

AGE-RELATED MEMORY LOSS (ARML) PROGRAM AND COGNITIVE AGING AND MEMORY (CAM) PROGRAM

2018 ANNUAL REPORT



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

*Prepared for the McKnight Brain Research Foundation by the
University of Florida McKnight Brain Institute and Institute on Aging*

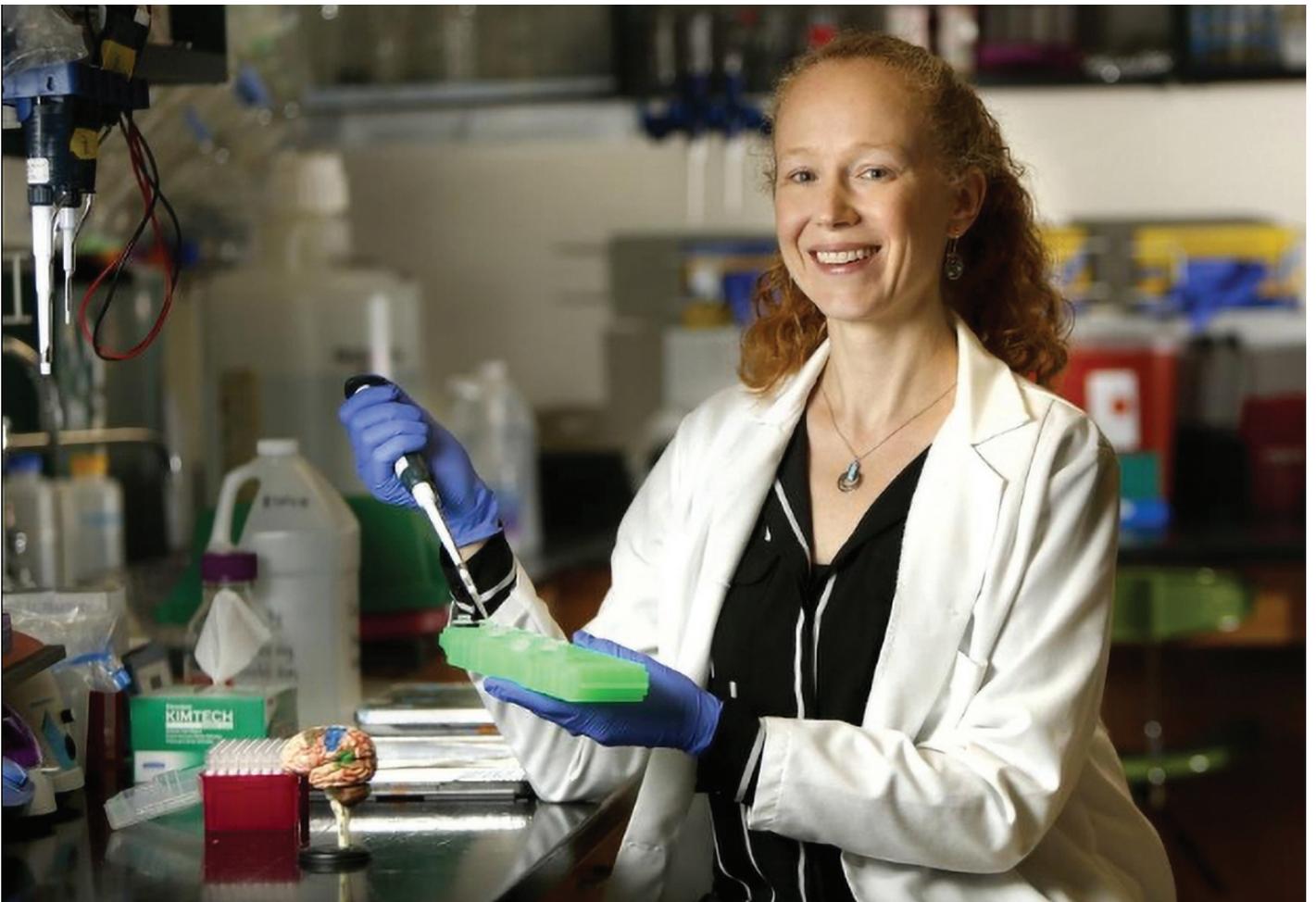
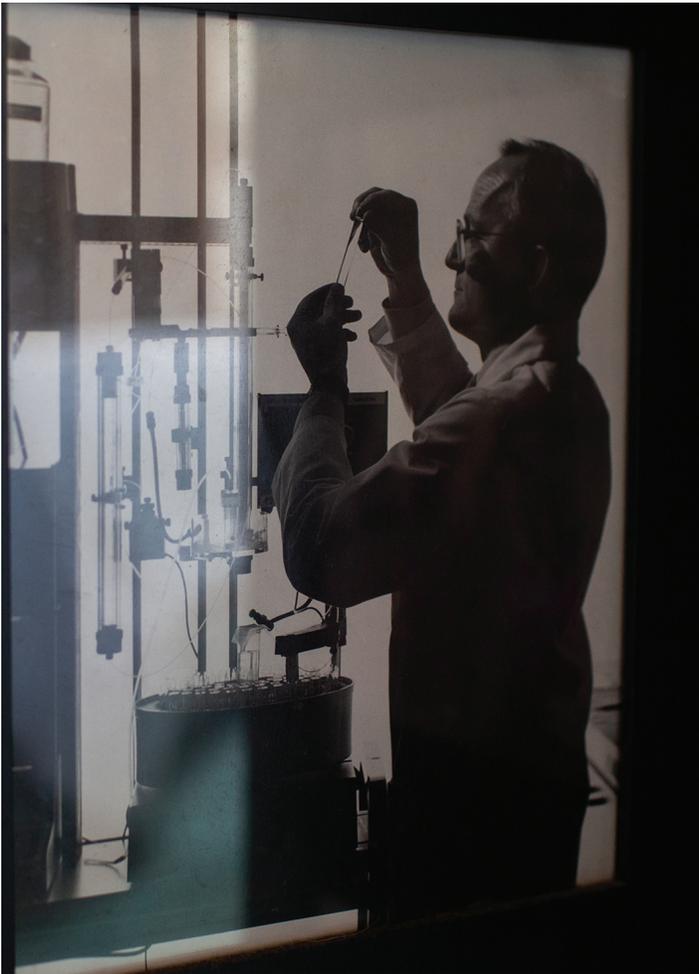


