pittsburgh, PA
2008-present	Adjunct Professor of Neurology, University of Pittsburgh School of Medicine
2008-2013	Vice President and Dean, University of Virginia School of Medicine, Charlottesville, VA; Physician in Chief, University of Virginia Health System
2008-2014	Professor of Neurology and Psychiatry and Behavioral Sciences, UVA School of Medicine
2013-2014	Visiting Professor, Department of Medical Ethics and Health Policy, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA [Sabbatical]
2014-2015	Visiting Scholar, Department of Radiology (PET Center) and Neurology, University of Pittsburgh School of Medicine/UPMC, Pittsburgh, PA [Sabbatical]
2015-present	Professor of Neurology Emeritus, University of Virginia
2015-present	Professor, Neurology and Neuroscience, Univ. of Florida College of Medicine, Gainesville, FL
2015-present	Deputy Director, McKnight Brain Institute, University of Florida
2015-2016	Interim Executive Director, McKnight Brain Institute, University of Florida
2015-present	Associate Director, 1Florida Alzheimer’s Disease Center

Other Experience and Professional Memberships

1994-2010	National Board of Directors, Alzheimer's Association, Chicago, IL; Vice-Chairman, 1998-2001
1997-2001	NIH Study Section, Neuroscience of Aging Review Committee (NIA) (Chair, 2002-2001)
1997-2001	Chair, Medical and Scientific Advisory Council, Alzheimer's Association
2002-2005	Chair, Medical and Scientific Advisory Panel, Alzheimer’s Disease International
2004-2010	Member & Vice President (2010), American Board of Psychiatry & Neurology (ABPN)
2004-2007	Member, Peripheral & Central Nervous System Drugs Advisory Committee, FDA; now advisor
2005-2015	Member, Board of Directors, American Society for Experimental NeuroTherapeutics (ASENT)
2008-2104	Founding Chair, ISTAART (International Society to Advance Alzheimer Research & Treatment)
2008-2013	Council of Deans, American Association of Medical Colleges (AAMC)
2009-2012	National Advisory Council, National Center on Complementary and Alternative Medicine (NCCAM; now National Center on Complementary and Integrative Health, NCCIH)
2013-2015	Council of Councils (National Advisory Council to the NIH Director for the Common Fund)

Honors

1972	Alpha Omega Alpha Research Award, University of Florida College of Medicine
1974	Roger Schnell Award for Excellence in Clinical Neurology (University of Florida)
1978-1979	National Research Service Award in Developmental Neurology (Neurochemistry) NINCDS
1980-1985	Teacher-Investigator Development Award, NINCDS
1988	Presidential Award, American Neurological Association
1994-present	*The Best Doctors in America*
2000	Distinguished Alumnus, University of Florida College of Medicine (“Wall of Fame”)
2003-present	Elected American College of Neuropsychopharmacology (ACNP)
2003-present	*America’s Top Doctors*

2003 Rita Hayworth Award, Alzheimer's Association
2005 Ronald and Nancy Reagan Research Institute Award for research/care/advocacy in AD.
2006 NIH Clinical Center Great Teachers Award
2008 Alzheimer's Association Zaven Khachaturian Award
2008-2013 James Carroll Flippin Professor of Medical Science, University of Virginia
2009-present Elected Fellow, American College of Physicians
2014--present Thompson Reuters Top 1% of Cited Papers
2015 Who's Who in America (Platinum edition)
2015-present Aerts-Cosper Professor of Alzheimer's Research, University of Florida
2017-present Who's Who in the World
2019 Albert Nelson Marquis Lifetime Achievement Award
2020 Henry Wishniewski Lifetime Achievement Award, (Alzheimer's Association International Conference)

C. Contributions to Science

Science (chosen from 500+ publications) https://www.ncbi.nlm.nih.gov/pubmed/?term=dekosky+s

1) Neurochemistry and synaptic plasticity in aging, MCI, and dementia

I was first to report (with Steve Scheff) the loss of synapses (by quantitative EM) in living humans with AD (biopsies), that synapse counts correlated with cognition, and that enlargement of residual synapses occurred with synaptic loss. I also demonstrated that unlike prior understanding, cholinergic enzymes were increased in the hippocampus and frontal cortex (but not other cortical areas) during MCI--a neuroplastic attempt to compensate for neurodegeneration, which then decreased as progression to AD occurred.

DeKosky, ST and Scheff, SW Synapse loss in frontal cortex biopsies in Alzheimer's disease: Correlation with cognitive severity. Annals of Neurology 27:457-464, 1990.

DeKosky, ST, Harbaugh, RE, Schmitt, FA, Bakay, RAE, Chui, HC…Senter, HJ, Markesbery, WR, and the Intraventicular Bethanecol Study Group. Cortical biopsy in Alzheimer's disease: Diagnostic accuracy and neurochemical, neuropathological and cognitive correlations. Annals Neurology 32:625-632, 1992.

DeKosky, ST, Ikonomovic, MD, Styren, SD, Beckett, L, Wisniewski, S, Bennett, D, Kordower, JH, and Muston, EJ. Up-regulation of choline acetyltransferase activity in hippocampus and frontal cortex of elderly subjects with mild cognitive impairment. Annals of Neurology 51:145-155, 2002.

Ikonomovic, MD, Klunk, WE, Abrahamson, EE, Wuu, J, Mathis, CA, Scheff, SW, Mufson, EJ and Cohen, A, Price, J, Weissfeld, L, James, J, Rosario, B, Bi, W, Nebes, R, Saxton, J, Snitz, B, Aizenstein, H, Wolk, D, DeKosky, ST, Mathis, C and Klunk, W. Basal cerebral metabolism may modulate the cognitive effects of Aβ in MCI: An example of brain reserve. J Neurosci 29:14770-8, 2009. PMCID: 2810461

2) Amyloid imaging in Alzheimer's Disease

I held the IND, was PI of the initial Program Project Grant, and led the clinical studies of the first PET amyloid imaging compound Pittsburgh Compound B (PiB). I participated in clinical study design, assessment of the relationship of amyloid load to clinical status and cortical metabolism as indexed by FDG-PET.

Ikonomovic, MD, Klunk, WE, Abrahamson, EE, Mathis, CA, Price, JC, Tsopelas, ND, Lopresti, BJ, Ziolko, S, Bi, W, Paljug, WR, Debnath, ML, Hope, CE, Isanski, BA, Hamilton, RL and DeKosky, ST Post-mortem correlates of in vivo PiB-PET amyloid imaging in a typical case of Alzheimer's disease. Brain 131:130-1645, 2008. PMCID 2408940

Wolk, DA, Price, JC, Madeira, C, Saxton, JA, Snitz, BE, Lopez, OL, Mathis, CA, Klunk, WE and DeKosky, ST. Amyloid imaging in dementias with atypical presentation. Alz. & Dementia 8:389-8, 2012 PMCID: 3517915

Snitz, BE, Weissfeld, LA, Lopez, OL, Kuller, LH, Saxton, J, Singhabu, DM, Klunk, WE, Mathis, CA, Price, JC, Ives, DG, Cohen, AD, McDade, E and DeKosky, ST. Cognitive trajectories associated with β-amyloid deposition in the oldest-old without dementia. Neurol 80:1378-1384, 2013. PMCID: PMC3662268

Golde TE, DeKosky ST, Galasko D. Alzheimer's disease: The right drug, the right time. Science. 14;362(6420):1250-1251, 2018. doi: 10.1126/science.aau0437.PMID: 30545877

3) Experimental Brain Trauma:

In the early 1990s (before transgenic mouse models were available), I studied TBI to study cascades similar to Alzheimer's. My lab demonstrated up-regulation of NGF and its control by IL1-beta, elevation of APP and A beta in TBI, and a number of interventions to stop elevation of A beta after injury, applicable to human studies.

DeKosky, ST Goss, JR, Miller, PD, Styren, SD, Kochanek, PM, and Marion, D. Up-regulation of nerve growth factor following cortical trauma. Experimental Neurology 130:173-177, 1994.

DeKosky, ST, Taffe, KM, Abrahamson, EA, Dixon, CE, Kochanek, PM, and Ikonomovic, MD Time course analysis of hippocampal nerve growth factor and antioxidant enzyme activity following lateral controlled cortical impact brain injury in the rat. Journal of Neurotrauma 21:491-500, 2004.

Abrahamson, EE, Ikonomovic, MD, Ciallella, JR, Hope, CE, Paljug, WR, Isanski, BA, Flood, DG, Clark, RSB, and DeKosky, ST Caspase inhibition therapy abolishes brain trauma-induced increases in Aß peptide: Implications for clinical outcome. Experimental Neurology 197:437-450, 2006.

Abrahamson, EE, Ikonomovic, MD, Dixon, DE and DeKosky, ST Simvastatin therapy prevents brain trauma-induced elevations in ß-amyloid peptide levels. Annals of Neurol 66:407-414 2009. PMID: 19798641

4) Human Brain Trauma:

With Bennet Omalu I described the first case of CTE in an American football player, then 4 additional cases. Our human brain tissue studies following acute TBI confirmed rapid up-regulation of APP, A□ and A□ plaques (within 2 hours), a risk factor for subsequent cognitive decline, suggesting acute post-TBI interventions and bringing study of AD and TBI together. We now study tau as a biomarker of CTE in living subjects.

Omalu, BI, DeKosky, ST, Minster, RL, Kamboh, MI, Hamilton, RL and Wecht, CH Chronic traumatic encephalopathy in a National Football League (NFL) player. Neurosurgery 57:128-134, 2005.

DeKosky, ST, Abrahamson, EE, Ciallella, JR, Paljug, WR, Wisniewski, SR, Clark, RS, and Ikonomovic, MD. Association of increased cortical soluble Aß42 levels with diffuse plaques after severe brain injury in humans. Archives of Neurology 64:541-544, 2007.

DeKosky, ST, Ikonomovic, MD and Gandy, S Traumatic brain injury: Football, warfare, and long-term effects. New England Journal of Medicine 363:1293-1296, 2010. PMID: 21265421

DeKosky, ST, Blennow, K, Ikonomovic, MD and Gandy, S. Acute and chronic traumatic encephalopathies: Pathogenesis and biomarkers. Nature Reviews Neurology 9:192-200, 2013. PMCID: 4006940

5) Mild Cognitive Impairment and Prevention of Dementia

I chaired the AAN Practice Parameter Committee that first defined MCI, showed multiple ways neuroplasticity occurred in MCI, had a leading role in the redefinition of MCI 10 years later, and directed the first prevention trial for AD, the NIH-funded GEM Study, using *Ginkgo biloba*. I have published multiple studies of MCI in imaging, cognition, and behavioral symptoms.

Petersen, RC, Stevens, JC, Ganguli, M…and DeKosky, ST (2001) Practice parameter: Early detection of dementia: Mild cognitive impairment (an evidence-based review). Neurology 56:1133-1142.

Albert, MS, DeKosky, ST, Dickson, D, Dubois, B, et al., The diagnosis of MCI due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement 7:270-279, 2011. PMCID: 3312027

DeKosky ST, Williamson JD, Fitzpatrick AL, Kronmal RA…Furberg CD. (2008) Ginkgo Evaluation of Memory (GEM) Study Investigators. Ginkgo biloba for prevention of dementia: a randomized controlled trial. JAMA. 19;300:2253-62. PMCID: PMC2823569.

Curiel, RE, Loewenstein, DA, Rosselli, M, Penate, A, Greig-Custo, MT, Bauer, RM, Guinjoan SM, Hanson KS, Li C, Lizarraga G, Barker WW, Torres, V, DeKosky, ST, Adjouadi, M, Duara, R. (2018). Semantic Intrusions and Failure to Recover from semantic interference in mild cognitive impairment: Relationship to amyloid and cortical thickness. Curr Alz Res. https://doi.org/10.2174/1567205015666180427122746

Golde TE, DeKosky ST, Galasko D. Alzheimer's disease: The right drug, the right time. Science. 14;362(6420):1250

D. Additional Information: Research Support and/or Scholastic Performance

U01 AG062368 Edwards (PI) 09/30/2018 - 05/31/2021
National Institute on Aging
Planning an Adaptive Clinical Trial of Cognitive Training to Improve Function and Delay Dementia
The purpose was to plan and pilot test ACTIVE MIND, a randomized clinical trial for persons with mild cognitive impairment (MCI). The objective was to plan and pilot tested MCI/dementia diagnoses procedures, IADL outcome measures, neuroimaging and biomarker assessments, 4 cognitive training arms and an active control among 60 participants with MCI.
Role: Co-Investigator

P30AG066506 (Golde PI) 04/01/2020 – 03/31/2025. 0.6 Calendar
NIH/NIA
1Florida Alzheimer's Disease Research Center
University of Florida and Mt. Sinai Medical Center AD Research Center
Major goals. The UF-MSMC ADRC will be focused on activities including identification of i) markers for earliest prodromal stages of cognitive impairment; ii) predictors of cognitive and functional decline in Hispanics and non-Hispanics. The ADRC facilitates testing of novel therapies for AD and related dementias in our diverse population, and provides community and professional training and education on AD and related dementias, thus having a broad state-wide impact. We recruit & train junior investigators to participate in research.
Role: Co-Investigator, Associate Director

U01 AG062368 Edwards (PI) 09/30/2018 - 05/31/2021
National Institute on Aging
Planning an Adaptive Clinical Trial of Cognitive Training to Improve Function and Delay Dementia
The purpose was to plan and pilot test ACTIVE MIND, a randomized clinical trial for persons with mild cognitive impairment (MCI). The objectives were to plan and pilot test MCI/dementia diagnoses procedures, IADL outcome measures, neuroimaging and biomarker assessments, examine 4 cognitive training arms and an active control among 60 participants with MCI.
Role: Co-Investigator

R01AG064587 (Bowers PI) 08/01/2019 – 04/30/2024 0.6 Calendar
NIH/NIA $34,060
Revitalizing Cognition in Older Adults at Risk for Alzheimer's Disease with near-Infrared Photobiomodulation
Major Goals: The goal of this study is to test a novel, low risk, low cost and potentially high impact brain stimulation approach for enhancing cognition in older adults at increased risk for Alzheimer's disease involving transcranial and intranasal delivery of near infrared (NIR) light via light emitting diodes, aka photobiomodulation
Role: Co-Investigator

1R01AG054077-01, (Woods PI) 05/01/2017 - 4/30/2021 0.6 Calendar
NIH/ NIA $65,912.82
Augmenting Cognitive Training in Older Adults - The ACT Grant
Goal: Enroll 360 healthy older adults between the ages of 65-89 into a study investigating the additive benefit of tDCS for cognitive training outcomes. This overarching goal affords two specific aims and one exploratory aim.

U01AG062368 (Woods PI) 06/01/2019 – 05/31/2021 1.2 Calendar
NIH/NIA $17,054.92
Planning an Adaptive Clinical Trial of Cognitive Training to Improve Function and Delay Dementia
The goal of this project is to simulate participant accrual and several treatment scenarios. For each scenario, we will determine statistical power and sample size required for trial success. The results of these statistical simulations will be applied to finalize an adaptive RCT design
Role: Co-Investigator

R21AG054876 (Williamson PI) 09/01/2017 - 05/31/2021 0.12 Calendar
NIH / NIA $368,225.95
Treatment of mild cognitive impairment with transcutaneous vagal nerve stimulation
This laboratory based, cross -over placebo controlled neuromodulation study is designed to assess the effects of transcutaneous vagal nerve stimulation of cognitive performance in patients with mild cognitive impairment. In addition, structural MRI will be used to quantify magnitude of response in the context of decline of structures critical in the progression of Alzheimer's disease (e.g., hippocampus).

9AZ15 (Smith PI) 05/07/2019 - 02/28/2021 0.12 Calendar
FDOH ED & ETHEL $5,136.98
Association of PET amyloid status with cognitive and functional outcomes of behavioral interventions in Mild Cognitive Impairment
Major Goals: 1: To examine the association of amyloid-PET imaging status with the best and worst outcomes from the PEACEOFMND multicomponent behavioral intervention; 2: To explore the incremental value of amyloid PET status beyond traditional MRI measures of baseline hippocampal volume in predicting best outcomes in the trial.
Role: Co-Investigator

OVERLAP
There is no scientific overlap between any of these studies.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Ebner, Natalie C

eRA COMMONS USER NAME (credential, e.g., agency login): NATALIE.EBNER

POSITION TITLE: Professor of Psychology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Free University Berlin, Berlin	BA	04/1998	Psychology
Free University Berlin, Berlin	MA	03/2001	Psychology
Free University Berlin, Berlin	PHD	05/2005	Psychology
Max Planck Institute for Human Development, Berlin, Germany	Postdoctoral	06/2007	Psychology
Yale University, Connecticut	Postdoctoral	07/2011	Psychology

Personal Statement

I am an expert in cognitive and socioemotional aging, decision making, and experimental aging neuroscience with extensive experience as investigation leader across various interdisciplinary research projects. I use a multi-methods approach that incorporates in-lab as well as real-life assessments and includes self-report, cognitive-behavioral measures, neuroimaging techniques, and hormone/neuropeptide markers. As a pre- and postdoctoral fellow at the Free University Berlin and the Max Planck Institute for Human Development, I have supervised behavioral research on emotion-cognition interactions across adulthood. As a postdoctoral fellow, and later as Associate Research Scientist at Yale University and as faculty at University of Florida (UF), I have expanded my research to examine neuropsychological changes associated with cognition-emotion interactions and decision making across adulthood. Methods applied to these studies include neuroimaging and eye-tracking as well as pharmacological (i.e., intranasal oxytocin administration) and real-life (i.e., simulated phishing) interventions. In addition to my primary appointment in the Department of Psychology at UF, I hold a joint appointment as faculty in the Florida Institute for Cyber Security Research. I am also affiliated with the Center for Cognitive Aging and Memory, the Institute on Aging (adjunct faculty), the McKnight Brain Institute, the Pain Research and Intervention Center of Excellence, and the Substance Abuse Training Center in Public Health on campus. I have received multiple awards, such as the Young Research Scientist Award from the German Psychological Association, the International Max Planck Research School on the Life Course Outstanding Alumni Award, the UF College of Liberal Arts and Sciences International Educator of the Year Award, the UF Research Foundation Professorship Award, and, recently, the UF College of Liberal Arts and Sciences Faculty Achievement Award. Since 2015, I have been a Kavli Fellow of the National Academy of Sciences. My body of work is documented in over 70 publications. Over the last 10 years, I have gained extensive expertise in supervision of post-bac, graduate, and postdoctoral trainees.

Representative Publications:

a. **Ebner NC**, Ellis DM, Lin T, Rocha HA, Yang H, Dommaraju S, Soliman A, Woodard DL, Turner GR, Spreng RN, Oliveira DS. Uncovering susceptibility risk to online deception in aging. J Gerontol B Psychol Sci Soc Sci. 2020 Feb 14;75(3):522-533. PubMed Central PMID: 29669133.
b. Horta M, Ziaei M, Lin T, Porges EC, Fischer H, Feifel D, Spreng RN, **Ebner NC.** Oxytocin alters patterns of brain activity and amygdalar connectivity by age during dynamic facial emotion identification. Neurobio. Aging 2019 June; 78: 42-51. PubMed Central PMCID: PMC6545147.

c. Rana M, Varan AQ, Davoudi A, Cohen RA, Sitaram R, **Ebner NC**. Real-time fMRI in neuroscience research and its use in studying the aging brain. Front Aging Neurosci. 2016 Oct;8:239. PubMed Central PMCID: PMC5067937.
d. **Ebner NC**, Johnson MR, Rieckmann A, Durbin KA, Johnson MK, Fischer H. Processing own-age vs. other-age faces: neuro-behavioral correlates and effects of emotion. Neuroimage. 2013 Sep;78:363-71. PubMed Central PMCID: PMC3684564.

B. Positions and Honors

Positions and Employment

2001 - 2005	Predoctoral Fellow, Free University Berlin & Max Planck Institute for Human Development, Berlin
2005 - 2007	Postdoctoral Fellow, Max Planck Institute for Human Development, Berlin
2007 - 2010	Postdoctoral Fellow, Yale University, Department of Psychology, New Haven, CT
2010 - 2011	Associate Research Scientist, Yale University, Department of Psychology, New Haven, CT
2011 - 2017	Assistant Professor, University of Florida, Department of Psychology, Gainesville, FL
2013 -	Adjunct Faculty, Cognitive Aging and Memory Clinical Translational Research Program (CAM-CTRP) University of Florida, Gainesville, FL
2015 -	Adjunct Faculty, Florida Institute for Cybersecurity Research (FICS), University of Florida, Gainesville, FL
2017 – 2020	Associate Professor, University of Florida, Department of Psychology, Gainesville, FL
2020 –	Professor, University of Florida, Department of Psychology, Gainesville, FL

Other Experience and Professional Memberships

2012 – 2018	Early Career Reviewer (ECR), National Institute of Health, Center for Scientific Review
2012 – 2018	Editorial Board: Cognition and Emotion
2012 – 2018	Editorial Board: Frontiers in Emotion Science
2016 –	Ad hoc Reviewer, Swiss National Science Foundation
2017 –	Ad hoc Reviewer, National Science Foundation
2018 –	Editorial Boards: Psychology and Aging; Journal of Experimental Psychology: General
2018	Ad hoc Member, Review Panel SPIP, National Institutes of Health
2019	Ad hoc Member, Review Panel MESH, National Institutes of Health
2020	Ad hoc Member, Review Panel BBBP, National Institutes of Health
2020	Editorial Board: Brain Aging
Membership	Association for Psychological Science (APS); International Society for Behavioral Neuroscience (ISBN); Social and Affective Neuroscience Society (SANS); Society for Cognitive Neuroscience (CNS); Society for Neuroscience (SfN); Florida Consortium on the Neurobiology of Cognition (FCNC)

Honors

2006	Heinz-Heckhausen-Jungwissenschaftlerpreis (Young Research Scientist Award), German Psychological Association
2014	International Max Planck Research School on the Life Course (LIFE) Outstanding Alumni Award, APA Board of Educational Affairs Award to Advance Interdisciplinary Education and Training in Psychology
2015	Kavli Fellow National Academy of Sciences
2016	UF Excellence Award -- Assistant Professors
2016	UF College of Liberal Arts and Sciences International Educator of the Year Award
2019	UF Research Foundation Professorship Award
2020	UF College of Liberal Arts and Sciences Faculty Achievement Award

C. Contributions to Science

Overview

My expertise in experimental behavioral aging research coupled with my background in affective, social, and cognitive neuroscience allows for a comprehensive view of brain-behavior relationships in the study of emotion, motivation, and social cognition in aging. I use a multi-methods approach in my research that combines convergent measures, including self-report, cognitive-behavioral measures, eye tracking, functional neuroimaging (fMRI, ERP), and, recently, highly innovative pharmacological (oxytocin administration),

neurofeedback training (real-time fMRI), and applied (cybersecurity related decision making) interventional approaches with the aim to integrate introspective, behavioral, and neuropsychological data.

Representative Publications:

a. Strickland-Hughes CM, Dillon KE, West RL, **Ebner, NC**. Own-age bias in face-name associations: Evidence from memory and visual attention in younger and older adults. Cognition. 2020 Mar. PMID: 32192981
b. Lussier D, Cruz-Almeida Y, **Ebner NC**. Musculoskeletal pain and brain morphology: Oxytocin's potential as a treatment for chronic pain in aging. Front Aging Neurosci. 2019;11:338. PubMed Central PMCID PMC6923678.
c. Frazier I, Lighthall NR, Horta M, Perez E, **Ebner NC**. CISDA: Changes in integration for social decisions in aging. Wiley Interdiscip Rev: Cogn Sci. 2019 May;10(3):e1490. PubMed PMID: 30605250.
d. **Ebner NC**, He Y, Fichtenholtz HM, McCarthy G, Johnson MK. Electrophysiological correlates of processing faces of younger and older individuals. Soc Cogn Affect Neurosci. 2011 Sep;6(4):526-35. PubMed Central PMCID: PMC3150862.

Decision Making and Aging

We aim at identifying adult age differences in cognitive, affective, and social influences on decision making, including in the applied contexts of health and computer security. We have shown that young and older adults differ in their use of future-time travel towards healthy decision making. In addition, we have developed an infrastructure that allows us to determine internet users' susceptibility to cyberattacks (e.g., phishing emails) in the natural setting of the participants' homes. This research has found evidence of a particular vulnerability in older compared to young internet users, combined with very low susceptibility awareness in the elderly. We have also developed a conceptual framework on social decision making in aging, which we submit to empirical test in ongoing research and which builds the basis of the proposed project.