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January 15, 2019

The McKnight Brain Research Foundation
The SunTrust Bank
Mail Code FL-ORL-2160
300 South Orange Avenue, Suite 1600
Orlando, FL 32801

Dear Trustees:

We would like to share our continued gratitude to the McKnight Brain Research Foundation (MBRF) for its generous support of the University of Florida's Age-Related Memory Loss (ARML) program and the Center for Cognitive Aging and Memory Clinical Translational Research (CAM).

In 2018, the faculty in the ARML and the CAM were incredibly successful in obtaining extramural support. Between the two programs, faculty were awarded six R01s, a U01, and career development awards. Faculty in the ARML program were awarded a T32 training grant, a strategic priority for UF Health. The CAM faculty were so successful that the expanded and renovated research space is near capacity and the numerous research studies necessitated the hiring of additional study coordinators, now totaling 18.

Demetrius Maraganore, MD, was successfully recruited to UF as a professor in neurology and is part of the CAM core faculty with a research emphasis on successful cognitive and brain aging. Focusing on scholarly activity, Dr. Woods published over 20 manuscripts and is being considered for early tenure and promotion. Dr. Bizon and Dr. Foster received the UF Research Foundation Professorship award, given to tenured faculty in recognition of distinguished current research and strong research studies having the promise of continuing distinction.

Lastly, the two MBRF-supported programs have developed a 5-year strategic plan that includes collaboration with other MBRF-supported locations in the US. The plan will be integrated into the MBI's strategic plan and we look forward to the ongoing accomplishments from these programs. Thank you again for your support.

Sincerely,



David R. Nelson, MD
Interim Senior Vice President, Health Affairs &
President, UF Health



J. Adrian Tyndall, MD
Interim Dean, College of Medicine



Michael G. Perri, PhD
Dean, College of Public Health and Health Professions Robert G.
Frank Endowed Professor

January 18, 2019

The McKnight Brain Research Foundation
SunTrust Bank
Mail Code FL-ORL-Suite 1600
300 South Orange Avenue, Suite 1600
Orlando, FL 32801

Dear Trustees,

We are pleased to submit the 2018 annual report of the activities of the ARML and CAM programs supported by the MBRF. The long-time enabling support of the MBRF and its members is deeply appreciated by both the members of the programs and the UF Health leadership. The aid of the MBRF has been vital to the discoveries made by our researchers, and with our work with other members of the aging research groups. Together, we have made exciting scientific advances toward understanding, treating, and preventing age-related memory loss. The multidisciplinary and unique foci of the ARML and CAM investigators, in comparative and human studies respectively, is a unique strength of our programs, and a source of recruiting of new faculty and new students to the field.

This year we celebrated a special milestone in the history of the McKnight Brain Institute (MBI)—the 20th anniversary of the opening of the building and a major advance to the interdisciplinary neuroscience at UF. Two events were held to commemorate this: a scientific program held at the Harn Museum of Art and a celebration at the new Cade Museum. The scientific program featured outstanding keynote speakers Mary Woolley, president of Research!America, the nation's largest non-profit public education and advocacy organization for medical and health research, and Jennifer French, executive director of the Neurotech Network and one of the world's first "bionic women." The evening also contrasted the accomplishments of the MBI's first 20 years with the exciting prospects for future research across the wide array of neuroscience research programs now affiliated with the MBI. We finished the year enjoying a superb evening with food, music, and remembrance of Bill Luttge and his efforts, and the MBRF's wonderful contribution to making the MBI a reality.