Representative Publications:

a. **Ebner NC**, Ellis DM, Lin T, Rocha HA, Yang H, Dommaraju S, Soliman A, Woodard DL, Turner GR, Spreng RN, Oliveira DS. Uncovering susceptibility risk to online deception in aging. J Gerontol B Psychol Sci Soc Sci. 2020 Feb 14;75(3):522-533. PubMed Central PMID: 29669133.
b. Frazier I, Lighthall NR, Horta M, Perez E, **Ebner NC**. CISDA: Changes in integration for social decisions in aging. Wiley Interdiscip Rev: Cogn Sci. 2019 May;10(3):e1490. PubMed PMID: 30605250
c. Lin T, Capecci D, Ellis D, Rocha H, Dommaraju S, Oliveira DS, **Ebner NC**. Susceptibility to spear-phishing emails: Effects of internet user demographics and email content. ACM Transactions on Computer-Human Interaction, 2019 Jul; 26(5):1-28 PubMed Central PMCID: PMC7274040.
d. Oliveira DS, Lin T, Rocha H, Ellis D, Dommaraju S, Yang H, Weir D, Marin S, **Ebner NC**. Empirical analysis of weapons of influence, life domains, and demographic-targeting in modern spam - An age-comparative perspective. Crime Science, 2019, 8:3. PMID: 31231604. PMCID: PMC6588014

Oxytocin and Socioemotional Aging

As summarized in recent theoretical papers, oxytocin is a neuropeptide with beneficial effects in social and emotional domains, mostly studied in healthy young adults, schizophrenia, and autism. Our group is the first to comprehensively study acute and chronic oxytocin effects in the context of emotional, motivational, and social-cognitive aging. We have developed a theoretical framework that allows us to examine the extent to which the neuropeptide oxytocin is associated with improved functioning in aging, considering gene-brain-behavior relationships using behavioral, (epi)genetic, pharmacological, and neuroimaging techniques. In this line of work, we have generated supportive evidence of benefits of oxytocin intranasal intervention on various functions in aging (e.g., affect, social decision making)

Representative Publications:

a. Horta M, Kaylor K, Feifel D, **Ebner NC**. Chronic oxytocin administration as a tool for investigation and treatment: A cross-disciplinary systematic review. Neurosci & Biobehav Rev. 2020 Jan; 108: 1-23. PubMed Central PMCID: PMC6949379.
b. Plasencia G, Luedicke JM, Nazarloo HP, Carter CS, **Ebner NC**. Plasma oxytocin and vasopressin levels in young and older men and women: Functional relationships with attachment and cognition. Psychoneuroendocrinology. 2019 Dec; PubMed Central PMCID: PMC6943921
c. **Ebner NC**, Chen H, Porges, E, Lin T, Fischer H, Feifel D, Cohen RA. Oxytocin's effect on resting-state functional connectivity varies by age and sex. Psychoneuroendocrinology. 2016 Jul;69: 50-59. PubMed Central PMCID: PMC4942126

d. **Ebner NC**, Horta M, Lin T, Feifel D, Fischer H, Cohen RA. Oxytocin modulates meta-mood as a function of age and sex. Front Aging Neurosci. 2015 Sep;7:175. PubMed Central PMCID: PMC4565056.

Own-Age Bias in Attention, Memory, and Emotion Perception

One line of my research builds on the fact that our environment is complex, and our cognitive system is limited, thus not all stimuli can be fully and simultaneously analyzed. There is evidence that emotional and self-relevant information is preferentially processed, possibly due to the highly practiced and elaborate knowledge structures associated with it as well as the greater personal and social costs of inattention or inaccurate memory. My research findings open new insights into how faces of different ages are processed and how they bias attention and memory. I show that this bias is affected by the emotional content of the faces and impacts memory for person-related information (e.g., personal goals and agendas). My results challenge and inform interpretations of face and emotion processing and age-related differences therein as older participants may be at a disadvantage relative to young participants when stimuli are faces of only young individuals. My findings are not only important from a developmental perspective, but they also place constraints on general theories of attention and memory and have various important implications for social interactions, emotional regulation, self-perceptions, psychological well-being, and health in adults of different ages.

Representative Publications:

a. Strickland-Hughes CM, Dillon KE, West RL, **Ebner, NC**. Own-age bias in face-name associations: Evidence from memory and visual attention in younger and older adults. Cognition. 2020 Mar. PMID: 32192981
b. **Ebner NC**, Luedicke J, Voelkle MC, Riediger M, Lin T, Lindenberger U. An adult developmental approach to perceived facial attractiveness and distinctiveness. Front Psychol. 2018 May;9:561. PubMed Central PMCID: PMC5949528.
c. **Ebner NC**, Johnson MR, Rieckmann A, Durbin KA, Johnson MK, Fischer H. Processing own-age vs. other-age faces: neuro-behavioral correlates and effects of emotion. Neuroimage. 2013 Sep;78:363-71. PubMed Central PMCID: PMC3684564.
d. **Ebner NC**, He Y, Fichtenholtz HM, McCarthy G, Johnson MK. Electrophysiological correlates of processing faces of younger and older individuals. Soc Cogn Affect Neurosci. 2011 Sep;6(4):526-35. PubMed Central PMCID: PMC3150862.

Complete List of Published Work in My Bibliography:
https://pubmed.ncbi.nlm.nih.gov/?term=natalie+ebner

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

Ed and Ethel Moore Alzheimer's Disease Research Program 20A15 Ebner (PI) 05/29/2020 - 06/30/2022
Determining Plasticity of Brain-Regulatory Mechanisms Related to Emotion Processing: A Neurofeedback Approach in Older Adults with Amnestic Mild Cognitive Impairment
The goal of this project is to determine plasticity in emotion processing regions in aging using neurofeedback based on real-time functional magnetic resonance imaging and to determine beneficial neurofeedback effects on emotion-regulatory skills in adults with amnestic Mild Cognitive Impairment.
Role: PI

NIH/NIA R01AG059809 Cruz-Almeida/Ebner (MPI) 08/01/2018 - 04/30/2023
Mechanisms of Oxytocin's Analgesia in Older Adults
The goal of this grant is to determine oxytocin's analgesic effect on chronic pain in aging.
Role: MPI

NIH/NIA - 1R01AG057764-01A1 Ebner/Spreng (MPI) 09/01/2018 – 06/30/2023
Uncovering and Surveilling Financial Deception Risk in Aging
The goal of this grant is to determine risk profiles to phishing susceptibility in aging and develop effective intervention tools (e.g., email warning).
Role: MPI

McKnight Research Foundation AGRDTD04-11-2018 Ebner/Wilson/Grilli/Levin (MPI) 05/01/2018 – 04/30/2021
Uncovering Risk Profiles of Deception and Mitigating Susceptibility to Scamming in Midlife and Older Age: A Novel Intervention Tool

The goal of this grant is to develop MERLIN as a decision-supportive intervention tool to reduce or prevent online deception in aging.
Role: MPI

NIH/NIA - R21AG057200 Ebner/Bowers (MPI) 03/01/2017 – 02/28/2021
Determining Plasticity of Brain-Regulatory Mechanisms Related to Emotion Processing: A Neurofeedback Approach in Aging and Parkinson Disease
The goal of this project is to determine plasticity in emotion processing regions in aging using neurofeedback based on real-time functional magnetic resonance imaging and to determine beneficial neurofeedback effects on emotion-regulatory skills in aging and Parkinson's Disease.
Role: MPI

Completed Research Support (Selection)

NSF 1814557 Oliveira (PI) 09/15/2018 –12/15/2019
SaTC: CORE: Small: FIRMA: Personalized Cross-Layer Continuous Authentication
The goal of this project is to develop and validate a tool that detects abnormality in computer use as a security solution.
Role: Co-PD/PI

NSF SaTC Medium SES-1513572 Oliveira (PI) 09/01/2015 - 12/15/2019
TWC: TTP Option: Medium: Collaborative Research: Developer Crowdsourcing: Capturing, Understanding, and Addressing Security-related Blind Spots in APIs
The goal of this project is to determine blind spots in programmer's attention when writing code.
Role: Co-PD/PI

NSF SaTC EAGERs SES-1450624 Oliveira (PI) 09/15/2014 - 08/31/2017
Age-Targeted Automated Cueing Against Cyber Social Engineering Attacks
The goal of this project is to develop and validate an open-source browser extension that provides visual security cues in an age-targeted fashion to protect older adults from web-based social engineering attacks during their everyday internet use.
Role: Co-PD/PI

OMB No. 0925-0001 and 0925-0002 (Rev. 03/2020 Approved Through 02-28-2023)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Fang, Ruogu

eRA COMMONS USER NAME (credential, e.g., agency login): ruogu.fang

POSITION TITLE: Assistant Professor, J. Crayton Pruitt Family Department of Biomedical Engineering

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Zhejiang University, Hangzhou	BS	06/2009	Information Engineering
The University of Hong Kong, HK	Exchange	06/2008	Electrical and Electronics Engineering
University of Cambridge, UK	Visiting Scholar	05/2009	Biotechnology
Cornell University, Ithaca, NY	PHD	08/2014	Electrical & Computer Engineering

A. Personal Statement

Dr. Fang is the Director of Smart Medical Informatics Learning and Evaluation (SMILE) Lab in the Biomedical Engineering Department. Dr. Fang is also a tenure-track Assistant Professor in the Department of Biomedical Engineering, with affiliation to Electrical and Computer Engineering, Computer and Information Science and Engineering, and Radiology. She is a biomedical data scientist with expertise in machine learning, neuroimaging, and brain dynamics modeling for neurological diseases. She is a pioneer in multimodal neuroimage analysis using machine learning and artificial intelligence, publishing a survey paper on health informatics in big data age, and multiple pioneering papers on dictionary learning, sparse representation, tensor total variation, and evolutionary deep learning for neuroimage analytics in flagship journals and leading, developing toolboxes on neuroimage analysis used by tens of laboratories worldwide, and serving as guest editor of Journal Computerized Medical Imaging and Graphics. Dr. Fang's work has been highlighted as the top 25 Hottest Papers in Medical Image Analysis Journal and won the Best Paper Award at International Conference on Image Processing. Dr. Fang's research specifically focuses on discovery and application of novel machine learning approaches for enhancing neuroimaging precision and brain dynamics quantification in adults with neurological diseases. Dr. Fang has expertise in multi-disciplinary neuroimaging analysis methodologies (optimization, sparsity, dictionary learning, machine learning, deep learning), extensive experience with hemodynamics-related neurological disorders, image restoration applications, and recent research with neurodegenerative diseases. Dr. Fang is the PI of the National Science Foundation CRII (Pre-CAREER) Award (NSF 1564892), NSF III Award (NSF 1908299), National Institute of Health Clinical Translational and Science Institute Award on brain dynamics modeling in multimodal neuroimaging.

a. Liu P, El Basha MD, Li Y, Xiao Y, Sanelli PC, **Fang R**. Deep Evolutionary Networks with Expedited Genetic Algorithms for Medical Image Denoising. Medical image analysis. 2019 May 1;54:306-15. PubMed PMID: 30981133; PubMed Central PMCID: PMC6527091

b. **Fang R,** Chen T, Sanelli PC. Towards robust deconvolution of low-dose perfusion CT: Sparse perfusion deconvolution using online dictionary learning. Medical image analysis. 2013 May 1;17(4):417-28. PubMed PMID: 23542422, PubMed Central PMCID: PMC4196260

c. Xiao Y, Liu P, Liang Y, Stolte S, Sanelli P, Gupta A, Ivanidze J, **Fang R.** STIR-Net: Deep Spatial-Temporal Image Restoration Net for Radiation Reduction in CT Perfusion. Frontiers in neurology. 2019;10. PMID: 31297079; PMCID: PMC6607281

d. **Fang R,** Zhang S, Chen T, Sanelli PC. Robust low-dose CT perfusion deconvolution via tensor total-variation regularization. IEEE transactions on medical imaging. 2015 Feb 20;34(7):1533-48.PubMed PMID: 25706579; PMCID: PMC4779066

B. Positions and Honors

Positions and Employment

2014-2017 **Tenure-Track Assistant Professor**, School of Computing and Information Engineering, Florida International University, Miami, FL.

2017- **Tenure-Track Assistant Professor**, J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, Gainesville, FL.

Professional Societies and Public Advisory Committees

2007- Fung Scholar, Li & Fung Groups, Hong Kong

2009- Member, Society of Women Engineers

2009- Reviewer for Nature Scientific Report, IEEE Transaction on Pattern Analysis and Artificial Intelligence, Medical Image Analysis, IEEE Transactions on Medical Imaging, IEEE Transaction on Image Processing, ACM Computing Survey, Pattern Recognition, IEEE Transaction on Circuits and Systems for Video Technology, Neuroradiology, Neurocomputing, Computerized Methods and Programs in Biomedicine, IEEE Transaction on Multimedia, IEEE Transaction on Instrumentation Measurement, Signal Processing Letter, Journal Electronic Imaging.

2010- Member, Institute of Electrical and Electronic Engineers (IEEE)

2010-2011 Vice President, China Entrepreneur Network

2011- Member, Medical Image Computing and Computer Assisted Intervention (MICCAI) Society

2012- Member, International Society for Optics and Photonics (SPIE)

2012- Member, American Society of Neuroradiology (ASNR) Research Scientist

2014 Managing Guest Editor, Special Issue on Sparsity Techniques in Medical Imaging, Computerized Medical Imaging and Graphics (CMIG)

2014 Co-Chair, the 2nd Workshop on Sparsity Techniques in Medical Imaging (STMI), Medical Imaging Computing and Computer Assisted Intervention Society (MICCAI) at Boston, MA

Honors

2007 Li & Fung Scholarship, sponsored by the Li & Fung Groups, Hong Kong

2009 Jacobs Scholar Fellowship, Cornell University

2010 Best PhD Poster Presentation Award, Engineering Research Conference, Cornell University

2010 Student Travel Award, IEEE International Conference on Image Processing, Hong Kong

2010 Best Paper Award, the 17th IEEE International Conference on Image Processing

2012 Cornell ECE Women's Conference Travel Grant, to attend the 15th International Conference on Medical Image Computing and Computer Assisted Intervention, Nice, France

2013 First Author for the paper recognized as the Top 25 Hottest Papers in the journal Medical Image Analysis, April – Sep. 2014.

2014 Student Travel Award, the 17th Annual International Conference on Medical Image Computing and Computer Assisted Intervention, Boston, USA.

2014 Hsien Wu and Daisy Yen Wu Memorial Award, Cornell University.

2016 Ralph Lowe Junior Faculty Enhancement Award, Oak Ridge Associated Universities

2016 Robin Sidhu Memorial Young Scientist Award, Society of Brain Mapping and Therapeutics

2018 UFII-CTSI Award, University of Florida Informatics Institute-Clinical Translational Science Institute

Extramural Service

2015 Reviewer, NSF Smart and Connected Health Panel

2016 Reviewer, NSF Smart and Connected Health Panel

2016 Reviewer, NIH Bio-Data Management and Analysis Study Section

2017 Reviewer, NSF Smart and Connected Health Panel

2017 Reviewer, NSF BIGDATA Panel

2017 Reviewer, NSF Big Data Spoke Panel

2017 Reviewer, NSF CRII

2018 Reviewer, NIH BMIT-A Study Section

2018 Reviewer, NSF Smart and Connected Community Panel

2018 Reviewer, NSF CRII Panel
2018 Reviewer, NSF CAREER Panel

C. Contributions to Science

1. **Neuroimage Analysis.** Over the past ten years, I have focused my research on the technical innovation and basic science application of neuroimage analysis using machine learning and optimization as novel approaches for neurological disease quantification and diagnosis. This work includes both multimodal neuroimage restoration in reduce radiation dose, brain dynamics deconvolution and quantification, and spatio-temporal super-resolution. The central finding is that data-driven and machine learning models can leverage the intra- and inter-personal similarity to achieve precise brain dynamics quantification in limited dose and resolution neuroimaging data. I was awarded the 2017 Ralph Lowe Junior Faculty Enhancement Award from the Oak Ridge Associated Universities for my scientific contributions to the field. My paper on sparse perfusion deconvolution for brain dynamics quantification has been highlighted as the top 25 Hottest Papers in Medical Image Analysis Journal. I am also PI of the NSF CRII and III grants on brain dynamics modeling. Collectively, this work provides me with a strong foundation in the technical elements and applications of neuroimaging analysis.
    a. **Fang R,** Chen T, Sanelli PC. Towards robust deconvolution of low-dose perfusion CT: Sparse perfusion deconvolution using online dictionary learning. Medical image analysis. 2013 May 1;17(4):417-28. PubMed PMID: 23542422, PubMed Central PMCID: PMC4196260
    b. **Fang R,** Karlsson K, Chen T, Sanelli PC. Improving low-dose blood–brain barrier permeability quantification using sparse high-dose induced prior for Patlak model. Medical image analysis. 2014 Aug 1;18(6):866-80. PubMed PMID: 24200529; PMCID: PMC4188431
    c. **Fang R,** Zhang S, Chen T, Sanelli PC. Robust low-dose CT perfusion deconvolution via tensor total-variation regularization. IEEE transactions on medical imaging. 2015 Feb 20;34(7):1533-48.PubMed PMID: 25706579; PMCID: PMC4779066
    d. **Fang R,** Gupta A, Huang J, Sanelli P. TENDER: Tensor non-local deconvolution enabled radiation reduction in CT perfusion. Neurocomputing. 2017 Mar 15;229:13-22.

2. **Machine Learning and Deep Learning Algorithm Innovation and Application.** My work in developing machine learning and deep learning algorithms has focused on auto machine learining and spatio-temporal modeling. I led and contributed to development and evolution of deep learning algorithms in medical image analysis, including expedited genetic algorithm for deep evolutionary networks, spatio-temporal restoration deep nets, and multi-scale deep neural networks for a broad spectrum of medical image applications, including medical image denoising, restoration, adipose tissue segmentation, and Parkinson's Disease differentiation.
    a. Liu P, El Basha MD, Li Y, Xiao Y, Sanelli PC, **Fang R.** Deep Evolutionary Networks with Expedited Genetic Algorithms for Medical Image Denoising. Medical image analysis. 2019 May 1;54:306-15. PubMed PMID: 30981133; PMCID: PMC6527091
    b. Xiao Y, Liu P, Liang Y, Stolte S, Sanelli P, Gupta A, Ivanidze J, **Fang R.** STIR-Net: Deep Spatial-Temporal Image Restoration Net for Radiation Reduction in CT Perfusion. Frontiers in neurology. 2019;10. PubMed PMID: 31297079; PMCID: PMC6607281
    c. Jiang F, Li H, Hou X, Sheng B, Shen R, Liu XY, Jia W, Li P, **Fang R**. Abdominal adipose tissues extraction using multi-scale deep neural network. Neurocomputing. 2017 Mar 15;229:23-33.
    d. Archer DB, Bricker JT, Chu WT, Burciu RG, McCracken JL, Lai S, Coombes SA, **Fang R,** Barmpoutis A, Corcos DM, Kurani AS. Development and validation of the automated imaging differentiation in parkinsonism (AID-P): a multicentre machine learning study. The Lancet Digital Health. 2019 Sep 1;1(5):e222-31. PubMed PMID: 32259098 PMCID: PMC7111208

3. **Computational Health Informtics** is an emerging research direction that integrates computational science, medicine, and information technology. With the advent of the big data age, my work has also contributed to the field of computational health informatics by estalibshing a survey of the current literature and extend the perfusion deconvolution research using information-based approaches such as non-local tensor total variation, sparsity techniques, and tissue-specific models. We have shown that the medical images have spatio-temporal self-similairty and tissue-specific patterns, to restore the high-quality images from the low-quality ones via dictionary learning and tensor total variation.

a. **Fang R,** Jiang H, Huang J. Tissue-specific sparse deconvolution for brain CT perfusion. Computerized Medical Imaging and Graphics. 2015 Dec 1;46:64-72. PMID: 26055434
b. **Fang R**, Chen T, Metaxas D, Sanelli P, Zhang S. Sparsity techniques in medical imaging. Computerized medical imaging and graphics: the official journal of the Computerized Medical Imaging Society. 2015 Dec;46(Pt 1):1. PubMed PMID: 26216851, PMCID: PMC4877683
c. **Fang R**, Pouyanfar S, Yang Y, Chen SC, Iyengar SS. Computational health informatics in the big data age: a survey. ACM Computing Surveys (CSUR). 2016 Jun 14;49(1):1-36.
d. Yang X, Bian J, **Fang R,** Bjarnadottir RI, Hogan WR, Wu Y. Identifying relations of medications with adverse drug events using recurrent convolutional neural networks and gradient boosting. Journal of the American Medical Informatics Association. 2020 Jan;27(1):65-72. PubMed PMID: 31504605

4. **Retinal image analysis using machine learning.** Retinal image analysis from the fundus and OCT images is an important channel for automated computer-assisted screening and diagnosis of various retinal, neurodegenerative, and cardiovascular diseases. I led and contributed to artificial intelligence, machine learning, and deep learning methods on analysis of both fundus images and optical coherence tomography (OCT) images. These analysis include image quality assessment, lesion detection, cup and disc segmentation, retinal layers segmentation, and vessel segmentation, which are important foundations to higher level disease diagnosis from retinal images.
    a. Liu, P., Kong, B., Li, Z., Zhang, S., **Fang, R.,** 2019. CFEA: Collaborative Feature Ensembling Adaptation for Domain Adaptation in Unsupervised Optic Disc and Cup Segmentation. Medical Image Analysis and Computer Assisted Intervention.
    b. Orlando JI, Fu H, Breda JB, van Keer K, Bathula DR, Diaz-Pinto A, **Fang R,** Heng PA, Kim J, Lee J, Lee J. et al. REFUGE Challenge: A unified framework for evaluating automated methods for glaucoma assessment from fundus photographs. Medical image analysis. 2020 Jan 1;59:101570. PMID: 31630011
    c. Masood S, **Fang R**, Li P, Li H, Sheng B, Mathavan A, Wang X, Yang P, Wu Q, Qin J, Jia W. Automatic choroid layer segmentation from optical coherence tomography images using deep learning. Scientific reports. 2019 Feb 28;9(1):1-8. PubMed PMID: 30816296 PMCID: PMC6395677
    d. Shen Y, Sheng B, **Fang R,** Li H, Dai L, Stolte S, Qin J, Jia W, Shen D. Domain-invariant interpretable fundus image quality assessment. Medical Image Analysis. 2020 Apr 1;61:101654. PubMed PMID: 32066065

Complete List of Published Work in my Bibliography:
https://scholar.google.com/citations?hl=en&user=LVb46zEAAAAJ

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

CISE Core Program Small NSF Fang (PI) 10/1/2019 – 9/30/2022
III: Small: Modeling Multi-level Connectivity of Brain Dynamics
This proposal focuses on a three-year research program to characterize and develop a multi-level connectivity model for brain dynamics and corresponding tools to significantly accelerate data-driven discoveries from dynamic neuroimaging data.
Role: PI

Phase I IUCRC University of Florida: Center for Big Learning NSF Li (PI) 01/01/2018 – 12/31/2022
With the vision of creating intelligence and leveraging collective wisdom from academia, industry, and governments, the CBL consortium focuses on large-scale deep learning (DL), intelligent platforms, and DL-enabled big data applications in a broad spectrum of disciplines.
Role: Co-I

UF CTSI TL1 NIH See (Student PI) 09/01/19 – 08/30/21
Predicting short-term and long-term effects of spinal cord stimulation: implications for clinical practice
The goal of this project is for the student to obtain training in clinical translational science on a project using machine learning and EEG signals to prediction short- and long-term outcomes in spinal cord stimulations for chronic pain patients.
Role: Mentor

Completed Research Support During Last Three Years

CISE CRII-1564892 NSF Fang (PI) 05/01/2016 – 04/31/2019
SCH: Characterizing, Modeling and Evaluating Brain Dynamics
This goal of this project is to develop a framework for data-driven brain dynamics characterization, modeling and evaluation that includes the new concept of a 5th dimension - brain dynamics - to complement the structural 4-D brain for a complete picture.
Role: PI

UFII-CTSI Pilot Award University of Florida Gong (PI) 06/01/2019 – 05/31/2020
Toward prevention of cardiotoxicity in cancer: a multimodal approach leveraging genomics, images and clinical data.
The goal of this project is to explore a novel approach to identify patients predisposed to cancer therapy-induced cardiotoxicity through interrogation of pharmacogenomics, medical images and clinical factors.
Role: Co-PI

UFII-SEED Award University of Florida Wu (PI) 08/01/2019 – 07/31/2020
Multimodal Visual-Text Learning from Clinical Narrative and Image for Early Detection of Diabetic Retinopathy
This study proposes to leverage the narrative clinical text to improve lesion detection from medical images via clinical Natural Language Processing (NLP). Our ultimate goal is to improve the early detection and prevention of vision-threatening diseases among rural and low-income areas by developing a low-cost, highly efficient system that can leverage both narrative clinical reports and medical images.
Role: Co-PI

UFII-CTSI Pilot Award UFII-CTSI Fang (PI) 06/01/2018 – 05/31/2019
Precision Dose: Personalized Radiation Dose Optimization for Multimodal Imaging
The goal of this project is to optimize personalized radiation dose in comprehensive brain imaging consisting of non-contrast CT (NCCT), CT angiography (CTA), and CT perfusion (CTP).
Role: PI

NSF REU SITE NSF Pissinou (PI) 02/01/2016-01/31/2019
ASSET: Research Experiences for Undergraduates in Advanced Secured Sensor Enabling Technologies
This project brings together fields of sensing, computing and communications to pioneer new core technologies along with supportive methods, architectures and tool-kits.
Role: Senior Personnel

Ralph Lowe Junior Faculty Award Oakridge University Association Fang (PI) 06/01/2016-5/31/2017
Modeling, Estimating and Reasoning in Limited Data Brain Dynamics
The goal of this study is to develop robust and data-driven techniques for the purpose of modeling, estimating functional parameters from the limited data brain images, and making decision support practical based on efficient direct estimation of the brain dynamics.
Role: PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Thomas C Foster

eRA COMMONS USER NAME (credential, e.g., agency login): Tom_Foster

POSITION TITLE: Professor and Evelyn F. McKnight Chair for Research on Cognitive Aging and Memory

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Arizona, Tucson AZ	BS	1981	Psychology
Bowman Gray, School of Medicine, W-S, NC	Ph.D.	1987	Physio/Pharm
University of Colorado, Boulder CO	Postdoctoral	1991	Neurophysiology and behavior

A. Personal Statement

My research focuses on understanding the relationship between age-related cognitive decline and mechanisms of brain aging. My long-term goal is the amelioration of memory deficits associated with aging and diseases of aging. My research program utilizes a combination of behavioral characterization with biochemical, molecular, and electrophysiological techniques and treatments (behavioral, pharmacological and viral) to obtain a vertically integrated perspective on neural aging, from the molecular to the cognitive level. Many of the molecular techniques are being applied to humans to obtain epigenetic markers of age-related cognitive decline. I have been continuously funded through NIH as a principle investigator since 1992 and my work includes over 140 publications on memory mechanisms and the aging brain. My lab has developed a battery of behavioral tasks that are sensitive to the onset and trajectory of age-related cognitive decline and control for sensory-motor or motivational factors. Other techniques that are routine in the lab include protocols for next generation RNA sequencing (Ion Proton), including examination of microRNA from exosomes, isolated from plasma in humans. In addition, we have developed techniques for examining DNA methylation as a mechanism for regulation of transcription. Our recent work demonstrates that microRNA and DNA methylation in blood can predict cognitive function in humans. We recently published several papers related to the idea that oxidative stress associated with inflammation and normal aging contributes to cognitive decline through redox regulation of the NMDA receptor. In addition, we have provide evidence for molecular mechanisms of cognitive reserve as a plasticity property that protects cognitive function.

Reviews related to our work:

a) **Foster**, TC. (2012) Dissecting the age-related decline on learning and memory tasks in rodent models: N-methyl-D-aspartate receptors and voltage-dependent Ca^{2+} channels in senescent synaptic plasticity. *Prog Neurobiol* 96:283-302. PMID: 22307057.
b) **Foster**, TC., Kyritsopoulos, A., and Kumar, A., (2017) Central role for NMDA receptors in redox mediated impairment of synaptic function during aging and Alzheimer's disease. Behav Brain Res, 322, 223-232. PMID: 27180169
c) Kumar, A., Yegla, B., **Foster**, TC. (2018) Redox signaling in neurotransmission and cognition during aging. Antioxid Redox Signal, 18, 1724-1745. PMCID: 5962336.
d) **Foster**, T.C. Senescent Neurophysiology: Ca^{2+} Signaling from the Membrane to the Nucleus. (2019) Neurobiology of Learning and Memory, 164, 107064 PMCID: 31394200

B. Positions and Honors

1. Positions and Employment

Assistant Professor, 1991-1992 Dept. Psych. University of Connecticut
Assistant Professor, 1992-1998, Dept. Psych. University of Virginia
Associate Professor, 1998-2003, Dept. Pharmacology, University of Kentucky Medical School
Associate Professor, 2003-2006, Dept. Neurosci, University of Florida
Professor 2006-present, Dept. Neurosci, University of Florida

2. Academic Honors and Awards

McKnight Chair for Research on Aging and Memory, University of Florida 2003-present
National Advisory Council on Aging NIH Method to Extend Research in Time (MERIT) Award (2011-2019)
Member of the planning Committee for the Cognitive Aging Summits I (2006), II (2010), III (2017)
Associate Editor *Frontiers in Aging Neuroscience* 2009-present
Section Editor *Experimental Gerontology* 2018-present
Editorial Board for *Aging Brain*
Member for > 10 NIH Special Emphasis Review Panels (2001-2015)
Member NIH IFCN-7 Study Section 1999-2004
Member NIH Learning and Memory study section (7/2014-6/2018)
Shannon Investigators Award, 1992

C. Contribution to Science

1. In general, my research has focused on understanding mechanisms for modifying synaptic transmission and their relationship to memory, particularly in the context of cognitive decline during aging. My early work employed *in vivo* recording and showed that neuronal discharge activity in the hippocampus, a brain structure involved in memory, could represent the history of experience and the association of sensory-motor information.
   a) **Foster**, TC., Christian, EP., Hampson, RE., Campbell, KA. and Deadwyler, SA. (1986) Sequential dependencies regulate sensory evoked responses of single units in the rat hippocampus. Brain Research 408:86-96. PMID: 3594233
   b) **Foster**, TC., West, MO., Hampson, RE. and Deadwyler, SA. (1988) Control of sensory activation of granule cells in the fascia dentata by extrinsic afferents: Septal and entorhinal inputs. Journal of Neuroscience 8:3869-3878. PMID: 3193182
   c) **Foster**, TC., Castro, CA. and McNaughton, BL. (1989) Spatial selectivity of rat hippocampal neurons: Dependence on preparedness for movement. Science 244: 1580-1582. PMID: 2740902

2. Synaptic plasticity is thought to mediate the associative and information storage properties of neurons. I employed electrophysiological techniques to determine the mechanisms for altered synaptic strength (quantal analysis) and provide illumination on age-related changes in mechanisms, which regulate the induction and expression of synaptic plasticity associated with cognitive decline. Recent work links impaired NMDA receptor function to inflammation and increased redox stress of aging.
   a) Norris, C.M., Korol, D.L. and **Foster**, T.C. (1996) Increased susceptibility to induction of long-term depression and long-term potentiation reversal during aging. Journal of Neuroscience 16: 5382-5392. PMID: 8757251
   b) Bodhinathan, K., Kumar A., **Foster**, T.C. Intracellular redox state alters NMDA receptor response during aging through Ca2+/calmodulin-dependent protein kinase II. Journal of Neurosciences 2010; 30(5):1914-1924.PM:20130200
   c) Guidi, M., Kumar, A., and **Foster** T.C. Impaired attention and synaptic senescence of the prefrontal cortex involve redox regulation of NMDA receptors. Journal of Neuroscience 2015, 35(9) 3966-3977. PMCID: 434819
   d) Kumar, A., Thinschmidt, J., and **Foster**, T.C. Mechanism for NMDA receptor hypofunction and redox sensitivity of hippocampal synaptic transmission during aging. (2019) Aging-US, 11, 5140-5157. PMCID: 6682512.

3. To examine the molecular signatures of aging and cognitive function, I have developed molecular techniques including isolation of exosomes, next generation sequencing of RNA and miRNA and DNA

methylation. The results characterize molecular markers and signaling pathways for age-related cognitive decline in specific brain regions that mediate the cognitive process of interest. In humans, an older DNA methylation clock, and miRNA from plasma exosomes predict both age and cognitive function.

a) Ianov, L., Rani, A., Beas, B. S., Kumar, A., and **Foster**, T.C. Transcription profile of aging and cognitive-related genes in the medial prefrontal cortex. Front Aging Neurosci, 2016, 8, 113. PMCID: 4868850.
b) Rani, A., O'Shea, A. Ianov, L., Cohen, R.A., Woods, A.J. **Foster**, T.C. miRNA in Circulating Microvesicles as Biomarkers for Age-Related Cognitive Decline. Front. Aging Neroci. 2017 9 (232) PMCID: 5632661
c) Ianov, L., De Both, M., Chawla, M.K., Rani, A., Kennedy, A.J., Piras, I., Day, J.J., Siniard, A., Kumar, A., Sweatt, J.D., Barnes, C.A. Huentelman, M.J. **Foster**, T.C. Hippocampal transcriptiomic profiles: Subfield vulnerability to age and cognitive impairment. Front Aging Neurosci 2018, PMCID: 4868850.
d) Cruz-Almeida, Y., Sinha, P., Rani, A., Huo, Z., Fillingim, R.B., **Foster**, T.C. Epigenetic Aging is Associated with Clinical and Experimental Pain in Community-Dwelling Older Adults, (2019) Molecular Pain, 15, PMCID: 6710702.

4. Much of my work has focused on modulation of the trajectory of cognitive decline including studies of the role of peripheral inflammation, hormone replacement, and cellular resilience to the stressor of aging.
   a) Kumar, A., Rani, A., Scheinert, R.B., Ormerod, B.K., and **Foster**, T.C. Nonsteroidal anti-inflammatory drug, indomethacin improves spatial memory and NMDA receptor function in aged animals. Neurobiology of Aging (2018), 70, 184-193. PMCID: 6119103.
   b) Febo, M., Rani, A., Yegla, B., Barter, J., Kumar, A., Wolff, C.A., Esser, K., And **Foster**, T.C. Longitudinal Characterization and Biomarkers of Age and Sex Differences in the Decline of Spatial Memory. (2020) Frontiers in Aging Neuroscience. 12: 34, PMCID: 7044155.
   c) Barter, J.D., Kumar, A., Rani, A., Colon-Perez, L. M., Febo, M., **Foste**r, T.C. Differential Effect of Repeated Lipopolysaccharide Treatment and Aging on Hippocampal Function and Biomarkers of Hippocampal Senescence (2020) Molecular Neurobiology, 57, 4045-4059. PMID: 32651758
   d) Smith, G. Rani, A., Kumar, A., Barter, J., Foster, T.C. Hippocampal Subregion Transcriptomic Profiles Reflect Strategy Selection during Cognitive Aging. Journal of Neuroscience, (2020) 40, 4888-4899. PMCID: 7326352.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/thomas.foster.1/bibliography/40906731/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

NIA R01 AG049711(PI: Foster) 09/01/2015 to 4/30/2020
Systemic inflammation in regulating the onset and progression of brain aging-1
The major goals of this project are to examine the hypothesis that systemic peripheral inflammation due to LPS will influence the onset and progression of age-related changes in NMDAR signaling mediating memory deficits.
Role: PI

NIA R01 AG052258 (PI Foster) 05/05/2016 to 4/30/2021
This project employs viral-mediated expression of specific cytokines in peripheral tissue to determine their effect on brain function.
Role: PI

NIA R01 AG037984-11 (PI: Foster) 9/15/2018 to 7/31/2013
The major goals of this project are to test the hypothesis that the beneficial effects of estrogen on cognition over the lifespan are due to transcriptional regulation of redox state and epigenetically mediated loss of function

NIA P30AG028740 (PI Pahor) 7/1/2006-3/31/2022
Claude D. Pepper Older Americans Independence Center
The mission of the University of Florida Older Americans Independence Center (OAIC) is to assess the risk factors of physical disability in older adults, develop and test effective prevention therapies, and train new investigators in research on aging and disability, while developing their leadership qualities.
Role: advice on animal models of aging and age-related cognitive decline

NIA RO1AG068205 (PI Kumar) 08/01/2020- 05/31/2022
Age-associated impaired executive function: Rescue by NMDA receptor upregulation

Completed Research Support

NIA R37 AG036800 Foster (PI Foster) 09/01/2014 to 08/31/19
The major goals of this project are to examine the hypothesis that age-related changes in NMDAR signaling mediate memory deficits and changes in synaptic plasticity. Aim 2 examines the idea that inflammation induces a redox-mediated NMDAR hypofunction.
Role: PI

NINDS R37 NS040389 (PI Ranum) 8/1/2015 – 7/31/2017
The purpose of this project is to use molecular genetic approaches to better understand the pathophysiology of spinocerebellar ataxia type 8. As part of this effort we have developed and are characterizing two distinct SCA8 transgenic models.
Role: advice on synaptic physiology and plasticity in transgenic animals

R21NS091435 (PI Notterpek) 9/1/2017 – 8/31/2017
This projects targets chaperone pathways for myelin repair in hereditary neuropathies
Role: advice on statistical analysis of behavior and transcription

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Joseph M. Gullett

eRA COMMONS USER NAME (credential, e.g., agency login): gullettj

POSITION TITLE: Research Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Florida	B.S.	05/2008	Psychology
University of Florida	M.S.	05/2013	Clinical Psychology
West Los Angeles VAMC	-	08/2017	APA Internship in Clinical Psychology
University of Florida	Ph.D.	08/2017	Clinical Psychology
University of Florida	Postdoctoral	08/2019	Neuropsychology

A. Personal Statement

I am a licensed neuropsychologist and Research Assistant Professor with the University of Florida Center for Cognitive Aging and Memory. I received my Ph.D. in clinical psychology from the University of Florida in August of 2017 after the completion of a one-year clinical internship in psychology at the West Los Angeles VA Medical Center. I have worked extensively in multimodal neuroimaging, including functional MRI and Diffusion methods to study populations with white matter pathology including older adults, Veterans with mild traumatic brain injury (mTBI), and people living with HIV (PLWH). My current work applies the methods of multimodal neuroimaging and neuropsychology to the study of cognitive aging as well as in Veterans with mTBI and PLWH and alcohol use disorders. I remain clinically-involved in the neuropsychological assessment of various populations, and collaborate as a licensed neuropsychologist both on a weekly clinical service as well as on a number of NIAAA-funded U-01 and R-01 grants focused on aging and PLWH. I recently completed a 1Florida Alzheimer's Disease Research Pilot Grant which generated the pilot data being included in a K-23 Clinical Trial submission to the National Institute of Aging, Neuroscience. This new and exciting area of focus, which includes the use of multi-modal neuroimaging to predict cognitive and intervention outcomes in older adults, is developing into my current area of research expertise.

B. Positions and Honors

Positions and Employment

2008-2011 Clinical Psychometrist, UF Neuropsychology Clinic, Gainesville, FL
2011-2016 Graduate Assistant, Department of Clinical & Health Psychology, Gainesville, FL
2016-2017 Psychology Intern, West Los Angeles VA Medical Center, Los Angeles, CA
2017-2018 Postdoctoral Clinical-Research Associate, Center for Cognitive Aging and Memory, Gainesville, FL
2018-2019 T32 Postdoctoral Fellow, Center for Cognitive Aging & Memory, Gainesville, FL

2019- Assistant Professor, Department of Clinical & Health Psychology, Gainesville, FL

Other Experience and Professional Memberships

2012-2017 Student Member, APA Division 40 (neuropsychology)

2016- Ad Hoc Reviewer, The Clinical Neuropsychologist
2018- Ad Hoc Reviewer, Neuropsychology Review
2019- Ad Hoc Reviewer, Human Brain Mapping
2019- Licensed Clinical Psychologist (PY10534)
2020- Ad Hoc Reviewer, Frontiers in Aging Neuroscience (review count: 2)
2020- Member, The International Neuropsychological Society
2020- Editorial Board Member, Frontiers in Aging Neuroscience
2020- Ad Hoc Reviewer, Human Brain Mapping
2020- Member, American Academy of Neurology (AAN)

C. Contributions to Science

1. Over my tenure as an assistant professor with the Center for Cognitive Aging and Memory, my scientific work has continued to focus on neuroimaging, clinical, and neuropsychological correlates of normal aging as well as HIV, morbid obesity, and cancer. Further, increased focus has been directed toward the impact of aging and neurodegenerative disease, including two first-author works focusing on novel white matter predictors of cognitive aging and data-based machine learning prediction of cognitive function.
   a. Gullett JM, O'Shea A, Lamb DG, Porges EC, O'Shea DM, Pasternak O, et al. The association of white matter free water with cognition in older adults. Neuroimage. 2020;
   b. Gullett JM, Chen Z, O'Shea A, Akbar M, Bian J, Rani A, et al. MicroRNA predicts cognitive performance in healthy older adults. Neurobiol Aging. 2020;
   c. Bryant VE, Gullett JM, Porges EC, Cook RL, Bryant KJ, Woods AJ, et al. History of Alcohol Consumption and HIV Status Related to Functional Connectivity Differences in the Brain During Working Memory Performance. Curr HIV Res. 2020;
   d. Cohen RA, Gullett JM, Porges EC, Woods AJ, Lamb DG, Bryant VE, et al. Heavy Alcohol Use and Age Effects on HIV-Associated Neurocognitive Function. Alcohol Clin Exp Res. 2019;

2. During the two years as postdoctoral fellow prior to starting my assistant professorship with the Center for Cognitive Aging and Memory, my scientific work focused on neuroimaging, clinical, and neuropsychological correlates of normal aging as well as HIV, alcohol use, and breast cancer-related cognitive phenomena.
   a. Gullett JM, Cohen RA, Yang GS, Menzies VS, Fieo RA, Kelly DL, et al. Relationship of fatigue with cognitive performance in women with early-stage breast cancer over 2 years. Psychooncology. 2019;
   b. Kuhn T, Jin Y, Huang C, Kim Y, Nir TM, Gullett JM, et al. The joint effect of aging and HIV infection on microstructure of white matter bundles. Hum Brain Mapp. 2019;
   c. Gullett JM, Lamb DG, Porges E, Woods AJ, Rieke J, Thompson P, et al. The Impact of Alcohol Use on Frontal White Matter in HIV. Alcohol Clin Exp Res. 2018;42(9):1640–9.
   d. Cohen RA, Siegel S, Gullett JM, Porges E, Woods AJ, Huang H, et al. Neural response to working memory demand predicts neurocognitive deficits in HIV. J Neurovirol. 2018;

3. In my early post-baccalaureate and graduate career, I focused my research endeavors on the use of diffusion tensor imaging and structural neuroimaging to investigate clinical phenomena within populations with TBI, PTSD, and temporal lobe epilepsy.

   a. Kuhn T, Gullett JM, Boutzoukas AE, Bohsali A, Mareci TH, FitzGerald DB, et al. Temporal lobe epilepsy affects spatial organization of entorhinal cortex connectivity. Epilepsy Behav. 2018;
   b. Kuhn T, Gullett JM, Nguyen P, Boutzoukas AE, Ford A, Colon-Perez LM, et al. Test-retest reliability of high angular resolution diffusion imaging acquisition within medial temporal lobe connections assessed via tract based spatial statistics, probabilistic tractography and a novel graph theory metric. Brain Imaging Behav. 2016;
   c. Gullett JM, Price CC, Nguyen P, Okun MS, Bauer RM, Bowers D. Reliability of three benton judgment of line orientation short forms in idiopathic parkinsons disease. Clin Neuropsychol. 2013;
   d. Ford A, Colon-Perez L, Triplett WT, Gullett JM, Mareci TH, FitzGerald DB. Imaging white matter in human brainstem. Front Hum Neurosci. 2013;

4. Through my collaborative efforts in other realms, I have also garnered expertise in various scientific topics, including cancer and obesity-related cognitive function, as well as the effect of TBI on neural sleep centers.
   a. Fernando HJ, Cohen RA, Gullett JM, Friedman J, Ayzengart A, Porges E, et al. Neurocognitive Deficits in a Cohort With Class 2 and Class 3 Obesity: Contributions of Type 2 Diabetes and Other Comorbidities. Obesity. 2019;
   b. Cohen RA, Gullett JM, Woods AJ, Porges EC, Starkweather A, Jackson-Cook CK, et al. Cytokine-associated fatigue prior to, during, and post-chemotherapy for breast cancer. J Neuroimmunol. 2019;
   c. Sullan MJ, Bohsali AA, Gullett JM, Goldstein J, Bauer RM, Mareci TH, et al. The Relationship Between Locus Coeruleus Volume and Measures of Sleep and Attentional Control in Veterans with Mild TBI. Clin Neuropsychol (Neuropsychology, Dev Cogn Sect D). 2015;29(3):324.
   d. Sullan M, Bohsali A, Gullett JM, Goldstein J, Bauer R, Mareci T, et al. The Locus Coeruleus and Sleep-Wake Disturbances in Veterans with mTBI. J Sleep med disord. 2014;1(1):1004.

5. Lastly, my interests also led me to explore the white matter connectivity of language centers using tractography in healthy adults, as well as publish a case study detailing a cautionary tale about MRI research with veterans.
   a. Bohsali AA, Triplett W, Sudhyadhom A, Gullett JM, McGregor K, FitzGerald DB, et al. Broca's area - Thalamic connectivity. Brain Lang. 2015;
   b. Ford AA, Triplett W, Sudhyadhom A, Gullett J, McGregor K, FitzGerald DB, et al. Broca's area and its striatal and thalamic connections: A diffusion-MRI tractography study. Front Neuroanat. 2013;
   c. FitzGerald DB, Gullett JM, Levy CE, Crosson BA. Delayed Diagnosis of Intracerebral Foreign Body From the Vietnam War. Mil Med. 2011;

Complete list of published work in my NCBI bibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/1Z3WHMZO4VfQQ/bibliography/53788754/public/?sort=date&direction=ascending

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

U01-AA020797-09 (MPIs: Cook, Cohen) 09/25/2011 – 06/30/2021
NIH/NIAAA
"Effects of Experimentally-Induced Reductions in Alcohol Consumption on Brain Cognitive, and Clinical Outcomes and Motivation for Changing Drinking in Older Persons with HIV Infection."
The goal of this study is to build on our past findings to determine the extent to which marked reductions in alcohol consumption over 4-weeks via contingency management (CM) improves cognitive performance, brain functions and pathophysiology, and HIV-associated health outcomes.
Role: Co-investigator

P01-AA019072-11 (PI: Kahler) 07/01/2020 – 05/31/2021
NIH/NIAAA
"Alcohol and HIV-Associated Brain Dysfunction."
The first goal of this study is to continue an ongoing line of research, extending current findings by incorporating functional neuroimaging (FMRI) approaches, along with additional magnetic resonance spectroscopy (MRS) methods that will enable us to delineate both functional and cerebral metabolic disturbances affecting specific functional brain systems that are associated with the interaction of ETOH and HIV, as well as alterations in functional connectivity within and between these systems. The second objective is to examine the extent to which reductions in ETOH consumption among heavy drinkers with HIV infection that result from a motivational intervention lead to improvements in these functional and metabolic neuroimaging measures, as well as neurocognitive performance.

R01-DK099334-05 (PI: Cohen) 06/25/2014 – 05/31/2021
NIH/NIDDK
"Obesity and Type-2 Diabetes: Bariatric Surgery Effects on Brain Function"
A prospective longitudinal cohort matched design will be used to assess changes in these neuroimaging indices, pre- and post-surgery and relative non-surgical obese controls. The groups will have equal proportions

of diabetics and non-diabetics with obesity, enabling us to test its influence. By examining obesity and weight loss in the context of bariatric surgery, this study capitalizes on a powerful natural experimental manipulation that can provide a unique window into the effects of obesity and weight loss on the brain

R01-AG061065-03 (MPIs: Cohen, Barve, Cook) 06/02/2020 – 05/31/2021
NIH/NIA
"Role of Gut Microbial Dysbiosis and Aging on HIV-Associated Neurocognitive and Brain Dysfunction"
The goal of this proposal is to conduct collaborative studies to understand the gut-brain relationship in older persons living with HIV-1 infection. The study will examine the role of gut-driven mechanisms on HIV-associated Neurocognitive Disorders (HAND) in the aging HIV+ population.