The ARML and CAM programs have continued to enjoy great success, as indicated in the enclosed report. Grant funding, qualifications of applicants to train in the programs, and their productivity are outstanding. Together with our collaborations with the other three McKnight Brain Institutes, the programs are also increasing their professional and public status; social media efforts have shown growth as well.

The CAM and ARML programs are truly jewels of the MBI. Wise selection by the leadership of faculty, post-doctoral fellows and graduate students have led to new NIH grants in both programs, at least half a dozen new PhDs awarded, and notably, a number of training grants, T32s, to attract and train the next generation of scientists to the field. Increased size of both programs has occurred in the past year, and in addition the programs have leveraged new pilots and other exploratory grants in collaboration with the department of aging and geriatric research.

New activities conceived by the MBI executive committee are designed to:

- further enhance neuroscience education,
- provide greater diversity in our trainees, and
- increase the visibility of, and recruiting capacity for, new faculty and trainees at UF and nationally.

Our outstanding science writer, Michelle Jaffee, and our Communications Director, Todd Taylor, not only help support these activities and publicize our work, but have the accomplishments of our researchers more visible on

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our continually updated and informative website (www.MBI.ufl.edu) and the MBI newsletter, The Brainstorm. Moreover, they have raised our visibility with invigorated Twitter, Facebook, and other social media sites. Data from all of these sources indicate that these efforts have succeeded in communicating the work supported by the MBRF to an increasingly widespread audience.

The MBI visiting scholars program and the ongoing recruitments in aging researchers have added to our broad educational programs, all of which complement the Luttge Lectureship and enable additional prominent brain aging investigators to visit the UF campus. For example, the MBI Research Evenings, feature short, thematically organized presentations and provide networking opportunities. Trainee Enhancement Opportunities, similar to UF Faculty Enhancement Opportunities, allow research fellows, clinical fellows and graduate students to increase their skills and develop new methodologies attending courses, learning new techniques, or exploring areas of neuroscience beyond their home labs, enabling recipients to become truly interdisciplinary in their views and skills.

We continue to support the Summer Neuroscience Internship Program (SNIP; directed by Dr. Sara Burke of ARML and Dr. Jada Lewis of the CTRND), with over 25 undergraduates, 60% of whom are under-represented minority students. Our Research Fellowship program continues to provide pilot funds to trainees and junior scientists, enhanced by collaboration and cost sharing with our colleagues in the department of aging and geriatric research. Importantly, as a part of our mission we fund MBI travel awards to neuroscientists at UF who do not have the funds to attend conferences both here and abroad.

If we could, we would name all of our fantastic faculty who have made extraordinary contributions to the MBRF programs, however, in this overview we will limit the narrative to a listing of those who have received new NIH grants and awards worthy of note. The ARML had three new R01s awarded this year, to Dr. Foster, Drs. Burke and Bizon, and another a multi-PI grant to Dr. Bizon. Dr. Burke received the McKnight Brain Institute Leadership award for 2018, and she was also honored with an Exemplary Teaching Award from the UF College of Medicine for her leadership of the SNIP. Dr. Bizon was awarded a UF Term Professorship in recognition of her work, and both Dr. Bizon and Dr. Foster were recognized with UF Research Foundation Awards, given both for their research accomplishments and for the likelihood of their continued excellent work.

The CAM program has had an equally outstanding year. Working from their new positions in the College of Public Health and Health Professions and their new labs in the MBI, they have increased their staff to 18 coordinators and 7 graduate students. In addition, 4 students received their PhDs. Dr. Cohen received two new R01s, and Dr. Woods received a U01 grant. Dr. Woods has been so productive that he is being proposed for early promotion and tenure. Dr. Williamson was awarded an R21, and Dr. Aprinda Indahlastari received the NYC Neuromodulation and North American Neuromodulation Society Young Investigator award, under Dr. Woods.

The ARML and CAM have developed a 5-year strategic plan, which includes collaborations with the other three MBRF sites. Since the MBI's strategic plan is programmatically based, it will be easy to integrate the MBRF plan, enhancing interactions among the MBRF-supported and other MBI programs to further elevate our science.

Finally, we continue to do upgrades to the laboratories and facilities to provide optimal space for our researchers to work, and to enable more recruiting to our basic, translational, and clinical research programs.

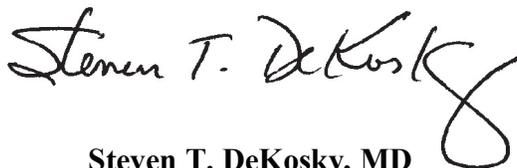
The CAM and ARML programs are exceeding our expectations, and we continue to be grateful to the MBRF Board for both your passion and support.

Sincerely,



Todd E. Golde, M.D., Ph.D.