Completed Research Support
AG047266 (Pilot PI: Gullett) 09/20/2019 – 09/30/2020
1Florida Alzheimer's Disease Center
"Machine Learning Diagnostic Prediction using Multi-modal Neuroimaging, Cognitive Performance, and Disease Progression Information"
The goal of the project is to provide highly accurate diagnostic prediction of stable versus progressive mild cognitive impairment using structural and functional MRI in combination with cognitive performance data.
Role: PI

NIAAA T32-AA25877 (PI: Cook) 09/01/2018-08/31/2019
"Translational Science Training to Reduce the Impact of Alcohol on HIV Infection"
The goal of this T32 project is to provide research training and expertise related to alcohol and HIV infection.
Role: Postdoctoral fellow

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Ashok Kumar

eRA COMMONS USER NAME (credential, e.g., agency login): Calcium

POSITION TITLE: Associate Professor of Neuroscience

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Lucknow, Lucknow	BS	1984	Life Sciences
University of Lucknow, Lucknow	MS.	1986	Zoology
Central Drug Research Institute, Lucknow	Ph.D.	1992	Pharmacology
Yale University, New Haven	Postdoctoral	1998	Neuroscience/Neurobiology of Aging

A. Personal Statement

Over the past two decades, my research is focused on delineating the mechanisms contributing to age-related cognitive impairment. Toward this goal, a central focus of my research involves the role of various interventions such as environmental enrichment, exercise, viral vector, and anti-inflammatory compounds in restoring/reversing age-associated impaired cognition, synaptic plasticity, and cell excitability. I along with Dr. Thomas Foster, have been instrumental in characterizing N-methyl-D-aspartate receptor (NMDAR) hypofunction during aging and its relationship with cognitive impairment (PMID: 20884759, PMID: 24089479, PMID: 21942371, PMID: 25740525, PMID: 27180169, PMID: 26732087, PMID: 30031231, PMID: 28467718, PMID: 30209673, PMID: 30504275); this work highlights a link between age-associated impaired cognition and a redox-mediated decline in NMDAR function. Our recent research findings (PMID: 30031231, PMID: 28928652) demonstrate that nonsteroidal anti-inflammatory compound improves neurogenesis, spatial memory, and NMDAR synaptic function. Aging by far the main risk factor for neurodegenerative disease including Alzheimer's disease (AD); the question remains "why are the elderly more vulnerable to AD?" Aging decreases NMDAR function at the synapse. We hypothesize that an oxidized redox state associated with aging influences GluN2B NMDAR synaptic localization/trafficking, particularly the extrasynaptic ones.

B. Positions and Honors

1. Position and Employment

2017-Present Associate Prof, Dept. of Neuroscience, Brain Institute, Univ. of Florida, Gainesville, FL.
2003 - 2017 Res Asst Prof, Dept. of Neurosci, Brain Institute, Univ. of Florida, Gainesville, FL.
2000 - 2003 Sr Research Associate, Dept. of Pharmacology, Univ. of Kentucky, Lexington, KY.
1997 - 1999 Res Associate, Dept. of Psychiatry, Yale University Sch. of Med, New Haven, CT.
1995 - 1997 Res Asso, Dept. of Pharmacodynamics, Univ. of Illinois at Chicago, Chicago, IL.
1987 - 1994 Research Fellow, Dept. of Pharmacology, Central Drug Res Institute, Lucknow.

2. Other Experience and Professional Memberships

1997- Member, Society for Neuroscience
1990- Life Member, Indian Society of Neuroscience

1990- Life Member, Indian Pharmacological Society

3. Editorial Service

Associate Editor: Frontiers in Neuropharmacology
Associate Editor: Frontiers in Aging Neuroscience
Section Editor: Behavioral and Brain Functions
Ad hoc Reviewer: Journal of Neurophysiology; Neurobiology of Learning and Memory; Neurobiology of Aging; Neuropharmacology; Neuropsychopharmacology; Synapse; Life Sciences; NeuroReport; Depression and Anxiety; Pharmacology, Biochemistry and Behavior; European Journal of Pharmacology; European Neuropsychopharmacology; Mechanisms of Aging and Development; Alzheimer's Research & Therapy; Hippocampus; Neuroscience; Brain Research; Neuroscience Letters; PLOS One; Behavioral Brain Research, Aging Cell, Antioxidant & Redox Signaling, Molecular Neurobiology, Neuroscience and Biobehavioral Reviews, Journal of Neuroscience; eNeuro.

4. Honors

2007 Awarded travel grant by Southeast Neural Network, Wakula Spring, FL.
1997 Junior Scientist Award by ASIOA, FASEB, New Orleans, LA.
1993 Prof P.C. Dandiya Gold Medal for best paper presentation, Indian Pharmacological Society, Hissar

C. Contributions to Science

Overall, my research is dedicated for understanding the influence of age-related changes in cognition over the life span. Towards this goal, my research focus is to delineate mechanisms that contribute to memory deficits associated with advanced age and develop possible therapeutic interventions including upregulation of NMDA receptor function and anti-inflammatory agents that could possibly restore/reverse/ or ameliorate age/neurodegenerative diseases-induced impaired synaptic and cognitive function.

1. My research demonstrate that the mechanism for altered synaptic plasticity thresholds during aging is due to calcium dysregulation (i.e. the calcium dysregulation hypothesis for senescent synapses). The mechanisms involve a decrease in calcium influx through NMDA receptors and increased calcium release from internal calcium stores (see below). My work on NMDA receptor function indicates that oxidative stress during aging underlies a redox-mediated NMDA receptor hypofunction. Furthermore, the redox-mediated decline in NMDA receptor function emerges in middle age and correlates with cognitive impairments. These results challenge the current clinical concept of using NMDA receptor antagonists for therapeutic intervention for memory decline. Our recent results suggests a major role for GluN2B in redox-mediated regulation of NMDA receptor during aging.

    i) **Ashok Kumar**, J.S. Thinschmidt, and T.C. Foster, Subunit contribution of NMDA receptor hypofunction and redox sensitivity of hippocampal synaptic transmission during aging, *Aging, 11 (14) 5140-5157* (2019), PMID: 31339863.
    ii) **Ashok Kumar** and T.C. Foster, Linking redox regulation of NMDAR synaptic function to cognitive decline during aging, *Journal of Neuroscience*, 40, 15710-15715 (2013), PMID: 24089479.
    iii) **Ashok Kumar**, Rani, A., Scheinert, R.B., Ormerod, B.K., and Foster, T.C. Nonsteroidal anti-inflammatory drug, indomethacin improves spatial memory and NMDA receptor function in aged animals. *Neurobiology of Aging* 70, 184-193, (2018), PMID: 30031231.
    iv) M. Guidi, **Ashok Kumar**, and T.C. Foster, Impaired attention and synaptic senescence of the prefrontal cortex involves redox regulation of NMDA receptors, *Journal of Neuroscience,* 35 (9), 3966-3977 (2015), PMCID: PMID: 25740525.

2. My work helped to characterize age-related changes in synaptic plasticity, long-term potentiation (LTP) and long-term depression (LTD) in the hippocampus. This body of work highlights that age-related differences in these two major forms of synaptic plasticity are largely due to a shift in the threshold synaptic activity required for induction rather than a difference in asymptotic levels of LTP and LTD. As part of this research I have examined the effects of receptors (metabotropic and muscarinic) that modulate cell signaling to influence synaptic plasticity thresholds.

i) **Ashok Kumar** and T.C. Foster, Shift in induction mechanisms underlies an age-dependent increase in DHPG-induced synaptic depression at CA3-CA1 synapses, *Journal of Neurophysiology***,** 98, 2729-2736 (2007), PMID: 17898145.
ii) **Ashok Kumar**, J. S. Thinschmidt, T.C. Foster, and M.A. King, Aging effects on the limits and stability of long-term potentiation and depression in rat hippocampal area CA1, *Journal of Neurophysiology*, 98 (2), 594-601 (2007), PMID: 17553951.
iii) **Ashok Kumar**, Carbachol-induced long-term synaptic depression is enhanced during senescence at hippocampal CA3-CA1 synapses, *Journal of Neurophysiology*, 104 607-616 (2010), PMID: 20505129.
iv) **Ashok Kumar** and Thomas C Foster, Interaction of DHPG-LTD and synaptic-LTD at senescent CA3-CA1 hippocampal synapses, *Hippocampus*, 24 466-475 (2014), PMID: 24390964.

3. The age-related increase in calcium released from internal stores contributes to a decrease in hippocampal cell excitability. I have employed *in vitro* single cell recording techniques to demonstrate that aging is associated with an increase in the calcium-dependent potassium-mediated afterhyperpolarization in male and female rats. The afterhyperpolarization limits the cell excitability and NMDA receptor activation, which normally depends on depolarization of the cell. My work provides evidence that the age-associated increase in the afterhyperpolarization influences the threshold for synaptic plasticity and could contribute to impaired cognitive performance.
   i) **Ashok Kumar** and T.C. Foster, 17β-estradiol benzoate decreases AHP in CA1 pyramidal neurons, *Journal of Neurophysiology***,** 88, 621-626 (2002), PMID: 12163515.
   ii) **Ashok Kumar** and T.C. Foster, Enhanced long-term potentiation during aging is masked by processes involving intracellular calcium stores, *Journal of Neurophysiology*, 91, 2437-2444 (2004), PMID: 14762159.
   iii) **Ashok Kumar** and T.C. Foster, Intracellular calcium stores contribute to increased susceptibility to LTD induction during aging, *Brain Research*, 1031, 125-128 (2005), PMID: 15621020.
   iv) K. Bodhinathan, **Ashok Kumar**, and T. C. Foster, Intracellular redox state alters NMDA receptor response during aging through Ca2+/Calmodulin-dependent protein kinase II, *Journal of Neuroscience* 30 (5)1914-1924 (2010), PMID: 20130200.

4. I have considerable expertise employing an *in vitro* slice electrophysiology to examine age-related changes in synaptic function, cell excitability, and senescent neural physiology. My work was the first to demonstrate an age-associated enhancement in afterhyperpolarization (AHP) in female senescent rats and delineated the role of estrogen-mediated reduction of the AHP amplitude. Furthermore, our work demonstrated that viral vector-mediated upregulation of estrogen receptor alpha improves age-associated cognitive and synaptic function. More recently, we demonstrated contribution of estrogen receptor subtypes, ER alpha, ER beta, and GPER1 in rapid estradiol-mediated enhancement of hippocampal synaptic function.
   i) **Ashok Kumar** and T.C. Foster, 17 beta-estradiol benzoate decreases the AHP amplitude in CA1 pyramidal neurons, *Journal of Neurophysiology*, 88, 621-626 (2002), PMID: 12163515.
   ii) L. A. Bean, **Ashok Kumar,** A. Rani, Mike Guidi, A. M. Rosario, E. T. Golde, and T.C. Foster, Re-opening of the critical window for estrogen therapy, *Journal of Neuroscience*, 35 (49) 16077-93 (2015), PMID: 26658861.
   iii) **Ashok Kumar**, L.A. Bean, A. Rani, Travis Jackson, T.C. Foster, Contribution of estrogen receptor subtypes, ERalpha, ERbeta, and GPER1 in rapid estradiol-mediated enhancement of hippocampal synaptic transmission in mice, *Hippocampus*, 25 (12) 1556-1566 (2015), PMID: 25980457.

5. It is hypothesized that the shift in synaptic plasticity mediates a decline in hippocampal-dependent episodic memory. Therefore, I initiated a number of studies examining the effect of various treatments on relationship between synaptic plasticity and cognition during aging. Our results demonstrate that social interaction, exercise, and expression of antioxidant enzymes could improve the synaptic function and ameliorate the cognitive performance.
   i) **Ashok Kumar** and T.C. Foster, Environmental enrichment decreases the augmented hippocampal afterhyperpolarization in senescent rats, *Brain Research***,** 1130 (1) 103-107 (2007), PMID: 17169341.
   ii) **Ashok Kumar**, A. Rani, O. Tchigranova, W.H. Lee, and T.C. Foster, Influence of late-life exposure to environmental enrichment or exercise on hippocampal function and CA1 senescent physiology, *Neurobiology of Aging,* 33, 828.e1-828.e17 (2012), PMID: 21820213.

iii) W.H. Lee, **Ashok Kumar**, A. Rani, J. Herrera, and T.C. Foster, Influence of viral vector-mediated delivery of superoxide dismutase and catalase to the hippocampus on spatial learning and memory during aging, *Antioxidant and Redox Signaling, 16* (4) 339-350 (2012), PMID: 21942371.

iv) R.B. Speisman, **Ashok Kumar**, A. Rani, T.C. Foster and B. K. Ormerod, Daily exercise improves memory, stimulates hippocampal neurogenesis and modulates immune and neuroimmune cytokines in aging rats, *Brain, Behavior, and Immunity,* 28, 25-43 (2013), PMID: 23078985.

URL Link to Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/ashok.kumar.3/bibliography/public/

D. Research Support

Ongoing Research Support

NIH-NIA, RO1AG037984 (Dr. Tom Foster PI and Dr. Kumar PI) 09/01/2018 to 07/31/2023
Estrogen signaling and cognition over the lifespan
Examines estrogen effects on memory function and delaying brain aging through regulation of transcription via the α-estrogen receptor.

NIH-NIA, RO1AG052258 (Dr. Tom Foster PI, Dr. Kumar Co-I) 05/05/2016 to 04/30/2021
Examines effects peripheral inflammation on cognitive and synaptic function over the course of aging.
Overlap: None.

NIH-NIA, R21AG068205 (Dr. Kumar PI) 09/01/2020 to 04/30/2022
Age-associated impaired executive function: Rescue by NMDA receptor upregulation.
Overlap: None.

Recently Completed Research Support:

NIH-NIA, R37AG036800 (Dr. Tom Foster PI, Dr. Kumar Co-I) 09/01/2015 to 08/31/2019
The major goals of this project are to examine the hypothesis that age-related changes in NMDAR signaling mediate memory deficits and changes in synaptic plasticity.
Overlap: None.

NIH-NIA, R01AG049711 (Dr. Tom Foster PI, Dr. Kumar Co-I) 09/01/2015 to 04/30/2020
Examines effects viral-mediated induced peripheral inflammation on cognitive function and NMDA receptor mediated synaptic transmission over the life span.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Lamb, Damon

eRA COMMONS USER NAME (credential, e.g., agency login): dglamb

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
University of Maryland, College Park, MD	BS	05/2003	Mathematics
University of Maryland, College Park, MD	BS	12/2003	Computer Engineering
University of Chicago, Chicago, IL	MS	12/2005	Computer Science
Marine Biological Laboratory, Woods Hole, MA	N/A	07/2009	Neural Systems & Behavior
Emory University, Atlanta, GA	PHD	08/2013	Neuroscience

A. Personal Statement

My long-term goal is to bridge cutting edge basic science and clinical/treatment focused research. The goal of this research proposal is to improve our understanding of autonomic function and modulations of learning and memory. In particular, I am investigating transcutaneous vagal nerve stimulation (tVNS) as a novel treatment for amnestic mild cognitive impairment (aMCI) to enhance cognition both in healthy individuals as well as amnestic mild cognitive impairment. tVNS is an exciting approach based on our understanding of the neurophysiological basis of memory and cognitive function, as well as pilot data. I look forward to extending our knowledge of this mechanistic impact of this innovative tool, laying a foundation for future clinical applications. I also have DARPA funding to further elucidate the neural circuit impacted by vagal nerve stimulation, providing complementary animal model data for the development of this approach. Apropos the mission of the Cognitive Aging and Memory Clinical Translational Research Program, my funded work on novel potential preventative treatments for aMCI (i.e., prodromal Alzheimer's) continues to show translational promise.

B. Positions and Honors

Positions and Employment

2001 - 2001 Product Engineer, Hughes Network Systems
2001 - 2004 Research Software Developer, University of Iowa
2002 - 2004 Research Assistant, Institute for Research in Electronics and Applied Physics, University of Maryland, College Park
2003 - 2004 Acoustic Modeling Software Developer, Acoustic Design Ahnert
2004 - 2007 Data Analyst, Brain-Body Center, University of Illinois, Chicago
2007 - 2013 Graduate Student, Emory University
2013 - 2017 Research Health Science Specialist, Brain Rehabilitation Research Center, Malcom Randall VAMC
2013 - 2018 Assistant Professor, University of Florida Departments of Neurology, Aging & Geriatrics, Clinical and Health Psychology
2017 - Research Health Scientist, Brain Rehabilitation Research Center, Malcom Randal VAMC
2018 - Assistant Professor, University of Florida Departments of Psychiatry, Neuroscience, Biomedical Engineering

Other Experience and Professional Memberships

- Member, Society for Neuroscience
- Member, American Association for the Advancement of Science

Honors

2005	Faculty Commendation, University of Chicago Department of Computer Science
2007 - 2009	NSF IGERT: Hybrid Neural Microsystems Fellow, Georgia Tech & Emory University
2009	MBL Neural Systems and Behavior Fellow, Frank R. Lillie Fellowship and Scholarship
2009	Scholar, Burroughs Wellcome Fund
2011 - 2013	Research Partners Fellow, Howard Hughes Medical Institute

C. Contribution to Science

1. Vagus nerve stimulation modulation of central nervous system function: While vagus nerve stimulation is best known as a treatment of certain forms of epilepsy, there is a growing appreciation for vagus stimulation as a tool for manipulation of central nervous system plasticity and of autonomic function. We are developing our understanding of how to apply vagus nerve stimulation to modulate neuroplasticity and to ameliorate complex disorders such as PTSD across multiple large-scale research efforts funded by the VA, NIH and DARPA. A portion of this work has been patented by the University of Florida.

    a. Lamb DG, Porges EC, Lewis GF, Williamson JB. Non-invasive vagal nerve stimulation effects on hyperarousal and autonomic state in patients with posttraumatic stress disorder and history of mild traumatic brain injury: preliminary evidence. Frontiers in medicine. 2017 Jul 31;4:124.
    b. JB Williamson, DG Lamb, ESC Porges. System and method for monitoring and controlling nervous system behavior using autonomic features - US Patent US10426956B2, 2019

2. Computational modeling of neuronal networks demonstrating complex, unexpected relationships: Neurons can have widely differing intrinsic membrane properties, in particular the density of specific conductances (or resistance to ionic flow through ion channels), but how these contribute to characteristic neuronal activity or pattern formation is not well understood. My biophysical modeling work on small neuronal networks investigated how these ionic conductances contribute to coordinated motor output. Previous work had elucidated relationships between pairs of conductances, but they were generally required to be similar in their time courses, although of opposing polarity. My work showed that much more complex relationships contribute to the output of neuronal networks, as well as providing an explanation of the basis for these relationships. Outside of the novel modeling approaches and the combination of algorithmic optimization approaches, computational tools, and biological data I used, this work has implications for the variability of individual response to psychoactive medication, and follow-up studies are ongoing.

    a. Günay C, Doloc-Mihu A, Lamb DG, Calabrese RL. Synaptic Strengths Dominate Phasing of Motor Circuit: Intrinsic Conductances of Neuron Types Need Not Vary across Animals. eNeuro. 2019 Jul 18;6(4):ENEURO.0417-18.2019. doi: 10.1523/ENEURO.0417-18.2019. PMID: 31270128; PMCID: PMC6709225.
    b. Lamb DG, Calabrese RL. Correlated conductance parameters in leech heart motor neurons contribute to motor pattern formation. PLoS One. 2013;8(11):e79267. PubMed PMID: 24260181; PubMed Central PMCID: PMC3832487.
    c. Lamb DG, Calabrese RL. Small is beautiful: models of small neuronal networks. Curr Opin Neurobiol. 2012 Aug;22(4):670-5. PubMed PMID: 22364687; PubMed Central PMCID: PMC3817830.
    d. Lamb DG, Calabrese RL. Neural circuits controlling behavior and autonomic functions in medicinal leeches. Neural Syst Circuits. 2011 Sep 28;1(1):13. PubMed PMID: 22329853; PubMed Central PMCID: PMC3278399.

3. Experimental and data analysis software & hardware: Throughout my scientific career I have applied my technical skills to the design, development, and deployment of computer software and hardware to enable my own and other investigators' research. An example of the data processing tools I have developed is CardioEdit/CardioBatch, which allows efficient raw data processing and analysis of electrocardiogram signals for the extraction of heart rate variability measures, which are an index of autonomic nervous system function. I used these tools to conduct collaborative research with both animal and human biological psychology researchers, but they were also made freely available to the research community. As a testament to the utility of this software, over 65 papers cite using my software to process and analyze

their data. In 2000, I developed a multi-center data collection and aggregation tool that enabled distributed, offline collection of child abuse and maltreatment information collected by social workers, police, and researchers. This tool has been a critical tool for at least 18 papers, and the ideas enabling flexible aggregation of multi-site data have led to subsequent tools developed by other scientific programmers. More applicable to the proposed investigation, I also programmed and built the initial hardware for the Dynamic Affect Recognition Experiment, a test of receptive emotional perception.

a. Bal E, Harden E, Lamb D, Van Hecke AV, Denver JW, Porges SW. Emotion recognition in children with autism spectrum disorders: relations to eye gaze and autonomic state. J Autism Dev Disord. 2010 Mar;40(3):358-70. PubMed PMID: 19885725.
b. Vaughan Van Hecke A, Lebow J, Bal E, Lamb D, Harden E, Kramer A, Denver J, Bazhenova O, Porges SW. Electroencephalogram and heart rate regulation to familiar and unfamiliar people in children with autism spectrum disorders. Child Dev. 2009 Jul-Aug;80(4):1118-33. PubMed PMID: 19630897.
c. Grippo AJ, Lamb DG, Carter CS, Porges SW. Social isolation disrupts autonomic regulation of the heart and influences negative affective behaviors. Biol Psychiatry. 2007 Nov 15;62(10):1162-70. PubMed PMID: 17658486; PubMed Central PMCID: PMC2144909.
d. Grippo AJ, Lamb DG, Carter CS, Porges SW. Cardiac regulation in the socially monogamous prairie vole. Physiol Behav. 2007 Feb 28;90(2-3):386-93. PubMed PMID: 17107695; PubMed Central PMCID: PMC1839927.

4. Time-resolved particle-beam emittance: Early in my research career, I gathered the first time-resolved particle-beam emittance data. This experiment looked into how a 100ns charged particle beam varied along its length. Such a measurement was technically challenging at many levels, and the success of this experiment relied on two key control systems I programmed: one controlling the electro-magnetic focusing and bending optics, and the other an adaptive control system for the beam-measurement apparatus. The data and the functional measurement system that resulted from this work directly contributed to journal papers and referred conference papers, and enabled other researchers to investigate otherwise inaccessible research questions.

a. Walter M, Quinn B, Lamb D, Bernal S, Godlove T, Haber I, Holloway M, Kishek RA, Li H, O'Shea PG, Reiser M. Experimental tests of the injection Y on the University of Maryland Electron Ring. Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment. 2005 May 21; 544(1-2):374-377.
b. Bernal S, Beaudoin B, Cui Y, Glanzer M, Godlove TF, Harris J, Holloway M, Haber I, Kishek RA, Lee W, Lamb D, Quinn B, Quirus M, Reiser M, Valfells A, Walter M, Wilson M, Yun R, Zou Y, O'Shea PG. Intense beam transport experiments in a multi-bend system at the University of Maryland Electron Ring. Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment. 2004 February 21; 519(1-2):380-387.
c. Walter M, Lamb D, Bernal S, Haber I, Kishek R, Li H, Quinn B, Snowel M, Valfells A, Reiser M, O'Shea P. Time resolved emittance measurement in the University of Maryland Electron Ring. Proceedings of the 2003 Particle Accelerator Conference. Particle Accelerator Conference; 2003; c2003.
d. Walter M, Quinn B, Lamb D, Bernal S, Godlove T, Haber I, Holloway M, Kishek R, Li H, O'Shea P, Reiser M. Experimental tests of the injection Y on the University of Maryland Electron Ring. Proceedings of the 2003 Particle Accelerator Conference. Particle Accelerator Conference; 2003; c2003.

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

IK2RX002490, Veterans Health Administration – Rehabilitation Research and Development
Lamb, Damon (PI)
03/01/18-02/28/23
Brain changed underlying emotional and executive alterations in TBI

Role: PI

1R01DK123329, NIDDK
Campbell-Thompson, Martha (PI)
08/01/20-07/31/24
Understanding pancreatic endocrine and exocrine loss in pre-type 1 Diabetes
Role: Co-I

I01RX003140, Veterans Health Administration – Rehabilitation Research and Development
Williamson, John (PI)
10/01/19-09/30/23
Transcutaneous vagal nerve stimulation improvement of sleep quality in veterans with PTSD with or without history of mild TBI
Role: Co-I

I50RX003000, Veterans Health Administration – Rehabilitation Research and Development
Bauer, Rus (Director)
10/01/19-9/3/24
Brain Rehabilitation Research Center
Role: Center Investigator

R21AG054876, NIA
Williamson, John (PI)
08/31/17-5/31/19 (NCE)
Treatment of mild cognitive impairment with transcutaneous vagal nerve stimulation
Role: Co-I

12179085, DARPA
Otto, Kevin (Contact PI)
01/01/17-12/31/20
Targeted Neuroplasticity Training
Role: Co-PI

Completed Research Support

0217BRRC-04, Brain Rehabilitation Research Center - Veterans Health Administration
Lamb, Damon (PI)
01/01/18-7/01/19
tVNS impacts on sleep architecture and autonomic features
Role: MPI

Veterans Health Administration – Rehabilitation Research and Development
Daly, Janis (Director)
10/01/13-9/3/19
Brain Rehabilitation Research Center
Role: Center Investigator

1R56HL127175, NIH-NHLBI
Williamson, John (PI)

09/08/15-08/31/16
Brain and cognition effects of cardio-resynchronization therapy in heart failure
Role: Co-Investigator

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Maciel, Carolina

eRA COMMONS USER NAME: cmaciel

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	START DATE MM/YYYY	END DATE MM/YYYY	FIELD OF STUDY
Universidade Federal Fluminense, Niteroi, Rio de Janeiro	MD	08/2003	07/2009	Medicine
New York-Presbyterian Hospital, Weill Cornell Medical College, New York, NY	Resident	06/2010	06/2011	Internal Medicine
New York-Presbyterian Hospital & Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, New York, NY	Resident	07/2011	06/2014	Neurology
Yale-New Haven Hospital, New Haven, CT	Clinical Fellow	07/2014	06/2016	Neurocritical Care
Yale-New Haven Hospital, New Haven, CT	Clinical Fellow	07/2016	06/2017	Critical Care Electroencephalography
Medical University of South Carolina, Charleston, SC	MSCR	08/2017	05/2019	Master of Science in Clinical Research

A. Personal Statement

I am a triple board-certified neurologist with formal training in neurocritical care, electrophysiology, and clinical research. This combination of training is ideal for my niche of study, which includes the mechanisms of secondary brain injury and outcome prediction in acute neurologic injuries. As a diverse scholar selected by the American Academy of Neurology to receive the TRANSCENDS award as first cohort, I had the opportunity to complete formal training in clinical research and clinical trials through a Master of Science program under a comprehensive mentorship for career development. The program was fundamental to equip me with the resources (from mentoring to training) I needed to thrive in a competitive scientific environment, write successful grant applications and maintain my scholarly productivity. I will employ this experience to guide trainees during all steps of the scientific process in translational science, from study design to dissemination of findings—in compliance with national and international scientific guidelines. I hold volunteer faculty appointments in two other institutions (Yale and University of Utah), which facilitates recruitment of other sites in multicenter trials and expands the outreach of TRANSCENDS, opening doors to trainees across all phases of their career development.

1. Simpkins AN, Busl KM, Amorim E, Barnett-Tapia C, Cervenka MC, Dhakar MB, Etherton MR, Fung C, Griggs R, Holloway RG, Kelly AG, Khan IR, Lizarraga KJ, Madagan HG, Onweni CL, Mestre H, Rabinstein AA, Rubinos C, Dionisio-Santos DA, Youn TS, Merck LH, **Maciel CB.** Proceedings from the Neurotherapeutics Symposium on Neurological Emergencies: Shaping the Future of Neurocritical Care. Neurocrit Care. 2020 Dec;33(3):636-645. PMID: 32959201

2. **Maciel CB**, Morawo AO, Tsao CY, Youn TS, Labar DR, Rubens EO, Greer DM. SSEP in Therapeutic Hypothermia Era. J Clin Neurophysiol. 2017 Sep;34(5):469-475. PMID: 28557905

3. Owusu KA, Dhakar MB, Bautista C, McKimmy D, Cotugno S, Sukumar N, Deng Y, Farooque P, Hirsch LJ, **Maciel CB**. Comparison of intranasal midazolam versus intravenous lorazepam for seizure termination

and prevention of seizure clusters in the adult epilepsy monitoring unit. Epilepsy Behav. 2019 Jul 30;98(Pt A):161-167. PMID: 31374472

B. Positions and Honors

Positions and Employment

2009 - 2010	ICU hospitalist, Hospital das Clinicas Alameda, Niteroi, RJ, Brazil
2017 -	Assistant Professor of Neurology, University of Florida, Gainesville, FL
2017 -	Adjunct Assistant Professor of Neurology, Yale University, New Haven, CT
2018 -	Director of Research for Neurocritical Care, University of Florida, Gainesville, FL
2019 -	Assistant Professor of Neurosurgery, University of Florida, Gainesville, FL
2019 -	Adjunct Assistant Professor of Neurology, University of Utah, Salt Lake City, UT
2019 - 2019	Chair, Neurotherapeutics Symposium 2019 – Neurologic Emergencies, Rochester/NY
2020 -	Member, Steering Committee, University of Florida Brain Injury, Rehabilitation, and Neuroresilience Center
2020 -	Member, Steering Committee, University of Florida Breathing Research and Therapeutics Center

Professional Memberships

2009 -	Member, Brazilian Medical Association
2011 -	Member, American Academy of Neurology
2015 -	Member, Neurocritical Care Society
2016 - 2017	Member, American Epilepsy Society
2016 -	Member, American Clinical Neurophysiology Society
2018 -	Member, American Heart Association
2018 -	Member, Society of Critical Care Medicine
2018 -	Member, Fundamentals of Neurocritical Care Committee, Neurocritical Care Society
2018 -	Member, Latin American Brain Injury Consortium
2018-	Member, International Society for Cerebral Blood Flow
2019 -	Member, Critical Care EEG Monitoring Research Consortium
2019 -	Invited Member, Clinical Research Subcommittee, American Academy of Neurology
2020 -	Invited Member, Stroke Council Early Career Development Committee, American Heart Association

Editorial Positions

2015 -	Ad hoc reviewer, Neurology
2015 -	Ad hoc reviewer, Neurocritical Care
2015 -	Ad hoc reviewer, Stroke
2017 -	Ad hoc reviewer, JAMA Neurology
2017 -	Ad hoc reviewer, Journal of Critical Care Medicine
2017 -	Ad hoc abstract reviewer, International Stroke Conference
2018 -	Ad hoc reviewer, Journal of Clinical Hypertension
2018 -	Assistant editor for eNeurologicalSci
2018 -	Ad hoc abstract reviewer, Neurocritical Care Society
2019 -	Ad hoc abstract reviewer, Society of Critical Care Medicine, American Academy of Neurology
2020 -	Ad hoc reviewer, Critical Care Explorations, Epilepsia, European Journal of Neurology

Honors and Awards

2013	Alumni Council's Distinguished Housestaff Award, Weill Cornell Medical Center
2014	Neurology Resident Teaching Award, Weill Cornell Medical College
2017	TRANSCENDS - Training in Research for Academic Neurologists to Sustain Careers and Enhance the Numbers of Diverse Scholars, American Academy of Neurology

C. Contribution to Science

1. **Neurologic outcome prediction in cardiac arrest.** We demonstrated the practice variability in outcome prediction despite multiple available guidelines and the limited performance of national and international guidelines in predicting poor outcomes, with the European Society of Intensive Care Medicine guidelines outperforming American guidelines. In a single center cohort, we highlighted that rates of brain death vary depending on the etiology of cardiac arrest; a striking 43% of deaths following resuscitation of overdose related cardiac arrests are attributed to brain death versus 6% in arrests from other etiologies. We explored the distinct clinical and electrophysiologic profile differences in post-anoxic myoclonus and exposed further the false positive rates of this phenomenon in predicting poor outcomes, as several individuals achieved a good outcome despite having myoclonus post-cardiac arrest (which used to be considered pathognomonic of poor outcome). We confirmed the high predictive value of absent N20 peaks for a poor outcome prediction of unresponsive cardiac arrest survivors treated with therapeutic hypothermia. We emphasized the pitfalls of current neuroprognostic tools and the importance of employing an immaculate technique. Finally, we raised awareness about an easily identifiable radiologic sign on computed tomography associated with severe diffuse anoxic brain injury and high-risk to progression to brain death, which, when recognized promptly, may assist in the identification of patients who will not benefit from continued brain resuscitation, such as targeted temperature management.

    a. **Maciel CB,** Barden MM, Youn TS, Dhakar MB, Greer DM. Neuroprognostication Practices in Post-Cardiac Arrest Patients: An International Survey of Critical Care Providers. Critical Care Medicine 2020 Feb;48(2):e107-e114. PMID: 31939809
    b. Zhou SE, **Maciel CB**, Ormseth CH, Beekman R, Gilmore EJ, Greer DM. Distinct predictive values of current neuroprognostic guidelines in post-cardiac arrest patients. Resuscitation. 2019 Jun;139:343-350. PMID: 30951843
    c. Ormseth CH*, **Maciel CB***, Zhou SE, Barden MM, Miyares LC, Beekman RB, Gilmore EJ, Greer DM. Differential outcomes following successful resuscitation in cardiac arrest due to drug overdose. Resuscitation. 2019 Apr 6; 139:9-16. PMID: 30965094 ***co-first authorship**
    d. Dhakar MB, Sivaraju A, **Maciel CB**, Youn TS, Gaspard N, Greer DM, Hirsch LJ, Gilmore EJ. Electro-Clinical Characteristics and Prognostic Significance of Post-Anoxic Myoclonus. Resuscitation. 2018 Oct;131:114-120. PMID: 29964146.

2. **Improving survival and neurologic recovery after cardiac arrest.** We summarized recent evidence and provided practical advice for the management of cardiac arrest survivors with an emphasis on halting secondary brain injury to achieve improved outcomes. These articles are important for the broad dissemination of the scientific progress made in the field of neurologic resuscitation, critical for the improvement of outcomes in cardiac arrest survivors. I performed the entirety of a comprehensive literature review and drafted the manuscripts.

    a. **Maciel CB**, Livesay S, Greene K, Greer DG. Hypoxic Ischemic Encephalopathy in Adults. Neurocritical Care Live. The Neurocritical Care Society, 6, August 2018. Web. 9/12/2018 Accessed.
    b. **Maciel CB**, Barden MM, Greer DM. Neurologic Recovery After Cardiac Arrest: a Multifaceted Puzzle Requiring Comprehensive Coordinated Care. Curr Treat Options Cardiovasc Med. 2017 Jul;19(7):52. PMID: 28536893.

3. **Understanding the role of potentially harmful EEG patterns and seizures in neurocritical illness.** We unveiled the previously unapprised seizure risk associated with primary intraventricular hemorrhages and raised awareness for the need to maintain a high suspicion of seizures in this setting and employ continuous electroencephalography monitoring. We reviewed the evidence of EEG findings and its prognostic implications as well as current standardized nomenclature and recommendations on the role of seizure prophylaxis in different acute brain injuries. This experience with scientific writing has contributed significantly to my critical literature appraisal skills, which has positioned me to write my own grants to support novel projects.

a. Sheikh ZB, Stretz C, **Maciel CB**, Dhakar MB, Orgass H, Petroff OA, Hirsch LJ, Gilmore EJ. Deep Versus Lobar Intraparenchymal Hemorrhage: Seizures, Hyperexcitable Patterns, and Clinical Outcomes. Crit Care Med. 2020 Jun;48(6):e505-e513. PMID: 32301843
b. Stretz C, Sheikh Z, **Maciel CB**, Hirsch LJ, Gilmore EJ. Seizures, Periodic and Rhythmic Patterns in Primary Intraventricular Hemorrhage. Annals of Clinical and Translational Neurology. 2018 September; 5(9):1104-1111. PMID: 30250866
c. **Maciel CB**, Hirsch LJ. Definition and Classification of Periodic and Rhythmic Patterns. J Clin Neurophysiol. 2018 May;35(3):179-188. PMID: 29718827.
d. Gilmore EJ, **Maciel CB**, Hirsch LJ, Sheth KN. Review of the Utility of Prophylactic Anticonvulsant Use in Critically Ill Patients with Intracerebral Hemorrhage. Stroke. 2016 Oct;47(10):2666-72. PMID: 27608820.

Complete List of Publications in My Bibliography: https://www.ncbi.nlm.nih.gov/sites/myncbi/carolina.maciel.1/bibliography/42347042/public/?sort=date&direction=descending

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

Maciel, Carolina 1/1/2021-12/31/2022
AMERICAN HEART ASSOCIATION 20IPA35380013 – Innovative Project Award
Early intervention augmenting GABA-ergic pathways: The VIGAB-STAT - VIGABatrin in post-anoxic STATus epilepticus
Role: PI. The goal of this project is to evaluate the feasibility of early GABA transaminase inhibition as adjunctive treatment for post-anoxic status epilepticus and characterize the pharmacokinetics of vigabatrin absorption in the post-cardiac arrest period.

Maciel, Carolina 4/1/2019-3/31/2021
CLAUDE D. PEPPER OLDER AMERICANS INDEPENDENCE CENTER AWD01736 – Junior Scholar Award and Pilot Grant
Brain Tsunamis After Cardiac Arrest and Microcirculatory Failure in Aging Brains
Role: PI. The goal of this project is to utilize neurophotonics to characterize the role of spreading depolarizations as primary and secondary brain injury mechanisms and outline the impact of aging on tissue responses to this phenomenon in rodents.

Completed Research Support

Maciel, Carolina 4/15/2019-4/14/2020
NINDS R13NS111956
Neurotherapeutics Symposium 2019 – Neurotherapeutics Symposium 2019 – accelerating the pace of translation in neurological emergencies by enhancing diverse workforce in neuroscience and promoting transdisciplinary team science.
Role: PI. The goal of this two-day conference is to promote new lines of research in neurocritical care, thereby stimulating advances in the evaluation and management of acute neurologic disorders. The Neurotherapeutics Symposium will facilitate the dissemination of new findings across overlapping scientific areas and promote longstanding transdisciplinary team science while using digital technology to nurture productive collaborations.

Maciel, Carolina 7/1/2018-7/1/2019
Departmental Funds – Neurology Department – New faculty package
Spreading depolarization in hypoxic-ischemic brain injury: a potential mechanism of secondary brain injury related to microcirculatory failure
Role: PI. The goal of this project is to utilize optic intrinsic signal imaging to characterize the occurrence and impact of spreading depolarizations in the early post-resuscitation period in a rodent model of cardiac arrest.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.

Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: MAURER, ANDREW

eRA COMMONS USER NAME (agency login): DREWMAURER

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Pittsburgh, Pittsburgh, PA	BS	12/2003	Neuroscience
University of Arizona, Tucson, AZ	PHD	12/2009	Neuroscience
University of Arizona, Tucson, AZ	Postdoctoral Fellow	06/2014	Neurobiology of Aging

A. PERSONAL STATEMENT

Throughout my scientific career, I have been focused on trying to understand the role of oscillations in shaping higher-cognitive processes. As a graduate student, I worked with Dr. Bruce McNaughton, acquiring skills in the acquisition and analysis of high-density single-unit electrophysiological recordings from awake-behaving rats. Much of my research focus was on combining neuron spiking data with local-field potentials in order to determine how spike timing is altered as a consequence of both location and time (i.e., theta phase precession). This research track was extended under the supervision of Dr. Carol A. Barnes, in which I continued to develop and implement high-level analyses to reveal novel computations of the CA1 subregion of the hippocampus (ref 1). This expertise will be applied to the analysis of oscillatory data to quantify hippocampal-prefrontal cortical circuit engagement in relation to higher cognitive function. Dr. Burke and I have 15 years of productive collaboration and I am excited to extend our research in the current proposal "*Preclinical Assays of Hippocampal-Prefrontal Cortical Circuit Engagement for Application in Therapeutic Development*."

After relocating to the University of Florida, where there is an active research focus on the neurobiology and cognition, I have become interested in the interactions across large networks of neurons in support of learning and memory and the role that oscillations play in governing neural computation. This continuing effort has yielded multiple network analytic papers from anatomical tracing and immediate early gene (ref 2) and single units (ref 3) as well as higher-order spectral analyses on continuous time-series data (ref 4) – all of which will prove useful in moving towards our goal of understanding information propagation in the brain.

1. **Maurer AP**, Lester AW, Burke SN, Ferng JJ, Barnes CA. Back to the future: preserved hippocampal network activity during reverse ambulation. J Neurosci. 2014 Nov 5;34(45):15022-31. PubMed PMID: 25378167; PubMed Central PMCID: PMC4220031.
2. **Maurer AP**, Johnson SA, Hernandez AR, Reasor J, Cossio DM, Fertal KE, Mizell JM, Lubke KN, Clark BJ, Burke SN. Age-related Changes in Lateral Entorhinal and CA3 Neuron Allocation Predict Poor Performance on Object Discrimination. Front Syst Neurosci. 2017 Jun 30;11:49. doi: 10.3389/fnsys.2017.00049. eCollection 2017. PMID: 28713251; PMCID: PMC5491840
3. **Maurer AP**, Burke SN, Diba K, Barnes CA. Attenuated Activity across Multiple Cell Types and Reduced Monosynaptic Connectivity in the Aged Perirhinal Cortex. J Neurosci. 2017 Sep 13;37(37):8965-8974. doi: 10.1523/JNEUROSCI.0531-17.2017. Epub 2017 Aug 11. PMID: 28821661; PMCID: In progress
4. Sheremet A, Burke SN, **Maurer AP**. Movement Enhances the Nonlinearity of Hippocampal Theta. J Neurosci. 2016 Apr 13;36(15):4218-30. doi: 10.1523/JNEUROSCI.3564-15.2016. PMID: 27076421 PMCID: PMC4829647

B. POSITIONS AND HONORS

Positions and Employment

2002 – 2004	Undergraduate Research Assistant, Dr. Bill Yates' Vestibular Research laboratory (U of Pitt), Pittsburgh, PA
2004 – 2008	Graduate Research Associate , Dr. Bruce McNaughton's Neural Systems, Memory and Aging Laboratory (U of Arizona), Tucson, AZ
2005 – 2006	Graduate Teaching Assistant, Course- "Memory mechanisms & Neural Computation", Tucson, AZ
2009 – 2014	Postdoctoral Research Fellow, Evelyn F. McKnight Brain Institute with Dr. Carol Barnes, Tucson, AZ
2014 -	Affiliate faculty member, Department of Biomedical Engineering, University of Florida, Gainesville, FL
2014 -	Assistant Professor, Department of Neuroscience, University of Florida, Gainesville , FL

Other Experience and Professional Memberships

2002 -	Member, Society for Neuroscience
2014 -	North Central Florida Chapter of the Society for Neuroscience

Honors

2003	Cum Laude, Unviersity of Pittsburgh
2007	Recipient of Conference Travel Award , Society for Neuroscience
2008	Recipient of the D.B. Marquis Behavioral Neuroscience Award, Behavioral Neuroscience Journal
2011	Recipient of the Ruth L. Kirschstein National Research Service Award, National Institute of Health

C. Contribution to Science

1. Prior to my thesis research, only two studies investigated hippocampal dynamics in the posterior/ventral region of the hippocampus. Therefore, I sought out to determine the firing rate characteristics of neurons in the intermediate portion of the hippocampus compared to the dorsal. We found that place field size was larger in more posterior regions, associated with a decreased rate of phase precession and a decreased sensitivity to velocity.
   a. Maurer AP, Vanrhoads SR, Sutherland GR, Lipa P, McNaughton BL. Self-motion and the origin of differential spatial scaling along the septo-temporal axis of the hippocampus. Hippocampus. 2005;15(7):841-52. PubMed PMID: 16145692.
   b. Maurer AP, Cowen SL, Burke SN, Barnes CA, McNaughton BL. Organization of hippocampal cell assemblies based on theta phase precession. Hippocampus. 2006;16(9):785-94. PubMed PMID: 16921501.
   c. Maurer AP, Cowen SL, Burke SN, Barnes CA, McNaughton BL. Phase precession in hippocampal interneurons showing strong functional coupling to individual pyramidal cells. J Neurosci. 2006 Dec 27;26(52):13485-92. PubMed PMID: 17192431.

2. Theta phase precession has long been thought to be a mechanism by which the brain temporally organizes events in order to facilitate learning and memory. The basic neuronal mechanisms, from ion channels to network dynamics governing this phenomenon, however, are not well understood. In order to elaborate and test the models of theta phase precession, I designed an experiment in which we trained rats to ambulate backwards, thereby, dissociating self-motion from head direction. These data support a view that head-direction input in not critical for theta phase precession.
   a. Maurer AP, McNaughton BL. Network and intrinsic cellular mechanisms underlying theta phase precession of hippocampal neurons. Trends Neurosci. 2007 Jul;30(7):325-33. PubMed PMID: 17532482.

b. Maurer AP, Lester AW, Burke SN, Ferng JJ, Barnes CA. Back to the future: preserved hippocampal network activity during reverse ambulation. J Neurosci. 2014 Nov 5;34(45):15022-31. PubMed PMID: 25378167; PubMed Central PMCID: PMC4220031.

3. One of the prominent characteristics of hippocampal pyramidal cell activity is their firing correlates with short-term predictions of future locations. Of course ambulatory characteristics will modulate both the future location and the distance covered. We have determined how ambulation alters firing patterns as well as tested models of hippocampal updating by training rodents to walk backwards on a linear track and found that when rodents walk backwards, hippocampal activity patterns continue to predict future locations regardless of head direction.
   a. Maurer AP, Burke SN, Lipa P, Skaggs WE, Barnes CA. Greater running speeds result in altered hippocampal phase sequence dynamics. Hippocampus. 2012 Apr;22(4):737-47. PubMed PMID: 21538659; PubMed Central PMCID: PMC3367321.
   b. Maurer AP, Lester AW, Burke SN, Ferng JJ, Barnes CA. Back to the future: preserved hippocampal network activity during reverse ambulation. J Neurosci. 2014 Nov 5;34(45):15022-31. PubMed PMID: 25378167; PubMed Central PMCID: PMC4220031.
4. While the size of hippocampal spatial receptive fields increases along the dorsal to ventral longitudinal axis, we asked the additional question on whether non-spatial factors could influence the firing rate charachteristics. By placing objects on the track, we showed that the spatial metric of hippocampal receptive fields can be reduced. This work produced new insights regarding the impact of sensory information along the hippocampal longitudinal axis and highlights the productive collaborative efforts of Dr. Burke and myself.
   a. Burke SN, Maurer AP, Nematollahi S, Uprety AR, Wallace JL, et al. The influence of objects on place field expression and size in distal hippocampal CA1. Hippocampus. 2011 Jul;21(7):783-801. PubMed PMID: 21365714; PubMed Central PMCID: PMC3314262.
   b. Burke SN, Maurer AP, Hartzell AL, Nematollahi S, Uprety A, et al. Representation of three-dimensional objects by the rat perirhinal cortex. Hippocampus. 2012 Oct;22(10):2032-44. PubMed PMID: 22987680; PubMed Central PMCID: PMC3447635.
   c. Burke SN, Maurer AP, Nematollahi S, Uprety A, Wallace JL, et al. Advanced age dissociates dual functions of the perirhinal cortex. J Neurosci. 2014 Jan 8;34(2):467-80. PubMed PMID: 24403147; PubMed Central PMCID: PMC3870932.
5. Interneurons have been hypothesized to provide the "scaffold" by which neuronal activity is structured within neural networks. In this sense, they can both govern the rate that information propagates through neural circuits as well as perform computational operations on the information. In light of these theories, we were enthusiastic to discover that putative basket cells exhibted theta phase precession, plausibly inherited from afferent pyramidal cell activity.
   a. Maurer AP, Cowen SL, Burke SN, Barnes CA, McNaughton BL. Phase precession in hippocampal interneurons showing strong functional coupling to individual pyramidal cells. J Neurosci. 2006 Dec 27;26(52):13485-92. PubMed PMID: 17192431.

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/myncbi/andrew.maurer.1/bibliography/43942059/public/?sort=date&direction=ascending

D. RESEARCH SUPPORT

2016/01/01-2020/11/31

1**R01**AG049722, NIH - National Institute on Aging

Burke, Sara (PI), **Maurer, Andrew** (Co-I)

Contribution of Declines in Functional Connectivity to Cognitive Aging.