Director
Director, 1Florida Alzheimer's Disease Research Center
Professor, Department of Neuroscience
College of Medicine

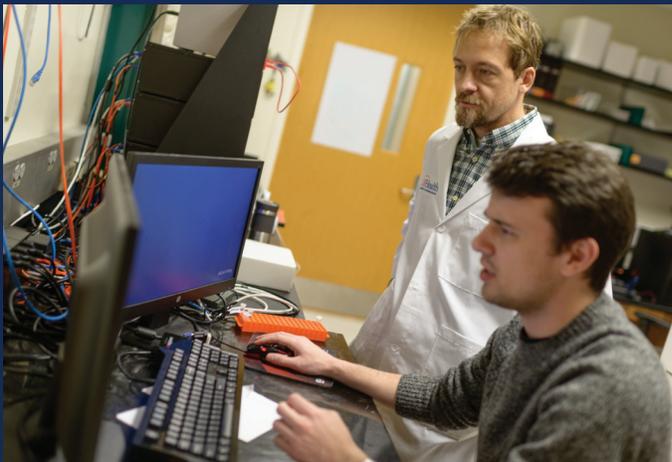
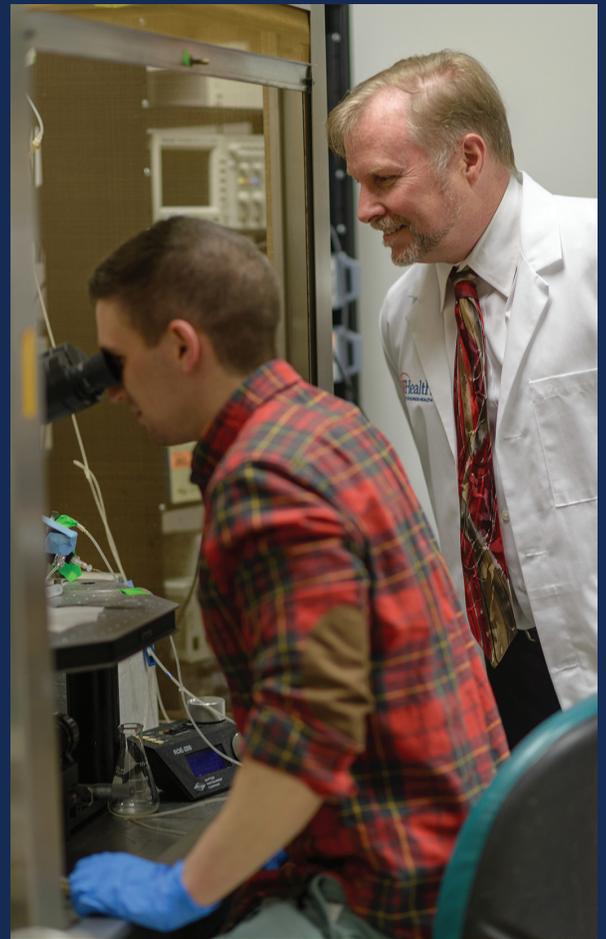


Steven T. DeKosky, MD

Deputy Director
Aerts-Cosper Professor of Alzheimer's Research
Associate Director, 1Florida ADRC
Professor of Neurology and Neuroscience

Age-related Memory Loss (ARML) Program and the Evelyn F. McKnight Chair for Brain Research in Memory Loss

2018 PROGRESS REPORT



Age-Related Memory Loss Program (ARML)

The ARML program consists of researchers dedicated to understanding and alleviation of age-related cognitive decline. MBRF sponsored support of ARML researchers is overseen by the ARML Program leadership consisting of Drs. Thomas Foster (Evelyn F. McKnight Chair for Research on Cognitive Aging and Memory and ARML Committee Chair), Lucia Notterpek (William T. and Janice M. Neely Professor and Chair of the Department of Neuroscience), Christiaan Leeuwenburgh (Chief, Division of Biology of Aging at the Institute on Aging and Leader of the Metabolism and Biomarkers and Research Career Development Cores), and Steven DeKosky (Rene Aerts-Virginia J. Cosper Professor of Alzheimer's Research and Deputy Director of the McKnight Brain Institute).

The ARML fund partially supports the faculty salaries of four principal investigators: Drs. Thomas Foster, Jennifer Bizon, Sara Burke, and Andrew Maurer. The four principal investigators of the ARML program continue to maintain a high level of productivity. Over the past year, the ARML faculty published at least 29 unique manuscripts (see Biosketches for details) and received NIH funding for three new research projects.

NIH/NIA R01AG037984 (PI Foster)

Title: Estrogen and Cognition over the Lifespan

The goal is to test the hypothesis that hormone replacement therapy improves cognition by enhancing NMDA receptors through redox regulation and that the closing of the therapeutic window for estrogen treatment is due to epigenetic mechanisms.