The major goal of this proposal is to interrogate prefrontal-medial temporal lobe interactions in order to determine how alterations in systems-level neural coordination in old animals produce cognitive impairments.

[No Overlap]

10% effort

2016/09/01-2021/8/31

1**R01**MH109548, NIH- National Institute of Mental Health

Maurer, Andrew (PI)

Testing and forecasting hippocampal theta wave propagation in learning and memory.

The goal of this proposal is to determine the biological underpinnings of the hippocampal traveling theta wave as well as develop a mathematical description that can anticipate ("forecast") the physiology in ventral locations using dorsal physiology.

[No Overlap]

24% effort

04/01/2017 - 03/31/2022

1**R01**AG055544, NIH - National Institute on Aging

Maurer, Andrew (PI)

Age-associated changes in hippocampal circuits and cognitive function.

The proposed research is relevant to public health because it provides an innovative approach for determining if age-related changes in the hippocampal circuit reflect adaptive plasticity or synaptic senescence. This will be achieved by linking local changes to overall synaptic function of hippocampal circuits. By understanding how local impairments alter systems-level network function, it will be possible to promote the development of interventions that broadly improve cognition in normal aging and Alzheimer's disease and meet a mission of the NIA to advance our understanding of age-related cognitive decline.

[No Overlap]

13% effort

09/01/18-07/01/23

R**01**NS071122, NIH – National Institute of Neurological Disorders and Stroke

Khoshbouei, Habibeh (PI)

Alpha-synuclein Regulates Dopamine Transporter Functions

Thee long-term goal of this study is to determine how dopamine transporter dysfunction following alpha-synuclein overexpression disrupts neuronal and network function, prior to cell loss.

[No Overlap]

10% effort

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Porges, Eric

eRA COMMONS USER NAME (credential, e.g., agency login): eporges

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Hampshire College, Amherst, MA	BA	01/2004	Cognitive Science
University of Chicago, Chicago, IL	MA	09/2012	Neuroscience
University of Chicago, Chicago, Illinois	PHD	08/2013	Neuroscience
University of Florida, Gainesville, FL	Postdoctoral Fellow	12/2015	Neuroscience

A. Personal Statement

Dr. Porges is currently an Assistant Professor in the Department of Clinical and Health Psychology at the University of Florida, a member of the Center for Cognitive Aging and Memory, an investigator on many ongoing studies of cognitive aging, and PI of an NIH K01 grant exploring cognitive and neurophysiological consequences of heavy drinking in people living with HIV. He has collaborated with Drs. Williamson and Lamb for over 6 years on a program of research employing transcutaneous vagal nerve stimulation (tVNS) in the context of PTSD and other anxiety spectrum disorders. He has expertise in the collection, analysis and interpretation of autonomic psychophysiological data in both laboratory and ecological ambulatory environments. He uses these methods to explore individual differences in central and peripheral response to stressors, with an emphasis on the ANS as a modulator of these responses. He has been integral in the development and implementation of transcutaneous vagal nerve stimulation (tVNS) at the University of Florida. He has been awarded an NIH/NIA R21 with Drs. Williamson (PI) and Lamb for the development of tVNS methodology in a mild cognitive impairment cohort, and recently was notified that a Veterans Administration Merit (R01 equivariant) would be funded supporting further application of tVNS in PTSD (Williamson PI). He has extensive experience in the design, collection, analysis and interpretation of Magnetic Resonance Imaging data, specifically fMRI, MRI, GABA MRS & DTI. For three years, he has served on the planning committee for the International Symposium on MR Spectroscopy of GABA and has hosted subsections, including those focused on GABA MRS in specific populations (e.g. aging). His doctoral training was in the field of Integrative Neuroscience, and was completed at the University of Chicago under the mentorship of Dr. Jean Decety.

1. Porges EC, Woods AJ, Edden RA, Puts NA, Harris AD, Chen H, Garcia AM, Seider TR, Lamb DG, Williamson JB, Cohen RA. Frontal Gamma-Aminobutyric Acid Concentrations Are Associated With Cognitive Performance in Older Adults. Biol Psychiatry Cogn Neurosci Neuroimaging. 2017 Jan;2(1):38-44. PubMed PMID: 28217759; PubMed Central PMCID: PMC5312683.

2. Cruz-Almeida Y, Porges E. Additional considerations for studying brain metabolite levels across pain conditions using proton magnetic resonance spectroscopy. Neuroimage. 2020 Sep 22;224:117392. PubMed PMID: 32971265.

3. Lamb DG, Porges EC, Lewis GF, Williamson JB. Non-invasive Vagal Nerve Stimulation Effects on Hyperarousal and Autonomic State in Patients with Posttraumatic Stress Disorder and History of Mild Traumatic Brain Injury: Preliminary Evidence. Front Med (Lausanne). 2017;4:124. PubMed PMID: 28824913; PubMed Central PMCID: PMC5534856.

4. Porges EC, Woods AJ, Lamb DG, Williamson JB, Cohen RA, Edden RAE, Harris AD. Impact of tissue correction strategy on GABA-edited MRS findings. Neuroimage. 2017 Nov 15;162:249-256. PubMed PMID: 28882635; PubMed Central PMCID: PMC5705271.

B. Positions and Honors

Positions and Employment

1999 - 2002	Emergency Medical Technician, Hampshire College Emergency Medical Services, Amherst, MA
2001 - 2002	Director of Hampshire College Emergency Medical Services, Hampshire College Emergency Medical Services, Amherst, MA
2002 - 2002	Project Manager, Greenleaf Medical, Palo Alto, CA
2003 - 2003	Intern, Beckman Institute for Advanced Science and Technology, University of Illinois at Urbana-Champaign, Urbana, IL
2004 - 2005	Research Coordinator , University of Illinois at Chicago, Chicago, IL
2006 - 2008	Lab Manager, Social Cognitive Neuroscience Lab, University of Chicago, Chicago, IL
2008 - 2013	Graduate Student, Integrative Neuroscience program, Department of Psychology, University of Chicago, Chicago, IL
2013 - 2015	Postdoctoral Associate, Center for Cognitive Aging and Memory, Institute on Aging, Department of Aging and Geriatric Research, University of Florida, Gainesville, FL
2016 -	Assistant Professor, Center for Cognitive Aging and Memory, Department of Clinical and Health Psychology, College of Public Health and Health Professions, University of Florida, Gainesville, FL

Other Experience and Professional Memberships

-	Ad Hoc Reviewer, Neuroimage
2010 -	Member, Society for Neuroscience
2011 -	Ad Hoc Reviewer, International Journal Psychophysiology
2011 -	Member, Society for Social Neuroscience
2012 -	Member, Cognitive Neuroscience Society
2012 -	Member, Society for Psychophysiological Research
2012 -	Social Neuroscience, Ad Hoc Reviewer
2013 -	Ad Hoc Reviewer, Developmental Review
2014 -	Review Editorial Board, Frontiers in Psychology; Emotion Science
2015 -	Review Editorial Board, Frontiers in Psychology, section Psychology for Clinical Settings
2015 -	Ad Hoc Reviewer, Experimental Gerontology

Honors

2010	Norman Henry Anderson Award, Department of Psychology at the University of Chicago
2011	Research Award, University of Chicago Psychology graduate student organization
2011	Norman Henry Anderson Award, Department of Psychology at the University of Chicago
2012	Student Poster Award, Society for Psychophysiological Research
2012	Travel Award, University of Chicago Psychology graduate student organization
2012	Norman Henry Anderson Award, Department of Psychology at the University of Chicago
2016	CTSA Institutional K Scholar, University of Florida

C. Contribution to Science

1. Neurocognitive aging: Neurochemical and anatomical changes that are protected by social behaviors are associated with changes in GABA concentrations and accelerated by physiological challenges such as HIV. My research has developed a theoretical framework to explain and predict these associated changes. Below are examples of recent work that investigates cognitive aging in a healthy aging cohort and an HIV+ population.

    a. Porges EC, Woods AJ, Edden RA, Puts NA, Harris AD, Chen H, Garcia AM, Seider TR, Lamb DG, Williamson JB, Cohen RA. Frontal Gamma-Aminobutyric Acid Concentrations Are Associated With

Cognitive Performance in Older Adults. Biol Psychiatry Cogn Neurosci Neuroimaging. 2017 Jan;2(1):38-44. PubMed PMID: 28217759; PubMed Central PMCID: PMC5312683.

b. Ebner NC, Chen H, Porges E, Lin T, Fischer H, Feifel D, Cohen RA. Oxytocin's effect on resting-state functional connectivity varies by age and sex. Psychoneuroendocrinology. 2016 Jul;69:50-9. PubMed PMID: 27032063; PubMed Central PMCID: PMC4942126.

c. Seider TR, Gongvatana A, Woods AJ, Chen H, Porges EC, Cummings T, Correia S, Tashima K, Cohen RA. Age exacerbates HIV-associated white matter abnormalities. J Neurovirol. 2016 Apr;22(2):201-12. PubMed PMID: 26446690; PubMed Central PMCID: PMC4783252.

d. Woods AJ, Porges EC, Bryant VE, Seider T, Gongvatana A, Kahler CW, de la Monte S, Monti PM, Cohen RA. Current Heavy Alcohol Consumption is Associated with Greater Cognitive Impairment in Older Adults. Alcohol Clin Exp Res. 2016 Nov;40(11):2435-2444. PubMed PMID: 27658235; PubMed Central PMCID: PMC5113749.

2. GABA MRS and advanced neuroimaging: Dr. Porges has over 6 years of experience with GABA MRS data collection and analysis methods. He currently is PI of an NIH grant (NIAAA) focused on the application of GABA MRS in clinical populations, and has in the past and continues to collaborate with many groups. His work has demonstrated the relationship of frontal cortical GABA, as measured with MRS to cognitive function, as well as the gradual age-related decrease of cortical GABA. He has demonstrated the impact that various tissue correction strategies have on the relationship of GABA to age and their comparatively smaller impact on the relationship of frontal cortical GABA to cognition. Dr. Porges served as a beta tester and developer of GABA MRS protocols and has provided contributions to Dr. Richard Edden's GABA MRS analysis software package (GANNET). Ongoing projects of Drs. Porges' employ GABA MRS in diverse populations including people living with HIV, chronic pain and aging. In addition to his GABA MRS work, Dr. Porges' has used novel applications of advanced multimodal imaging methods. This work has including specific and unique functional connectivity from amygdala sub-nuclei to cortical targets that are predicted by psychopathic traits.

a. Porges EC, Woods AJ, Lamb DG, Williamson JB, Cohen RA, Edden RAE, Harris AD. Impact of tissue correction strategy on GABA-edited MRS findings. Neuroimage. 2017 Nov 15;162:249-256. PubMed PMID: 28882635; PubMed Central PMCID: PMC5705271.

b. Cruz-Almeida Y, Porges E. Additional considerations for studying brain metabolite levels across pain conditions using proton magnetic resonance spectroscopy. Neuroimage. 2020 Sep 22;224:117392. PubMed PMID: 32971265.

c. Porges EC, Woods AJ, Edden RA, Puts NA, Harris AD, Chen H, Garcia AM, Seider TR, Lamb DG, Williamson JB, Cohen RA. Frontal Gamma-Aminobutyric Acid Concentrations Are Associated With Cognitive Performance in Older Adults. Biol Psychiatry Cogn Neurosci Neuroimaging. 2017 Jan;2(1):38-44. PubMed PMID: 28217759; PubMed Central PMCID: PMC5312683.

d. Yoder KJ, Porges EC, Decety J. Amygdala subnuclei connectivity in response to violence reveals unique influences of individual differences in psychopathic traits in a nonforensic sample. Hum Brain Mapp. 2015 Apr;36(4):1417-28. PubMed PMID: 25557777; PubMed Central PMCID: PMC4837469.

3. Neuroendocrine function: Neuroendocrine functions related to individual variability in response to stressors, including high-intensity social stimuli, can impact the quality of interpersonal relationships and health outcomes. At the extremes, these differences can lead to interpersonal conflict or the strengthening of social bonds. I have had a long-term interest in exploring central and peripheral physiological predictors (e.g., autonomic activity and endocrine measures) of individual differences in response to high-intensity stimuli (e.g., violence and parental interaction). I have used salivary and blood for hormone assays, including cortisol. Note: Smith and Porges are co-first authors on "Oxytocin receptor gene variation predicts empathic concern and autonomic arousal while perceiving harm to others."

a. Porges EC, Smith KE, Decety J. Individual differences in vagal regulation are related to testosterone responses to observed violence. Front Psychol. 2015;6:19. PubMed PMID: 25759673; PubMed Central PMCID: PMC4338751.

b. Carter CS, Porges EC. Parenthood, stress, and the brain. Biol Psychiatry. 2011 Nov 1;70(9):804-5. PubMed PMID: 21986092.

c. Ebner NC, Chen H, Porges E, Lin T, Fischer H, Feifel D, Cohen RA. Oxytocin's effect on resting-state functional connectivity varies by age and sex. Psychoneuroendocrinology. 2016 Jul;69:50-9. PubMed PMID: 27032063; PubMed Central PMCID: PMC4942126.

d. Smith KE, Porges EC, Norman GJ, Connelly JJ, Decety J. Oxytocin receptor gene variation predicts empathic concern and autonomic arousal while perceiving harm to others. Soc Neurosci. 2014 Feb;9(1):1-9. PubMed PMID: 24295535; PubMed Central PMCID: PMC3923324.

4. Patients with TBI often develop Post-Traumatic Stress Disorder (PTSD). This syndrome, defined and diagnosed by psychological and behavioral features, is associated with symptoms such as anxiety, anger, increased arousal, and vigilance, as well as flashbacks and nightmares. Several of the symptoms observed in PTSD may be in part the result of altered autonomic nervous system (ANS) activity in response to psychological and physical challenges. Brain imaging has documented that TBI often induces white matter damage to pathways associated with the anterior limb of the internal capsule and uncinate fasciculus. Since these white matter structures link neocortical networks with subcortical and limbic structures that regulate autonomic control centers, injury to these pathways may induce a loss of inhibitory control of the ANS. Our work suggests that TBI-induced damage to networks that regulate the ANS increase vulnerability to PTSD. This provides the possibility that vulnerability to PTSD can be measured in patients with TBI.

   a. Lamb DG, Porges EC, Lewis GF, Williamson JB. Non-invasive Vagal Nerve Stimulation Effects on Hyperarousal and Autonomic State in Patients with Posttraumatic Stress Disorder and History of Mild Traumatic Brain Injury: Preliminary Evidence. Front Med (Lausanne). 2017;4:124. PubMed PMID: 28824913; PubMed Central PMCID: PMC5534856.

   b. Williamson JB, Porges EC, Lamb DG, Porges SW. Maladaptive autonomic regulation in PTSD accelerates physiological aging. Front Psychol. 2014;5:1571. PubMed PMID: 25653631; PubMed Central PMCID: PMC4300857.

   c. Falchook AD, Porges EC, Nadeau SE, Leon SA, Williamson JB, Heilman KM. Cognitive-motor dysfunction after severe traumatic brain injury: A cerebral interhemispheric disconnection syndrome. J Clin Exp Neuropsychol. 2015;37(10):1062-73. PubMed PMID: 26340588.

   d. Williamson JB, Heilman KM, Porges EC, Lamb DG, Porges SW. A possible mechanism for PTSD symptoms in patients with traumatic brain injury: central autonomic network disruption. Front Neuroeng. 2013 Dec 19;6:13. PubMed PMID: 24391583; PubMed Central PMCID: PMC3867662.

5. Individual differences in central and peripheral nervous system response to violent stimuli: Violence is a salient stimulus and an important environmental signal with survival consequences, conveying information about potential threats to personal health and safety. This research employed a multilevel approach to identify features that contribute to individual differences in peripheral and central physiological responses to observed violence. Studies (a) and (b) employed behavioral manipulations that altered the within-subject relationship to violent stimuli. Study (c) employed functional connectivity analyses of brain imaging data and demonstrated that the modulation of neurophysiological recruitment of specific brain areas was related to individual differences in subjective appraisals. Study (d) employed measures of peripheral physiology to demonstrate an inverse relationship between parasympathetic tone and testosterone release to observed violence, demonstrating the influence of autonomic regulation on physiological response to external stimuli. The work presented here demonstrates across different methods that individual responses to observed violence can be predicted by preexisting traits and manipulated by altering a participant's relationship to the stimuli.

   a. Yoder KJ, Porges EC, Decety J. Amygdala subnuclei connectivity in response to violence reveals unique influences of individual differences in psychopathic traits in a nonforensic sample. Hum Brain Mapp. 2015 Apr;36(4):1417-28. PubMed PMID: 25557777; PubMed Central PMCID: PMC4837469.

   b. Smith KE, Porges EC, Norman GJ, Connelly JJ, Decety J. Oxytocin receptor gene variation predicts empathic concern and autonomic arousal while perceiving harm to others. Soc Neurosci. 2014 Feb;9(1):1-9. PubMed PMID: 24295535; PubMed Central PMCID: PMC3923324.

   c. Porges EC, Decety J. Violence as a source of pleasure or displeasure is associated with specific functional connectivity with the nucleus accumbens. Front Hum Neurosci. 2013;7:447. PubMed PMID: 23964226; PubMed Central PMCID: PMC3741555.

d. Lamm C, Porges EC, Cacioppo JT, Decety J. Perspective taking is associated with specific facial responses during empathy for pain. Brain Res. 2008 Aug 28;1227:153-61. PubMed PMID: 18619426.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/eric.porges.1/bibliography/public/

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

K01 AA025306-01A1, NIH/NIAAA
Porges, Eric (PI) 2017-2022
Cognitive and functional deficits associated with reduced cortical GABA in HIV-infected heavy drinkers.
This project will investigate important hypotheses regarding the relationship between regional cerebral GABA concentrations and cognitive flexibility in HIV+ heavy drinkers.
Role: PI

NIH R21AG054876 2017-2020
Williamson, John (PI)
Treatment of mild cognitive impairment with transcutaneous vagal nerve stimulation (tVNS).
The goal of this funding is to determine if tVNS can enhance cognitive performance during stimulation in patients with amnestic mild cognitive impairment and whether structural changes in brain regions relevant for memory encoding (e.g., hippocampus) predict response. Acute tVNS induced changes to GABA+, measured via edited MRS, is a component of this protocol.
Role: Co-I

Center for Cognitive Aging and Memory (CAM), McKnight Brain Research Foundation
Porges, Eric (PI) 09/01/18-ongoing
CAM Pilot Study: Attentive Brain Study
This study complements the above R21, enrolling a cognitively intact, normal aging cohort. The goal of this study is to explore the acute consequences of transcutaneous vagal nerve stimulation (tVNS) on memory, as well as functional connectivity (fMRI), and neurometabolite (MRS) in this population.
Role: PI

R01AG054077-04, NIH/NIA
Woods, Adam (PI) 2016-2021
This randomized clinical trial examines the effect of augmenting cognitive training with transcranial direct current stimulation (TDCS) to maximize cognitive and functional outcomes older adults experiencing age-related cognitive decline. Change in well-validated measures of everyday abilities and neurocognitive function will serve as outcome measures. Functional and structural neuroimaging biomarkers of neural plasticity and learning (fMRI, GABA MRS, etc.) will measure intervention-associated alterations in specific brain regions impacted by cognitive aging.
Role: CO-I

NIH R01DK123329 2020-2024
Campbell-Thompson, Martha (PI)
Understanding pancreatic endocrine and exocrine loss in pre-type 1 diabetes.
Recent data suggest that first-degree relatives of patients with T1D have a smaller pancreas than control subjects, including those without islet- autoantibodies. The goal of this project is to employ the collaborative, multicenter TrialNet study of relative pancreas volume and morphological changes using noninvasive radiology with correlations to β-cell and acinar cell functions and genotype. The data and analyses emanating from this multicenter study have the potential to greatly improve our understanding of the endocrine-exocrine interactions during the natural history of T1D and may thus change the way we view T1D pathogenesis.
Role: Co-I

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Simpkins, Alexis

eRA COMMONS USER NAME (credential, e.g., agency login): ASIMPKINS

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Augusta State University	BS	2001	Chemistry
Medical College of Georgia	PHD	2010	Vascular Biology
Medical College of Georgia	MD	2010	
Medical College of South Carolina	OTH	2018	Masters of Clinical Research
Johns Hopkins Hospital	Resident	2014	Neurology Residency
NIH/NINDS, Stroke Branch	Resident	2017	Vascular Neurology Fellowship
Medical College of South Carolina	MS	2019	Masters of Clinical Research

A. Personal Statement

My prior career training and expertise, make me a perfect fit for conductive age related and cognitive research. After obtaining my MD.PhD. at the Medical College of Georgia with my graduate research focusing on stroke and vascular biology in 2010, I completed my neurology residency training at Johns Hopkins University in 2014. During my neurology residency, was funded support through the R 25 institutional grant to complete 6 months of research on neural repair and inflammation. I then completed a 3-year clinical and research vascular neurology fellowship at the NIH/NINDS Stroke Branch in 2014 where I focused on neuroimaging and biomarkers of ischemic stroke where I published research demonstrating the dynamic changes that happen after acute ischemic stroke and its importance in determining neurologic outcome. I have completed my Master's of Clinical research in the competitive TRANSCENDS program through the American Academy of Neurology, where I have received extensive training in team science. I have worked in collaboration with Dr. Adam Woods using transcriptomic data from the ACTIVE study and volumetric assessment of white matter lesions. We were able to demonstrate that inflammation plays a role in the presence of white matter hyperintensities in aging subjects before developing cognitive dysfunction. This translational project investigated signatures of miRNA from exosomes isolated from serum in patient's pre-mild cognitive impairment correlates with white matter hyperintensities on MRI. In addition, I have conducted projects on vascular cognitive impairment and effects of aging on cardiac markers of stroke. I was awarded a junior investigator award for the at the HEADS-UP pre-symposium of the International Stroke Conference on research project demonstrating health care disparities in trends in vascular dementia diagnosis in patients included in the National Inpatient Sample. My goal is to continue to evaluate effects of aging on vascular disease and biomarkers of stroke.

1. Simpkins A. Impact of Race-Ethnic and Economic Disparities on Rates of Vascular Dementia in the National Inpatient Sample Database from 2006-2014. Journal of Stroke and Cerebrovascular Diseases. 29. 104731. 10.1016/j.jstrokecerebrovasdis.2020.104731.
2. Simpkins AN, Janowski M, Oz HS, Roberts J, Bix G, Doré S, Stowe AM. Biomarker Application for Precision Medicine in Stroke. Transl Stroke Res. 2019 Dec 18;. doi: 10.1007/s12975-019-00762-3. [Epub ahead of print] Review. PubMed PMID:31848851.
3. Simpkins AN, Dias C, Norato G, Kim E, Leigh R. Early Change in Stroke Size Performs Best in Predicting Response to Therapy. Cerebrovasc Dis. 2017;44(3-4):141-149. PubMed PMID: http://www.ncbi.nlm.nih.gov/pubmed/28683442/; PubMed Central PMCID: PMC5629107.

4. Simpkins AN, Dias C, Leigh R. Identification of Reversible Disruption of the Human Blood-Brain Barrier Following Acute Ischemia. Stroke. 2016 Sep;47(9):2405-8. PubMed PMID: 27462115; PubMed Central PMCID: PMC5111547.

B. Positions and Honors

Positions and Employment

2002-04 & 2008-10: Medical Student, Medical College of George, Augusta, GA
2004-2008: Graduate Student, Medical College of Georgia, Augusta, GA (Mentor: John D. Imig PhD.)
2010-2011: Internship, Department of Internal Medicine Medical College of Georgia, Augusta GA
2011-2014: Neurology Resident, Johns Hopkins Hospital, Baltimore, MD.
2014-2015: Vascular neurology fellow at the National Institute of Health
2015-2016: Chief vascular neurology fellow at the National Institute of Health
2016-2017: Vascular neurology fellow at the National Institute of Health
2017-current: Assistant Professor of Neurology at the University of Florida, Gainesville FL
2017- 2019: Graduate Student, Medical University of South Carolina, Charleston, SC

Other Experience and Professional Memberships

2003 Research Journal Seminar Director, for the summer Research Apprentice Program at the Medical College of Georgia, Georgia
2011-14; American Academy of Neurology
2017-19 American Heart Association
2017-19 Reviewer of abstracts for the International Stroke Conference
2017-19 AAN TRANSCENDS program Scholar graduate
2017-19 Contributor, Blogging Stroke, Stroke Journal
2018-20 Stroke Early Career Cerebrovascular Development Committee Member for the AHA Stroke Council
2018-20 International Stroke Genetics Consortium (ISGC)
2018-20 NIH Collaborator Position
2018-20 Assistant Editor, eNeurologicalScience, World Federation of Neurology, Elsevier
2019 Reviewer for Student Scholarships in Cardiovascular Disease and Stroke for AHA Scientific Council Early Career Committee
2019 Delaware INBRE Developmental Research Pilot Program Study Panel – Grant reviewer July 2019
2020 Editorial Board member, Journal of Neuroimaging, April 2020
###

Honors

2007 Donald J. Reis Memorial Trainee Award, American Physiology Society (APS)
2007 Acres of Diamonds Award, Minority Trainee Research Forum
2007 Caroline Tum Suden/Frances Hellebrandt Award, APS
2008 Epoxide Hydrolase in Toxicology and Pharmacology Symposium Travel Award, American Society for Pharmacology and Experimental Therapeutics (ASPET)
2008 Minority Graduate Student Travel Award, ASPET
2008 Caroline Tum Suden/Frances Hellebrandt Award, APS
2008 Runner-up Graduate Student Best Abstract Award, ASPET
2009 VA Chief of Neurology Award, Medical College of Georgia
2001-2010 Stoney Brook Scholarship
2016 Travel Award for Winter Conference on Brain Research
2016 Travel Award for the American Neurological Association Conference
2017 First Prize winner of the 2016 Progress and Innovation Award, Stroke Journal
2017 TRANSCENDs Scholar, American Academy of Neurology
2019 Best Poster Award at the International Genetics Consortium, St. Louis, Illinois
2019 Recognized at top 10% abstract from International Stroke Conference for abstract “Secondary Stroke Prevention with Aspirin and Clopidogrel in CYP2C19*17 Carriers Increases Risk of Major Non-CNS Bleeding” of 2019
2019 Fastest Door To Needle time for administration of thrombolysis to acute stroke patients of 2018 of 16 minutes for UF Shands
2019 Stroke Council Diversity Travel Award, American Heart Association
2019 Awarded Service Key for Patient Care, University of Florida
2019 Best Poster Award at the International Genetics Consortium, St. Louis, Illinois, October 2019.

2020 HEADSUP Junior Investigator Travel Award, International Stroke Conference, American Heart Association February 2020.

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C. Contribution to Science

1. *Combine with 3. Acute Stroke Management. 1 should be cog and aging*

I have contributed on two facets of age-related cognitive decline and memory loss. I have worked in collaboration with Dr. Adam Woods using data from patients within the ACTIVE study. This translational project investigated signatures of miRNA from exosomes isolated from serum in patient's pre-mild cognitive impairment correlates with white matter hyperintensities on MRI. An abstract with our findings was presented at the American Academy of Neurology in April 2020. We found an association between miRNA transcripts and white matter hyperintensities in aging patients pre-cognitive decline that suggests that inflammation plays a role in the early pre-symptomatic state of white matter disease. In addition, in collaboration with the institutional Clinical Translational Science Institute (CTSI) and Sepsis Aging Research group at the University of Florida, I have presented and mentored projects on vascular cognitive impairment and effects of aging on cardiac markers of stroke. I was awarded a junior investigator award for the at the HEADS-UP pre-symposium of the International Stroke Conference on research project demonstrating health care disparities in trends in vascular dementia diagnosis in patients included in the National Inpatient Sample. Also, I mentored 2 resident projects presented at international conferences. Dr. Aisha Elfasi's abstract was accepted as a moderated poster for the In-hospital treatment & vascular cognitive impairment session of the International Stroke Conference, February 2020, and Dr. Natalie Buchwald's abstract on regional differences in hospital setting and insurance coverage for was presented as an oral poster presentation during the Vascular Cognitive Impairment session at the International Stroke Conference February 2020.

Peer Reviewed Publications:

Simpkins A. Impact of Race-Ethnic and Economic Disparities on Rates of Vascular Dementia in the National Inpatient Sample Database from 2006-2014. Journal of Stroke and Cerebrovascular Diseases. 29. 104731. 10.1016/j.jstrokecerebrovasdis.2020.104731.

Elfasi A, Mankowski RT, Moore FA, Ghita GL, Villani K, Anton SD, Brackenridge SC, Brumback B, Efron P, Leeuwenburgh C, Moldawer LL, Simpkins AN. Abstract TMP91: Pre-Sepsis P-wave Terminal Force in Lead V1 (PTFV1) as a Predictor of Atrial Fibrillation, In-Hospital Mortality, and Cognition in Sepsis Patients. Stroke. 2020;51(Suppl_1):ATMP91-ATMP. doi: doi:10.1161/str.51.suppl_1.TMP91.

Buchwald N, Elfasi A, Yu C, Simpkins AN. Abstract WP481: Regional Differences in Hospital Setting and Insurance Coverage in Patients Included in the National Inpatient Sample Database 2006-2014 With Vascular Dementia. Stroke. 2020;51(Suppl_1):AWP481-AWP. doi: doi:10.1161/str.51.suppl_1.WP481.

Simpkins AN, Boutzoukas E, O'Shea A, Rani A, Foster T, Cohen R, Woods A. miRNA from Exosomes in Older Adults that have Asymptomatic White Matter Hyperintensities Suggest Role for Brain Inflammation in Precursor Stage to Cognitive Impairment. Neurology Apr 2020, 94 (15 Supplement) 1620.

Simpkins A, Chen Z, Youn T, Kelly A, Khanna A, Wilson C, Bian J, Hogan W, Nagaraja N. Regional Reductions in the Frequency of Vascular Dementia Were Detected in the West Amongst Patients Included in the National Inpatient Sample Database from 2006–2014, Neurology Apr 2020, 94 (15 Supplement) 4827.

Elfasi A, Moore F, Mankowski R, Ghita G, Villani K, Anton S, Brakenridge S, Brumback B, Efron P, Elie M, Leeuwenburgh C, Moldawer L, Simpkins AN. Utility of Pre-sepsis P-wave Terminal Force in Lead V1 (PTFV1) as a Predictor of Atrial Fibrillation and Ischemic Stroke in Patients with Sepsis. Neurology Apr 2020, 94 (15 Supplement) 4867

2. *Demonstrating mechanisms of vascular and neural protection using soluble epoxide hydrolase inhibitors using animal models of ischemic stroke and vascular remodeling*. As stroke still remains one of the leading causes for long-term disability in adults, novel interventions to reduce morbidity beyond

what our current therapies offer are needed. I worked with Dr. John Imig on novel inhibitors of the epoxide pathway in animal in vivo models of ischemic stroke during graduate school. Epoxyeicosatrenoic acids (EETs) are anti-apoptotic, angiogenic, anti-inflammatory, and anti-nociceptive lipids synthesized in astrocytes by cytochrome P450 (CYP) 2C11, a hypoxia inducible enzyme, and are released upon activation of glutamate receptors or by hypoxia. The rapid degradation of EETs by the soluble epoxide hydrolase enzyme (SEH) is one of the largest impediments to using EETs as a pharmacological agent. Pharmacologic use of SEH inhibitors (SEHi) have been shown to increase EET levels and promote EET downstream effects *in vivo.* The findings during my graduate work showed that chronic SEH inhibition decreases infarct size induced by middle cerebral artery occlusion independent of lowering blood pressure in spontaneously hypertensive stroke prone rats (SHR-SP) rats and Wistar Kyoto (WKY) rats via vascular and neuroprotection. The chronic protective effect in SHRSP rats was associated increased cerebral microvessel density and trends for down regulation of pro-apoptotic mediators after 6 weeks of SEHi. In particular, Mapk8ip, a JNK pathway mediator, was found to be up-regulated in the brain tissue of WKY rats. Moreover, we were able to show that knocking out the gene expression of SEH in mice impaired the response to vascular wall and endothelial injury. The compilation of this work has been published in 3 articles which in combination have been cited 120 times. This work has also prompted further expansion into the role of SEHi and EETs in neural repair and the modulation of inflammatory response using exogenous EETs and SEHi.

Peer Reviewed Publications:

Simpkins AN, Rudic RD, Schreihofer DA, Roy S, Manhiani M, Tsai HJ, Hammock BD, Imig JD. Soluble Epoxide Inhibition is Protective Against Cerebral Ischemia via Vascular and Neural Protection. The American Journal of Pathology. 2009 Jun; 174(6): 2086-2095. PMCID: PMC2684174.

Simpkins AN, Rudic RD, Roy S, Tsai HJ, Hammock BD, Imig JD. Soluble Epoxide Inhibition Modulates Vascular Remodeling. American Journal of Physiology - Heart and Circulatory Physiology. 2010 Mar: 298(3): H795-806. PMCID: PMC2838550.

Imig JD, Simpkins AN, Renic M, Harder DR. Cytochrome P450 Eicosanoids and Cerebral Vascular Function. Expert Reviews in Molecular Medicine. 2011 Jan; 13; Article number e7. PMCID: PMC3613250.

3. *Identification of imaging biomarkers in ischemic stroke.* Although MRI has been studied in the setting of acute ischemic stroke, imaging biomarkers for use in clinical trials are still lacking. Several MRI biomarkers have been proposed, including a diffusion lesion volume (FIV) at 24 hours after acute ischemic stroke onset, and evidence of early reperfusion (PER). However, neither of these biomarkers account for the previously well described early changes in apparent diffusion coefficient lesion volumes (ECS) that occur within the first 24 hours. I was co-first author on case report that demonstrated how clinical infarcts can vary during the hyperacute period of acute ischemic stroke. In addition, I have worked with Dr. Richard Leigh during my clinical research stroke fellowship at the NIH to investigate the utility of MRI imaging biomarkers in predicting clinical outcome. Here we used the natural history of stroke MRI registry pipeline created by Dr. Leigh, which allows for automated lesion volumes calculations on co-registered images to test the hypothesis that ECS are predictive of early neurologic improvement and perform more effectively as a diagnostic test than FIV and PER. The findings of this study show that single time point measurements such as FIV and PER are less effective imaging biomarkers and may not be optimal imaging biomarkers for use in phase II clinical trials. In addition, I have demonstrated a CT correlated for MRI HARM that may be useful for evaluated blood brain disruption.

   Peer Reviewed Publications:

   Majidi S, Simpkins AN, Leigh R. The Efficacy of IV Tissue Plasminogen Activator for Restoring Cerebral Blood Flow in the Hours Immediately after Administration in Patients with Acute Stroke. J Neuroimaging. 2019 Mar;29(2):206-210. doi: 10.1111/jon.12587. Epub 2018 Dec 3. PubMed PMID:30508260; PubMed Central PMCID:PMC6403008.

Simpkins AN, Dias C, Norato G, Eunhee K, Leigh R, on behalf of the NIH Natural History of Stroke Investigators. Early Changes in ADC Volume is an Imaging Biomarker of Early Neurologic Improvement in Ischemic Stroke Treatment. Cerebrovascular Diseases. Cerebrovasc Dis. 2017 Jul 7;44(3-4):141-149.

Simpkins AN, Janowski M, Oz HS, Roberts J, Bix G, Doré S, Stowe AM. Biomarker Application for Precision Medicine in Stroke. Transl Stroke Res. 2019 Dec 18;. doi: 10.1007/s12975-019-00762-3. [Epub ahead of print] Review. PubMed PMID:31848851.

Kim-Tenser M, Mlynash M, Lansberg MG, Tenser M, Bulic S, Jagadessan B, Simpkins AN, Albers GW, Marks MP, Heit J. CT Perfusion Core and ASPECT Score Prediction of Outcomes in DEFUSE3. International Journal of Stroke. Int J Stroke. 2020 Mar 31

De Prey J, Yu C, Echevarria FD, Barreto I, Rees JH, DeJesus RO, Simpkins AN. Iodinated Contrast Extravasation on Post-Revascularization Computed Tomography Mimics Magnetic Resonance Hyperintense Acute Reperfusion Marker: A Case Study. J Stroke Cerebrovasc Dis. 2020 Sep 15;29(12):105294. doi: 10.1016/j.jstrokecerebrovasdis.2020.105294. Epub ahead of print. PMID: 32992195.

4. *Evaluation of Reversible Blood Brain Barrier Disruption in Acute Ischemic Stroke in Humans using permeability imaging.* During my research fellowship, I have also been working on a second project with Dr. Leigh that focuses on the blood brain barrier (BBB) during very early time points of ischemic stroke and its association with hemorrhagic transformation. Dr. Leigh has developed an innovative method for detecting BBB permeability using contrast enhanced MR imaging, which he has previously published and validated. While ischemic stroke *in vitro* and *in vivo* data suggest that BBB disruption during cerebral is a dynamic process, we are the first to demonstrate that blood brain barrier disruption can be reversible after thrombolysis in humans. Moreover, we also demonstrated while the non-reversible focal BBB disruption is significantly associated with hemorrhagic transformation while reversible BBB disruption was not. In addition to this work, I have contributed to research on blood brain barrier disruption with novel findings such as ocular blood brain barrier disruption and detection of ischemic stroke and the association between blood brain barrier disruption, white matter disease, and stroke recovery.

   Peer Reviewed Publications:

   Simpkins AN, Dias C, Leigh R. Identification of Reversible Disruption of the Human Blood-Brain Barrier Following Acute Ischemia. Stroke. 2016 Sep;47(9):2405-8. PubMed PMID: 27462115; PubMed Central PMCID: PMC5111547.

   Hitomi E, Simpkins AN, Luby M, Latour LL, Leigh RJ, Leigh R. Blood-ocular barrier disruption in acute stroke patients. Neurology. 2018 Feb 7;PubMed PMID: 29438039.

   Gupta N, Simpkins AN, Hitomi E, Dias C, Leigh R. White Matter Hyperintensity-Associated Blood-Brain Barrier Disruption and Vascular Risk Factors. J Stroke Cerebrovasc Dis. 2018 Feb;27(2):466-471. PubMed PMID: 29100854; PubMed Central PMCID: PMC5808404.

   Nadareishvili Z, Simpkins AN, Hitomi E, Reyes D, Leigh R. Post-Stroke Blood-Brain Barrier Disruption and Poor Functional Outcome in Patients Receiving Thrombolytic Therapy. Cerebrovasc Dis. 2019;47(3-4):135-142. doi: 10.1159/000499666. Epub 2019 Apr 10. PubMed PMID:30970357; PubMed Central PMCID:PMC6610790.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/alexis.simpkins.3/bibliography/public/

D. Additional Information: Research Support and/or Scholastic Performance

NINDS Intramural Project:

Title of Project: National Institutes of Neurological Disorders and Stroke/NIH, Evaluation, Pathogenesis, and Treatment of Patients with or at Risk for Cerebrovascular Disease (A Natural History/Disease Pathogenesis Protocol).
Grant/Protocol Number: (01-N-0007)
Participation: 2014 - Present
Principle Investigator: Lawrence Latour, PhD.
Goal and Role of Person in Biographical Sketch: I am currently working on blood transcriptome and MRI imaging biomarkers of acute ischemic stroke. The goal is to find biomarkers that can isolate patients who may be at higher risk of hemorrhagic transformation and stroke progression. We are using advanced transcriptome analysis with next generation RNA sequencing of mRNA and microRNA in patients that have been imaged with MRI prior to and after acute ischemic stroke treatment.

R25 NINDS Research Education Program for Residents and Fellows in Neurology and Neurosurgery
Title of Project: Enhancement of neural repair from ischemia via soluble epoxide hydrolase inhibition
Grant/Protocol Number: RFA-NS-09-003
Dates of Funding: July 2013 – June 2014
Principle Investigator: Argye Hillis, M.D.
Goal and Role of Person in Biographical Sketch: I submitted a project during neurology residency to evaluate the role of soluble epoxide hydrolase inhibitions effects on neural repair from ischemic insult.

Individual F31 Pre-doctoral Fellowship
Title of Project: "Vascular Protection by Epoxide Hydrolase Inhibition in Cerebral Ischemia"
Grantor: National Heart, Lung, & Blood Institute/ NIH/ DHHS
Grant/Protocol Number: 1 F31 HL087723-01
Dates of funding: April 2007- May 2010
Graduate Student, Vascular Biology Department at the Medical College of Georgia, Georgia
Principle Investigator, Dr. John D. Imig 08/2004 - 05/2008
Goal and Role of the Person in the Biographical Sketch: I completed and defended my thesis work on the protective effects of soluble epoxide hydrolase inhibitors in cerebral ischemia and vascular remodeling. The mechanisms of cerebral protection against cerebral ischemia via chronic soluble epoxide inhibition in hypertensive and normotensive animals were investigated. In addition, the role of soluble epoxide hydrolase enzyme in vascular remodeling was investigated via animal models of carotid ligation and wire induced femoral artery injury.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: John B Williamson

eRA COMMONS USER NAME (credential, e.g., agency login): wjohnb

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
The Florida State University, Tallahassee FL	BA	04/1996	Psychology
Virginia Polytechnic Institute and State University, Blacksburg, VA	PhD	05/2004	Clinical Psychology, Neuropsychology
University of Chicago, Chicago IL	Resident	07/2004	Clinical Psychology Internship
University of Illinois, Chicago	Postdoctoral Fellow	07/2006	Neuropsychology
University of Illinois, Chicago	Postdoctoral Fellow	07/2008	Neuroscience

A. Personal Statement

I am a clinical psychologist with specialization in neuropsychology. I am an affiliate investigator with the Center for Cognitive Aging and Memory. I also hold a position within the Center for OCD and Anxiety Related Disorders and I am the leader of the Cognitive and Emotion Function initiative at the Brain Rehabilitation Research Center at the North Florida/South Georgia VAMC. My research team has been strongly involved in the development of tVNS methods and application. I currently have NIA funding using tVNS to affect cognitive performance in patients with amnestic mild cognitive impairment as well as by the MBRF pairing tVNS with cognitive training in older adults. I completed two pilot projects funded by the BRRC to examine the impact of tVNS on hyperarousal symptoms in patients with PTSD and to examine the effects of tVNS on sleep architecture in the same population. We recently received Merit Review (VA R01) funding to follow-up the latter pilot and that project started last October. I have been the PI or Co-I on multiple funded grants from the federal government (NIH, DOD, VA) that employ cognitive and affective neuroscience as well as psychophysiology approaches. I have worked with vagally mediated systems research for many years. In addition to work on tVNS, I continue mechanistic studies using multi-modal neuroimaging in aging, traumatic brain injury, post-traumatic stress disorder, and cerebrovascular disease.

B. Positions and Honors

Positions and Employment

2008-2012 Research Health Scientist, Dept of Veteran Affairs, Gainesville FL
2009-2012 Research Assistant Professor, Department of Neurology University of Florida
2012-2018 Assistant Professor Department of Neurology, University of Florida
2012- Research Psychologist, Dept of Veteran Affairs, Gainesville, FL
2012- Affiliate Investigator, Center for Cognitive Aging and Memory, McKnight Brain Foundation
2016- Assistant Professor, Department of Neuroscience, University of Florida
2018- Assistant Professor (tenure track), Department of Psychiatry, University of Florida
2018- Lead, Cognitive and Emotion Function Initiative, Brain Rehabilitation Research Center, Dept of Veteran Affairs, Gainesville FL

2018- Investigator, Center for OCD and Anxiety Related Disorders, Department of Psychiatry, University of Florida

Other Experience and Professional Memberships

2002 Member, International Neuropsychological Society
2008- Member, Florida Society of Neurology
2013- Member, American Academy of Clinical Neuropsychology
2019 Member, American Psychological Association
2020 Member, International Society to Advance Alzheimer's Research and Treatment (ISTAART)

C. Contributions to Science

1. *Advanced understanding of neurophysiological and cognitive consequences of mood and personality trait differences.* Dr. Williamson's early research focused on the role of differences in fronto-subcortical brain systems and laterality as a function of subclinical individual differences in mood and personality states and traits in the manifestation of autonomic mobilization to regional brain tasks. We demonstrated that, in a college-aged population, high trait hostility resulted in elevated autonomic responses to tasks that recruited right hemisphere resources and that performance on these right hemisphere tasks was also degraded compared to their low trait hostility peers. Further we showed motor asymmetries in children and men with symptoms of depression and hostility. This research has been replicated multiple times by other groups and lead to a capacity model for understanding the interaction of personality traits on psychophysiological profiles that have been correlated to cardiovascular and cerebrovascular diseases later in life. These vagally mediated brain systems overlap with those in consideration in PTSD, another area of contribution.
   a. **Williamson JB**, Harrison DW. Functional cerebral asymmetry in hostility: A dual task approach with fluency and cardiovascular regulation. *Brain and Cognition* 2003; *52:167*-174.
   b. Demaree HA, Higgins D, **Williamson JB**, Harrison DW. Asymmetry in handgrip strength and fatigue in low- and high- hostile men. *International Journal of Neuroscience* 2002; 112:415-428.
   c. Everhart DE, Harrison DW, Shenal BV, **Williamson JB**, Wuensch KL. Grip-strength, fatigue and motor perseveration in anxious men without depression. *Neuropsychiatry, Neuropsychology and Behavioral Neurology* 2002; 15:122-142.
   d. Emerson CS, Harrison DW, Everhart D, **Williamson JB**. Hand fatigue asymmetry in motor performances of depressed boys. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology* 2001; 14:130-134.

2. *Furthered the knowledge base of factors relating to cognition, emotion and autonomic disturbance in cerebrovascular disease and neurological injury.* Because of relationships between autonomic disruptions in trait hostility and other mood related features to later development of cardiovascular and cerebrovascular disease, Dr. Williamson became interested in the bases of vascular dementia and the contributions of vascular factors to the development of cognitive and emotional dysfunction in the elderly. These interests led to numerous studies of vascular cognitive impairment (VCI) (dementia precursor) that showed the contribution of white matter hyperintensitites to VCI and also led to Dr. Williamson's early work on the use of diffusion tensor imaging as a sensitive tool for assessing the relationship of regional white matter disruption to cognitive and mood indicators. Further, Dr. Williamson was funded by an F32 to study the relationship of white matter disease to mobilization of autonomic resources to perform cognitive tasks.
   a. **Williamson JB**, Nyenhuis DL, Pedelty L, Byrd S, Jhaveri M, Wang C, deTeledo-Morrell L, Sripathirathan K, Gorelick P. Baseline differences between Vascular Cognitive Impairment No Dementia reverters and nonreverters. *Journal of Neurology, Neurosurgery, and Psychiatry* 2008; 79:1208-1214.
   b. **Williamson JB**, Nyenhuis Dl, Stebbins GT, Gorelick PB. Regional differences in apparent white matter integrity, cognition and mood in patients with ischemic stroke. *Journal of Clinical and Experimental Neuropsychology* 2010: 32, 673-681.
   c. **Williamson JB**, Lewis GF, Grippo A, Lamb D, Harden E, Handleman M, Lebow J, Carter CS, Porges SW. Autonomic predictors of recovery following surgery: A comparative study. *Autonomic Neuroscience* 2010:156, 60-66.
   d. **Williamson JB**, Lewis GF, Nyenhuis DL, Stebbins GT, Murphy C, Handelman M, Harden E, Heilman KM, Gorelick PB, Porges SW. The effects of cerebral white matter changes on cardiovascular

responses to cognitive and physical activity in a stroke population. *Psychophysiology* 2012; 49:1618-1628.

3. *Elucidated impact of chronic lateralized stroke on spatial cognition as well as normal perturbations of sensory performance on laterality of spatial cognition and autonomic support.* These efforts led to several related lines of investigation to examine risk factors contributing to the development of spatial performance deficits in patients with cerebrovascular disease.
   a. **Williamson JB**, Haque S, Harciarek M, Burtis DB, Lamb D, Zilli E, Heilman KM. The influence of stimulus proximity on judgments of spatial location in patients with chronic unilateral right and left hemisphere stroke. *Journal of Clinical and Experimental Neuropsychology* 2014; 36:787-793.
   b. Finney G, **Williamson JB**, Burtis DB, Drago V, Mizuno T, Jeong Y, Crucian G, Haque S, Heilman KM. Effects of chronic right hemisphere damage on the allocation of spatial attention: Alterations of accuracy and reliability. *Journal of the International Neuropsychological Society* 2015; 21:1-5.
   c. Burtis DB, Heilman KM, Mo J, Wang C, Lewis GF, Davilla MI, Ding M, Porges SW, **Williamson JB**. The effects of constrained left and right monocular viewing on the autonomic nervous system. *Biological Psychology* 2014; 100:79-85.
   d. **Williamson JB**, Lamb DG, Burtis DB, Haque S, Kesayan T, Heilman K. Right hemispatial ipsilesional neglect with chronic right hemisphere strokes. *Journal of Clinical and Experimental Neuropsychology* 2018 May;40(4):347-356.