NIH/NIA R21AG058240 (multiple-PI with Burke and Bizon)

Title: Interactions of Perirhinal Tau Pathology and Aging in Cognitive Dysfunction

The goal of this award is to determine in the interaction between tau pathology, age, and declines in stimulus discrimination.

NIH/ NIA 1R01AG060778-01 (multiple-PI with Bizon)

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.

We are very proud of our ARML investigators who received recognition for achievements and contributions to science:

- Dr Sara Burke McKnight Brain Institute Leadership Award (2018).
- Dr. Burke was recognized with an Exemplary Teaching Award from the University of Florida College of Medicine due in part to her leadership in the UF Summer Neuroscience Internship Program (SNIP)

Two of our members received recognition from the University of Florida for scholarly achievements and outstanding research:

- Dr. Jennifer Bizon received a University of Florida Term Professor award in recognition of recent meritorious achievements and academic accomplishments.
- Dr. Bizon and Dr. Foster received University of Florida Research Foundation Professorship awards, which are given in recognition of faculty who have a distinguished current record of research and a strong research agenda that is likely to lead to continuing distinction in their fields.

ARML Program Activities

Research Support

The ARML leadership approved funding for several new projects. In many cases, the support contributed to the success in obtaining additional funding from NIA or the Claude D. Pepper Older Americans Independence Center:

- Natalie Ebner, Ph.D. and Yenisel Cruz-Almeida, Ph.D. *Oxytocin and Aging: A Neuro-Behavioral Analysis of Social Cognition and Prosocial Behavior in Young and Older Adults*. This project received R01 funding from NIA.
- Joseph McQuail, Ph.D. Postdoctoral Fellow (Bizon lab) *Mitochondrial Mechanisms of Age-Related Physical and Cognitive Decline*. This project received funding as a Pepper Junior Scholar Award.
- Brittney Yegla, Ph.D. Postdoctoral Fellow (Foster lab) *Exosomal Mediation of Exercise-Induced Benefits in Aging*. This study received funding as a Pepper Pilot and Exploratory Study.
- Sarah A. Johnson, Ph.D. Postdoctoral Fellow (Burke lab) to support an NIH K99/R00 award by helping to defray the costs of establishing and maintaining the colony of aged transgenic TH-Cre rats.
- Sara Burke Ph.D. received funding to support acquisition of touchscreen chambers and a high throughput Keyence BZX Fluorescence Microscope.

Several projects received letters of support from the ARML leadership:

- Andrew Liu Ph.D. Study *Circadian and Sleep Deregulation by Neuroinflammation in Traumatic Brain Injury and Aging*. Submitted as a Pepper Pilot and Exploratory project.
- Shinichi Someya, Ph.D. Study *Estrogen and Prevention of Hearing Loss*. Submitted as a Pepper Pilot and Exploratory project.

Developing the next generation of scientists

Training Grants

A major goal of the ARML program is the development and support of new scientists dedicated to innovative research in the understanding and alleviation of age-related memory loss. The ARML program was integral to the submission of two training grants to increase support for graduate students and postdoctoral fellows:

- A T32 grant “Clinical and Translational Pre-doctoral Training in Alzheimer’s Disease and Related Dementias” (Lewis/Bizon PIs) was funded. This grant will fund graduate students interested in Alzheimer’s Disease and Related Dementias and will include ARML support for those interested in research and training in cognitive changes associated with normal aging.
- A T32 grant was been submitted (Manini PI) to support post-doctoral trainees in a program focused on translational research addressing the multi-factorial causes and consequences of age-related decline. This proposal received a respectable priority score (31); however, it was not in the fundable range and will be resubmitted.

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Mentoring Graduate Students and Postdoctoral Fellows

Graduate students and postdoctoral scholars are mentored by the ARML faculty, who present their research at scientific meetings. During the past year associates of the ARML program presented their research at the McKnight Brain Research Foundation poster session at the Society for Neuroscience. We are delighted with our members that presented their work, including Abbi Hernandez, Ph.D. (Burke lab) who was awarded first place and Ms. Jolie Barter (Foster lab) who received honorable mention.

Graduate students and postdoctoral scholars from ARML labs have been recognized with accolades for their research, including funding for their research projects:

- Abbi Hernandez, Ph.D. (Burke lab) received an MBI Trainee Enhancement Opportunity Award
- Sarah Johnson, Ph.D. (Burke lab) received the highly regarded and competitive NIH K99 Pathway to Independence Award.

Two students received Bryan Robison awards:

- Dr. Caesar Hernandez (Bizon Lab) and Jolie Barter (Foster lab) were recognized for their neuroscience research.
- Dr. Hernandez also received a silver medal in the UF Medical Guild competition.

Promoting Collaboration and Communication

The support of the MBRF has been fundamental in collaborative efforts and maintaining communication among ARML researchers at the four MBRF academic sites. The following represents a subset of collaborations across MBRF-sponsored institutions and within UF. In many cases, these collaborations result in funded projects, published papers, or grants submitted to NIH. In addition, several collaborations provide examples of the translational potential of ARML discoveries and techniques.