4. *Provided theoretical model to advance the understanding of traumatic brain injury on manifestation of emotional dysregulation and also the impact of chronic emotional dysregulation on aging. Developed mechanistic information on use of noninvasive vagal nerve stimulation to affect symptoms of PTSD.* TBI and PTSD are both critical issues that affect today's Veteran population. Understanding neurological mechanisms of emotional disruption in this population is critical to developing appropriate treatments. The presented models provide clear testable hypotheses that may lead to effective diagnosis and treatments for this population. This work is ongoing and we are developing several lines of inquiry from the project including a recently funded CDA-2 (Damon Lamb) on tVNS and its impact in the context of our model on GABA and fMRI shifts in the limbic system in patients with mTBI/PTSD and the proposed merit submission integrating my mechanistic work (CDA-2) and the impact of tVNS on emotional cognition/autonomic behavior.
   a. **Williamson JB**, Heilman KM, Porges EC, Lamb DG, Porges SW. A possible mechanism for PTSD symptoms in patients with traumatic brain injury: central autonomic disruption. *Frontiers in Neuroengineering* 2013 Dec 19; 6:13.
   b. **Williamson JB**, Porges EC, Lamb DG, Porges SW. Maladaptive autonomic regulation in PTSD accelerates physiological aging. *Frontiers in Psychology* 2015 Jan 21;5:1571.
   c. Lamb DF, Porges EC, Lewis GF, **Williamson JB**. Non-invasive vagal nerve stimulation effects on hyperarousal and autonomic state in patients with posttraumatic stress disorder and history of mild traumatic brain injury: preliminary evidence. *Frontiers in Medicine* 2017 July 31; 4:124.
   d. Wilson MA, Liberzon I, Lindsey ML, Lokshina Y, Risbrough VB, Sah R, Wood SK, **Williamson JB**, Spinale FG. Common pathways and communication between the brain and heart: Connecting post-traumatic stress disorder and heart failure. *Stress* 2019 Sep;22(5):530-547.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/john.williamson.2/bibliography/48036192/public/?sort=date&direction=ascending

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

VAMC I01RX003140 11/01/2019-10/31/2023
Transcutaneous vagal nerve stimulation improvement of sleep quality in Veterans with PTSD with or without history of mild TBI. The goal of this project is to optimize dosing and determine the effects of tVNS on sleep architecture and next morning autonomic function (hyperarousal) in patients with PTSD and mTBI.
Role: PI

NIH 1R01AG061065 09/30/2018-8/31/2023
Role of gut microbial dysbiosis and aging on HIV-associated neurocognitive and brain dysfunction

The goal of this project is to determine mechanisms of gut microbial dysbiosis to brain dysfunction as assessed via multi-modal neuroimaging in the context of cognitive deficits associated with HIV.
Role: Co-I

DOD DN180041 05/01/2019-04/31/2022
Biomarker based precision medicine approach to traumatic brain injury subphenotypes.
The goal of this funding is to determine injury characteristic features of TBI and their relationship to different expressions of behavioral outcomes.
Role: Site-PI

McKnight Brain Research Foundation 2019-2022
Paired cognitive training and transcutaneous vagal nerve stimulation in older adults.
The purpose of this longitudinal multi-institution pilot project is to assess the enhancing effects of tVNS on neuroplasticity as indicated by MRI methods and skill acquisition in older adults.
Role: PI

NIH R21AG054876 09/01/2017-08/31/2021 (no-cost extension)
Treatment of mild cognitive impairment with transcutaneous vagal nerve stimulation.
The goal of this funding is to determine if tVNS can enhance cognitive performance during stimulation in patients with amnestic mild cognitive impairment and whether structural changes in brain regions relevant for memory encoding (e.g., hippocampus) predict response.
Role: PI

State of Florida 2020-2021
A feasibility study of real-time monitoring of Posttraumatic Stress Disorder related sleep disturbances and other symptoms among patients on medical marijuana.
Role: Co-I

Brain Rehabilitation Research Center 2020-2021
Transcutaneous vagal nerve stimulation modulation of sleep quality and cognition in older veterans with subjective cognitive impairment. This pilot award is a designed to determine the effect of tVNS at night on cognitive performance in older people with subjective cognitive impairment.
Role: PI

Completed Research Support (Recent)
VAMC BRRC Pilot Award 2018-2019
Non–invasive vagal nerve stimulation modification of sleep architecture and emotion in Veterans with PSTD.
The goal of this funding is to provide pilot data for the effect of transcutaneous vagal nerve stimulation on sleep quality and morning mood and cognition in patients with TBI and PTSD.
Role: PI

VAMC 1 LK2RX000707-09 CDA-2 4/01/2012 – 03/31/2018
White matter changes and mild TBI: Emotional and autonomic consequences.
The goal of this funding was to extend knowledge of white matter damage contributions after TBI to the development of emotional dysregulation in Veterans with PTSD.
Role: PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Woods, Adam

eRA COMMONS USER NAME (credential, e.g., agency login): ajwoods

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
University of Alabama at Birmingham, Birmingham, AL	BS	05/2003	Psychology
George Washington University, Washington, DC	PHD	05/2010	Cognitive Neuroscience
University of Pennsylvania, Philadelphia, PA	Postdoctoral Fellow	06/2013	Cognitive Neuroscience

A. Personal Statement

Dr. Woods is Associate Director of the Center for Cognitive Aging and Memory (CAM) in the McKnight Brain Institute at UF. Dr. Woods is also an Associate Professor in the Department of Clinical and Health Psychology at UF, with a joint appointment to Neuroscience. He is a cognitive neuroscientist with expertise in non-invasive brain stimulation, neuroimaging, and cognitive training for working memory and speed of processing/attention. He is a national leader in the field of neuromodulation, leading the largest transcranial electrical stimulation (tES) and near infrared photobiomodulation trials to date, multiple cognitive training trials, publishing the first comprehensive textbook in the field of tES, and multiple field standards papers. Dr. Woods' research specifically focuses on discovery and application of novel non-invasive interventions for enhancing cognitive function in adults with and without neurodegenerative disease. Dr. Woods has expertise in multi-disciplinary cognitive neuroscience methodologies (MRI/fMRI, electrophysiology, non-invasive brain stimulation), extensive experience with aging-related cognitive disorders, cognitive training applications, and past research with neurological diseases. Over the past five years, Dr. Woods has established one of the largest and most well-funded neuromodulation laboratories in the United States. He is PI of the first and largest phase III RCT for tES using transcranial direct current stimulation (tDCS) and cognitive training, the ACT study (R01AG054077, n=360), the largest phase II near infrared photobiomodulation trial (R01AG064587, n=168), one of the largest phase II tES trials, the Stimulated Brain Study (K01AG054077, n=80), as well as an R21 and U01 investigating the effects of neuromodulation on the aging brain (R21MH112206, U01AG062368). He also serves as co-I on multiple other NIH funded grants focused on neuromodulation of cognitive aging, chronic pain, and mobility using transcranial electrical stimulation (RF1MH114290, R37AG033906, R21AG053736). Each of these studies attempts to enhance cognitive and brain function through neuromodulation. In addition, Dr. Woods is currently undertaking an NIA funded remote assessment of 300+ older adults for evaluation of COVID-19 impact on cognition, brain health, mental health and well-being over a 1-year study period.

a. Nissim N, O'Shea A, Indahlastari A, Telles R, Richards L, Porges E, Cohen R, Woods AJ. Effects of in-scanner bilateral frontal tDCS on functional connectivity of the working memory network in older adults. Front Aging Neurosci. 2019 Mar 15;11: 51. PubMed PMID: 30930766; PubMed Central PMCID: PMC6428720

b. Woods AJ, Cohen R, Marsiske M, Alexander GE, Czaja SJ, Wu S. Augmenting cognitive training in older adults (The ACT Study): Design and Methods of a Phase III tDCS and cognitive training trial. Contemp Clin Trials. 2017 Dec 5;65:19-32. PubMed PMID: 29313802.

c. Nissim N, Nissim N, O'Shea A, Indahlastari A, Telles R, Richards L, Porges E, Cohen R, Woods AJ. Effects of in-scanner bilateral frontal tDCS on functional connectivity of the working memory network in older adults. Front Aging Neurosci. 2019 in press. PubMed PMID: pending.

d. Woods AJ, Antal A, Bikson M, Boggio PS, Brunoni AR, Celnik P, Cohen LG, Fregni F, Herrmann CS, Kappenman ES, Knotkova H, Liebetanz D, Miniussi C, Miranda PC, Paulus W, Priori A, Reato D, Stagg C, Wenderoth N, Nitsche MA. A technical guide to tDCS, and related non-invasive brain stimulation tools. Clin Neurophysiol. 2016 Feb;127(2):1031-1048. PubMed PMID: 26652115; PubMed Central PMCID: PMC4747791.

B. Positions and Honors

Positions and Employment

2010 - 2013	Post-doctoral Fellow, University of Pennsylvania, Philadelphia, PA
2013 -	Assistant Professor, University of Florida, Gainesville, FL
2014 -	Assistant Director, Center for Cognitive Aging and Memory, Gainesville, FL

Other Experience and Professional Memberships

2005 -	Member, Association for Psychological Science
2005 -	Member, International Neuropsychological Society
2010 -	Member, Society for Neuroscience
2014 -	Junior Fellow, World Academy of Arts and Sciences
2015 -	Ad Hoc Reviewer, US Veteran's Administration
2016 -	Ad Hoc Reviewer, National Institutes of Health
2016 -	Member, American Psychological Association

Honors

2006 - 2009	Graduate Research Fellowship , National Science Foundation
2010 - 2013	Post-doctoral Fellowship, Intellectual and Developmental Disabilities Research Center, Children's Hospital of Philadelphia
2014 - 2016	KL2 Scholar, University of Florida Clinical Translational Science Institute
2015 - 2015	Young Investigator Award in Neuromodulation, NYC Neuromodulation 2015
2018-2020	University Preeminence Term Professorship, University of Florida, College of Public Health and Health Professions
2019	Tenure, University of Florida

C. Contribution to Science

Transcranial Electrical Stimulation. Over the past eight years, I have focused my research on the technical and basic science application of non-invasive electrical brain stimulation techniques as novel interventions for enhancement of cognitive function. This work includes both transcranial direct current stimulation and transcranial magnetic stimulation. To further the field, I co-founding a CME certified practical training course in tES that has trained over 950 researchers and students to safely and consistently apply this method of non-invasive brain stimulation. I have published numerous field standards papers aimed at enhancing replicability and safety for the method and the first textbook in the field, in addition to exploring its impact on a variety of cognitive functions in the brain. I was awarded the 2015 NYC Neuromodulation Young Investigator Award for my scientific and educational contributions to the field. Furthermore, I am also PI of the first Phase III tDCS randomized clinical trial, as well as the largest tDCS study to date. Collectively, this work provides me with a strong foundation in the technical elements and application standards of tES.

a. McLaren ME, Nissim NR, Woods AJ. The effects of medication use in transcranial direct current stimulation: A brief review. Brain Stimul. 2018 Jan - Feb;11(1):52-58. PubMed PMID: 29066167; PubMed Central PMCID: PMC5729094.
b. Szymkowicz SM, McLaren ME, Suryadevara U, Woods AJ. Transcranial Direct Current Stimulation Use in the Treatment of Neuropsychiatric Disorders: A Brief Review. Psychiatr Ann. 2016 Nov;46(11):642-646. PubMed PMID: 27885309; PubMed Central PMCID: PMC5117191.
c. Bikson M, Grossman P, Thomas C, Zannou AL, Jiang J, Adnan T, Mourdoukoutas AP, Kronberg G, Truong D, Boggio P, Brunoni AR, Charvet L, Fregni F, Fritsch B, Gillick B, Hamilton RH, Hampstead BM, Jankord R, Kirton A, Knotkova H, Liebetanz D, Liu A, Loo C, Nitsche MA, Reis J, Richardson JD, Rotenberg A, Turkeltaub PE, Woods AJ. Safety of Transcranial Direct Current Stimulation: Evidence Based Update 2016. Brain Stimul. 2016 Sep-Oct;9(5):641-61. PubMed PMID: 27372845; PubMed Central PMCID: PMC5007190.
d. Kessler SK, Minhas P, Woods AJ, Rosen A, Gorman C, Bikson M. Dosage considerations for transcranial direct current stimulation in children: a computational modeling study. PLoS One. 2013;8(9):e76112. PubMed PMID: 24086698; PubMed Central PMCID: PMC3785412.

Neuroimaging and Magnetic Resonance Spectroscopy. My work in neuroimaging and spectroscopy has focused on understanding the brain networks and neurometabolites that underlie cognitive processes and how these processes are altered by age and medical disorders exacerbating aging of the human brain. This work has primarily used structural and functional magnetic resonance imaging and diffusion weighted imaging, but now includes magnetic resonance spectroscopy. Through multimodal neuroimaging, this work aims to identify markers predictive of cognitive decline in older adults, as well as markers of intervention effectiveness. This work has been central to identification of neural intervention targets for tES.

a. Porges EC, Woods AJ, Lamb DG, Williamson JB, Cohen RA, Edden RAE, Harris AD. Impact of tissue correction strategy on GABA-edited MRS findings. Neuroimage. 2017 Nov 15;162:249-256. PubMed PMID: 28882635; PubMed Central PMCID: PMC5705271.
b. O'Shea A, Cohen RA, Porges EC, Nissim NR, Woods AJ. Cognitive Aging and the Hippocampus in Older Adults. Front Aging Neurosci. 2016;8:298. PubMed PMID: 28008314; PubMed Central PMCID: PMC5143675.
c. Porges EC, Woods AJ, Edden RA, Puts NA, Harris AD, Chen H, Garcia AM, Seider TR, Lamb DG, Williamson JB, Cohen RA. Frontal Gamma-Aminobutyric Acid Concentrations Are Associated With Cognitive Performance in Older Adults. Biol Psychiatry Cogn Neurosci Neuroimaging. 2017 Jan;2(1):38-44. PubMed PMID: 28217759; PubMed Central PMCID: PMC5312683.
d. Woods AJ, Hamilton RH, Kranjec A, Minhaus P, Bikson M, Yu J, Chatterjee A. Space, time, and causality in the human brain. Neuroimage. 2014 May 15;92:285-97. PubMed PMID: 24561228; PubMed Central PMCID: PMC4008651.

Working Memory/Executive Function. One area of my work investigates the impact of aging and stroke on working memory and executive function. My recent work in age-related change in working memory/executive function includes both behavioral and neuroimaging based identification of therapeutic neural targets for tES. This work spans investigation of early development (age 2-18 years) to effects in later life (ages 60+) and following focal lesions to frontal and parietal brain systems.

a. Nissim NR, O'Shea AM, Bryant V, Porges EC, Cohen R, Woods AJ. Frontal Structural Neural Correlates of Working Memory Performance in Older Adults. Front Aging Neurosci. 2016;8:328. PubMed PMID: 28101053; PubMed Central PMCID: PMC5210770.
b. Woods AJ, Göksun T, Chatterjee A, Zelonis S, Mehta A, Smith SE. The development of organized visual search. Acta Psychol (Amst). 2013 Jun;143(2):191-9. PubMed PMID: 23584560; PubMed Central PMCID: PMC3651801.
c. Woods AJ, Mark VW. Convergent validity of executive organization measures on cancellation. J Clin Exp Neuropsychol. 2007 Oct;29(7):719-23. PubMed PMID: 17896197.
d. Mark VW, Woods AJ, Ball KK, Roth DL, Mennemeier MS. Disorganized search is not a consequence of neglect. Neurology. 2004; 63(1):78-84.

Attention. Over the past ten years, I have studied attentional processes in the brain using a variety of tES and attention research methods in spatial neglect following stroke and health cognitive populations to understand the relative contributions of frontal and parietal systems in attention.

a. Woods AJ, Lehet M, Chatterjee A. Context modulates the contribution of time and space in causal inference. Front Psychol. 2012;3:371. PubMed PMID: 23162484; PubMed Central PMCID: PMC3498891.
b. Woods AJ, Mennemeier M, Garcia-Rill E, Huitt T, Chelette KC, McCullough G, Munn T, Brown G, Kiser TS. Improvement in arousal, visual neglect, and perception of stimulus intensity following cold pressor stimulation. Neurocase. 2012;18(2):115-22. PubMed PMID: 22013983; PubMed Central PMCID: PMC3266979.
c. Woods AJ, Mennemeier M, Garcia-Rill E, Meythaler J, Mark VW, Jewel GR, Murphy H. Bias in magnitude estimation following left hemisphere injury. Neuropsychologia. 2006;44(8):1406-12. PubMed PMID: 16434066; PubMed Central PMCID: PMC4420160.
d. Mennemeier M, Pierce CA, Chatterjee A, Anderson B, Jewell G, Dowler R, Woods AJ, Glenn T, Mark VW. Biases in attentional orientation and magnitude estimation explain crossover: neglect is a disorder of both. J Cogn Neurosci. 2005 Aug;17(8):1194-211. PubMed PMID: 16197678; PubMed Central PMCID: PMC4442679.

Cognitive Aging Interventions. Much of my current and past work focuses on successful cognitive aging interventions, in a variety of populations. This work has evaluated not only the cognitive and functional consequences of aging and various disorders, but also improvement in these processes following intervention. This line of my research attempts to identify novel markers (e.g., neuroimaging, etc.) and methods for prevention (e.g,. tES, anti-inflammatory intervention) of age and disease related cognitive.

a. Anton SD, Woods AJ, Ashizawa T, Barb D, Buford TW, Carter CS, Clark DJ, Cohen RA, Corbett DB, Cruz-Almeida Y, Dotson V, Ebner N, Efron PA, Fillingim RB, Foster TC, Gundermann DM, Joseph AM, Karabetian C, Leeuwenburgh C, Manini TM, Marsiske M, Mankowski RT, Mutchie HL, Perri MG, Ranka S, Rashidi P, Sandesara B, Scarpace PJ, Sibille KT, Solberg LM, Someya S, Uphold C, Wohlgemuth S, Wu SS, Pahor M. Successful aging: Advancing the science of physical independence in older adults. Ageing Res Rev. 2015 Nov;24(Pt B):304-27. PubMed PMID: 26462882; PubMed Central PMCID: PMC4661112.
b. Woods AJ, Cohen RA, Pahor M. Cognitive frailty: frontiers and challenges. J Nutr Health Aging. 2013 Sep;17(9):741-3. PubMed PMID: 24154645; PubMed Central PMCID: PMC4471842.
c. Woods AJ, Mark VW, Pitts AC, Mennemeier M. Pervasive cognitive impairment in acute rehabilitation inpatients without brain injury. PM R. 2011 May;3(5):426-32; quiz 432. PubMed PMID: 21570030; PubMed Central PMCID: PMC3275913.
d. Mark VW, Woods AJ, Mennemeier M, Abbas S, Taub E. Cognitive assessment for CI therapy in the outpatient clinic. NeuroRehabilitation. 2006;21(2):139-46. PubMed PMID: 16917160.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/adam.woods.1/bibliography/45511051/public/

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

NIA R01AG064587 (Woods, Adam; Bowers, Dawn; Alexander, Gene; MPIs) 08/01/19-04/31/24
National Institutes of Health
Revitalizing Cognition in Older Adults at Risk for Alzheimer's Disease with Near-Infrared Photobiomodulation
This five-year R01 multisite Phase II randomized clinical trial will investigate the impact of near-infrared (NIR) photobiomodulation on cognition and mitochondrial function in older adults at risk for Alzheimer's disease. University of Florida (parent site) and the University of Arizona will perform a six-week intervention using NIR and assess changes in cognition, functional brain response and mitochondrial function (31P magnetic resonance spectroscopy) in a population of 168 older adults.
Role: MPI

NIA R01AG054077 (Woods, Adam; Cohen, Ronald; Marsiske, Michael; MPIs) 09/01/16-08/31/21
National Institutes of Health
Augmenting Cognitive Training in Older Adults (ACT)
This study is a Phase III definitive multi-site randomized clinical trial with an adaptive design that will establish the benefit of delivering adjunctive transcranial direct current stimulation (tDCS) with cognitive training in older adults to combat cognitive aging. This trial measures both trial success and intervention mechanisms using multimodal neuroimaging and magnetic resonance spectroscopy, as well as comprehensive neurocognitive and functional assessment.
Role: MPI

NIA T32AG020499 (Marsiske/Woods/Smith; MPIs) 05/01/20-04/30/25
National Institutes of Health $1,788,970
Research Training in Non-Pharmacological Interventions for Cognition in Aging, MCI, and Alzheimer's Disease
This pre-doctoral training grant will provide dedicated research training to PhD students in non-pharmacological intervention methods for remediating age-related cognitive decline, cognitive symptoms of MCI and AD as well as methods for potentially preventing conversion to MCI and AD. The training program is designed around three substantive areas: 1) behavioral interventions, 2) multi-component compensatory interventions, and 3) non-invasive brain stimulation interventions. The training grant provides training to 6 predoctoral students per year.
Role: MPI

NIA U01AG062368 (Edwards, Jerri; PI) 09/30/18-05/31/21 (NCE)

National Institutes of Health
Planning an adaptive clinical trial of cognitive training to improve function and delay dementia
This two-year U01 project will develop the infrastructure for a large Phase II/III clinical trial investigating the impact of various forms of cognitive training on functional abilities and dementia conversation in patients with mild cognitive impairment. I will lead the UF site on this trial and will also lead the neuroimaging and data management for the pilot trial and in the subsequent full trial submission. This grant involves sites at University of South Florida (parent site), University of California San Francisco and the University of Florida.
Role: Site PI

NIA K01AG050707-A1 (Woods, Adam; PI) 09/30/16-05/31/21
National Institutes of Health
Neuromodulation of Cognition in Older Adults
The goal of this study will be to investigate the ability of transcranial direct current stimulation to enhance the effectiveness of cognitive training targeting attention, speed of processing, and working memory function in older adults. Training will focus on cognitive aging interventions and advanced magnetic resonance imaging and spectroscopy methods.
Role: PI

NIA R37AG033906 (Fillingim, Roger; PI) 06/01/19-04/31/24
National Institutes of Health
Understanding Pain and Limitations in Osteoarthritic Disease
The goal of this project is to evaluate transcranial direct current stimulation and mindfulness based stress reduction, alone and in combination, as treatments of chronic osteoarthritic knee pain in a 2 site phase II trial.
Role: Co-I

NIMH R21MH112206 (Woods, Adam; Ding, Mingzhou; MPIs) 01/15/18-/12/31/21 (NCE)
National Institutes of Health
Stimulating Theta Oscillations to Enhance Working Memory
This project will the impact of transcranial alternating current stimulation (tACS) on working memory network synchrony in the theta band of EEG using electrophysiology and functional magnetic resonance imaging.
Role: MPI

NIMH RF1MH114290-01 (Sadlier, Rosalind; PI) 07/19/17-07/18/21
National Institutes of Health
Mechanism and dosimetry exploration in transcranial electrical stimulation using magnetic resonance current mapping methods
The goal of this project is to pioneer an objective measure of current flow in the brain using state of the art magnetic resonance imaging methods combined with in scanner application of tDCS and tACS. This project will also assess the relationship between activation in working memory related regions from an NBACK fMRI task and correspondence of change following F3-F4 in scanner tDCS.
Role: Co-I

VA Merit Review (Clark, David; PI) 08/01/19-07/31/23
Cerebral networks of locomotor learning and retention in older adults
This four-year Merit application extends the ongoing collaborative work in R21AG053736 to investigate the impact of tDCS paired with complex walking as an intervention for mobility decline in older adults to a larger Phase II trial with increased mechanistic insight through multimodal neuroimaging. I will lead all aspects of tDCS clinical trial implementation in the trial.
Role: Co-I

McKnight Brain Research Foundation (Woods/Bowers, MPIs) 05/1/18-04/31/20
Near infrared brain stimulation in older adults.
The goal of this funding is to use near infrared brain stimulation to improve cognition, 31P MRS markers of ATP, and functional neuroimaging biomarkers of cognitive and metabolic decline in healthy aging in a 2-site phase II pilot trial.
Role: MPI