- The 'Perirhinal Cortex' working group published a review for *Trends in Neurosciences* with MBRF faculty members from UF (Burke, Bizon, Bauer), Arizona (Ryan, Barnes), and Alabama (Roberson). This collaboration is serving as a foundation for future grant proposals.
- A collaboration between UF (Maurer) and Arizona (Barnes) will examine oscillations of brain activity in young and aged primates.
- A collaboration was established among UF faculty (Leeuwenburgh, Esser, Febo, Foster) with two major goals: To create an animal colony, for aging animals locally, in order to assist junior faculty interested in aging research; and to conduct longitudinal studies on cognitive decline following recommendations of the Cognitive Aging Summit III. This project received funding from the Pepper Center Metabolism & Translational Sciences Core.
- A collaboration with Yenisel Cruz-Almeida from the Department of Aging & Geriatric Research and the Cognitive Aging & Memory Clinical Translational Research Program (CAM-CTRP) will examine whether "epigenetic age" predicts different behavioral and brain variables. The Foster lab will provide epigenetic data from blood samples. A grant submission is expected in 2019.
- A collaboration among several UF clinical departments and the ARML group will examine the interaction of aging and sepsis on functional outcomes. This has resulted in a grant submission. In addition, a program project grant is planned for 2019. Project 4 (Price, Elie, Foster) involves

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examination of cognition impairment/resilience with markers of inflammation, brain aging, and measures of biological and cognitive reserve in patients, and the development of an animal model.

There are no easy solutions to age-related cognitive decline. This complex and multifaceted problem requires the collaborative efforts supported by the MBRF. The ideas and work by ARML faculty are considered significant, as evidenced by newly funded research projects, and MBRF support ensures the continued progress and productivity of ARML researchers.

Sincerely,

A handwritten signature in red ink, appearing to read "Tom Foster".

Thomas C. Foster, Ph.D.
Professor in the Department of Neuroscience and Genetics and Genomics Program
and Evelyn F. McKnight Chair for Research on Cognitive Aging and Memory
University of Florida, Evelyn F. and William L. McKnight Brain Institute

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Active Federal Funding as PI

PI	Project Number	Project Title	NIH Institute	FY	FY Total Cost
Foster, Thomas C	R37AG036800	SIGNALING CASCADES AND MEMORY DEFICITS DURING AGING	NIA	2018	\$ 291,924
Foster, Thomas C	R01AG049711	SYSTEMIC INFLAMMATION IN REGULATING THE ONSET AND PROGRESSION OF BRAIN AGING	NIA	2018	\$ 307,500
Foster, Thomas C	R01AG052258	SYSTEMIC INFLAMMATION IN REGULATING THE ONSET AND PROGRESSION OF BRAIN AGING	NIA	2018	\$ 375,000
Foster, Thomas C	R01AG037984	ESTROGEN AND COGNITION OVER THE LIFESPAN	NIA	2018	\$ 380,967
Bizon, Jennifer L	R01AG029421	Neural Mechanisms of Cognitive Decline in Aging	NIA	2018	\$ 303,060
Bizon, Jennifer L	RF1AG060778	DECISION MAKING AND BASOLATERAL AMYGDALA DYSFUNCTION IN AGING	NIA	2018	\$ 600,932
Bizon, Jennifer L/Burke Sara N	R21AG058240	INTERACTIONS OF PERIRHINAL TAU PATHOLOGY AND AGING IN COGNITIVE DYSFUNCTION	NIA	2018	\$ 190,625
Lewis, Jada M/Bizon, Jennifer L	T32AG061892	CLINICAL AND TRANSLATIONAL PRE-DOCTORAL TRAINING IN ALZHEIMER'S DISEASE AND RELATED DEMENTIAS	NIA	2018	\$ 302,193
Burke, Sara N	R01AG049722	THE CONTRIBUTION OF DECLINES IN FUNCTIONAL CONNECTIVITY TO COGNITIVE AGING	NIA	2018	\$ 375,166
Maurer, Andrew P	R01AGT055544	AGE-ASSOCIATED CHANGES IN HIPPOCAMPAL CIRCUITS AND COGNITIVE FUNCTION	NIA	2018	\$ 380,952
Maurer, Andrew P	R01MN109548	TESTING AND FORECASTING HIPPOCAMPAL THETA WAVE PROPAGATION IN LEARNING AND MEMORY	NIMH	2018	\$ 459,892

SUMMARY OF SCIENTIFIC ACHIEVEMENTS SINCE LAST REPORT:

Jennifer Bizon, PhD

- 8 new publications (1 additional under review), including in *The Journal of Neuroscience*, *Trends in Neuroscience*, *Neurobiology of Aging* and *eNeuro*.
- Multiple invited presentations and >12 poster presentations across 5 international meetings, with both undergraduate and graduate students winning numerous awards for their presentations
- Received both UF Term and Research Foundation Professorships
- New Grants:
 - RF1 (\$2,085,477.00 direct)
 - R21 (\$275,000.00 direct)
 - T32 (\$1,059,365.00).
 - Phase II DARPA grant (approximately \$200,000 to my laboratory)
 - co-sponsored funded K99/R00 (NIA) to SA Johnson
 - sponsored K01 (NIA) to JA McQuail
 - sponsored McKnight Brain Institute fellowship to Shelby Blaes.

Sara N. Burke, PhD

2018 was marked by a number of scientific achievements in the Burke laboratory. These include the identification of 'hub' neurons that are more vulnerable in advanced age (Hernandez et al., 2018, *Neurobiology of Aging*). Hub neurons are cells that have long-range projections and are more likely to be active. Higher activity levels and the need for long distance axonal transport is metabolically costly, rendering these neurons susceptible to energy imbalances that emerge during aging. Additionally, we have shown that a ketogenic diet is able to lead to both peripheral and brain health benefits in aged animals (Hernandez et al., 2018, *Journal of Gerontology*; Hernandez 2018, *Frontiers in Aging Neuroscience*) and have been funded to continue to pursue this work. Finally, we have continued to reverse translate human cognitive aging into animal models by further testing the face validity of our rodent mnemonic similarity task (Burke et al., 2018; *Frontiers in Systems Neuroscience*; Johnson et al., 2018, under revision *Frontiers in Systems Neuroscience*).

Other notable accomplishments in the 2017-2018 academic year include:

1. My first graduate student, Dr. Abbi R. Hernandez, completed and defended her PhD on March 23, 2018.
2. I recruited a new graduate student that I co-mentor with Dr. Maurer (Nicolas DiCola).
3. I served on 12 student committees, 1 student graduated with a PhD (Dr. Sruti Rayaprolu) and another student graduated with a masters degree (Constantine Kyritsopoulos).
4. I served on the mentorship panel for 3 postdoctoral fellows (Drs. Orsini, McQuail and Colon-Perez) that received NIH funding or submitted career development grants that scored in the fundable range. Dr. Orsini will be transitioning to research independence next year.
5. I continued to direct the Summer Neuroscience Internship Program and obtained funding and housing for 12 students to conduct summer research at UF.
6. I received the American Psychological Association Early Career Award for Distinguished Contribution in Cognitive and Behavioral Neuroscience (2017), and the McKnight Brain Institute Leadership Award (2018).
7. I served as Co-Director for one of the Neuroscience Graduate Program Core Principles courses (GMS6022). I also was an instructor in the Clinical Neuroanatomy Course for medical students (GMS6020), and I gave several additional lectures.
8. I chaired a symposium at an international meeting and gave 4 invited talks/seminars.

9. In November 2017 I served as an opponent for Ingrid Åmellem dissertation defense, entitled “Regulation of neurogenesis in the dentate gyrus and its role in anxiety-related behaviour in mice,” at the Norwegian University of Science and Technology, Kavli Institute for Systems Neuroscience in Trondheim, Norway. Notably, this Institute is directed by the 2014 Nobel Laureates Drs. May-Britt Moser and Edvard Moser.

Thomas C. Foster, PhD

Our research has been directed at two mechanisms of age-related cognitive decline, *impaired synaptic plasticity* and *epigenetic mechanisms for resiliency*. In examining these mechanisms, we employ animal models to examine age-related differences in response to inflammation and hormones.

Impaired synaptic plasticity: Impaired episodic memory is one of the earliest indicators of age-related cognitive decline. This rapid and flexible form of memory depends on synaptic plasticity, mediated by N-methyl-D-aspartate receptors (NMDARs). Our research demonstrates that an age-related decrease in episodic memory is due to a decrease in NMDAR function. In turn, the decrease in NMDAR function is linked to basic mechanisms of aging, increasing oxidative stress and inflammation. Published work defined inflammation as one source for increased oxidative stress (Kumar et al., 2018a). Non-steroidal anti-inflammatory drug (NSAID) treatment 1) enhanced episodic memory and 2) promoted NMDAR-dependent synaptic plasticity by 3) acting on redox state to increase NMDAR function.

We conclude that the mechanism for impaired cognitive function involves metaplasticity, defined as the plasticity of a plasticity mechanism (i.e. decrease NMDAR function Kumar et al., submitted). Moreover, in the case of normal aging and the onset of cognitive impairment, NMDAR hypofunction may be treatable since hypofunction emerges early, as a component of reversible redox signaling, rather than irreversible oxidative damage. In contrast, oxidative damage is more apparent with advanced age and neurodegenerative disease (Kumar et al., 2018b). In the case of treating inflammation, it is important to recognize that systemic inflammation and neuroinflammation play an important role in tissue repair, the response to toxic agents, and likely influence resilience to neurodegenerative disease. Other considerations include the increased use of NSAIDs by the elderly for pain relief and obstacles for NSAID treatment due to problems with efficacy and possible adverse effects that NSAIDs may create for the elderly. Thus, there may be better approaches than chronic anti-inflammatory treatments or NSAIDs may be combined with other anti-inflammatory treatments. For example, in another study (Yegla and Foster submitted) we found that food restriction decreased plasma markers of chronic systemic inflammation associated with aging. Thus, future studies will determine if manipulations of lifestyle factors that improve cognition (i.e. diet and exercise) are linked to NMDA receptor redox regulation.

Epigenetic mechanisms for resiliency: Gene expression in the aging brain depends on transcription signals generated by senescent physiology, interacting with genetic and epigenetic programs. In turn, environmental factors influence epigenetic mechanisms, such that an epigenetic-environmental link may contribute to the accumulation of cellular damage, susceptibility or resilience to stressors, and variability in the trajectory of age-related cognitive decline. Epigenetic mechanisms, DNA methylation and histone modifications, alter chromatin structure and the accessibility of DNA. Furthermore, small non-coding RNA, termed microRNA (miRNA) bind to messenger RNA (mRNA) to regulate translation. We published a paper describing one epigenetic mechanism (HDAC3 inhibition requires BET reader proteins) for the regulation of memory and transcription of genes linked to memory function (Sator et al., in press). In addition, we published a review paper outlining a hypothesized role for epigenetics in mediating changes in resiliency and brain reserve during aging. These ideas form part of the basis for a new NIH grant, which was funded this year (Foster PI).

Andrew Maurer, PhD

This marks the 2nd year of the Maurer lab. We have diligently spent the last year acquiring personnel and equipment. This past year, we were fortunate enough to begin recordings from old and young animals. We are negotiating a potential young/aged primate collaboration with Dr. Carol Barnes at the University of Arizona EMBL. We have published eight papers within the last year.

PUBLICATIONS IN PEER REVIEWED JOURNALS:

Jennifer Bizon, PhD

1. Hernandez CM, Orsini CA, Labiste CC, Wheeler AR, Ten Eyck TW, Bruner MM, Sahagian JJ, Harden SW, Frazier CJ, Setlow B, Bizon JL. *The changing role of the basolateral amygdala during intertemporal choice in aging. Under Review.*

2. Blaes SL, Orsini CA, Holik HM, Stubbs TD, Ferguson SN, Heshmati SC, Bruner MM, Wall SC, Febo M, Bruijnzeel AW, **Bizon JL**, Setlow B. (2018) Enhancing effects of acute exposure to cannabis smoke on working memory performance. *Neurobiol Learning and Memory* pii: S1074-7427(18)30277-6. doi: 10.1016/j.nlm.2018.12.001.
3. Orsini CA, Hernandez CM, **Bizon JL**, Setlow B. (2018) Deconstructing value-based decision making via temporally selective manipulation of neural activity: insights from rodent models. *Cogn Affect Behav Neurosci*. Epub ahead of print.
4. Blaes SL, Orsini CA, Mitchell M, Bezhold SM, Spurrell MS, **Bizon JL**, Setlow B (2018) Monoaminergic modulation of decision making under risk of punishment in a rat model. *Behavioural Pharmacology*. 29(8):745-761.
5. Hernandez CM, McQuail JA, Schwabe M, Burke SN, Setlow B, **Bizon JL** (2018) Age-related declines in prefrontal cortical expression of metabotropic glutamate receptors that support working memory. *eNeuro* 28:5(3) pii: ENEURO.0164-18.2018.
6. McQuail JA, Krause EG, Setlow B, Scheur DA, **Bizon JL** (2018) Stress-induced corticosterone secretion covaries with working memory in aging. *Neurobiology of Aging* 71:156-160.
7. Orsini CA, Heshmati SC, Garman TS, Wall SC, **Bizon JL**, Setlow B (2018) Contributions of medial prefrontal cortex to decision making involving risk of punishment. *Neuropharmacology* 139:205-216.
8. Burke SN, Gaynor LS, Barnes CA, Bauer RM, **Bizon JL**, Roberson ED, Ryan L. Shared functions of perirhinal and parahippocampal cortices: implications for cognitive aging. *Trends in Neuroscience*. 41(6):349-359.
9. 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(48): 11537-11548.

Sara N. Burke, PhD

1. Gaynor LS, Curiel RE, Penate A, Rosselli M, **Burke SN**, Wicklund M, Loewenstein DA, Bauer RM (2018). Visual Object Discrimination Impairment as an early predictor of Mild Cognitive Impairment and Alzheimer's disease. Under revision, *Journal of the International Neuropsychological Society*.
2. Colon-Perez LM, Turner SM, Lubke KN, Febo M*, **Burke SN*** (2018). *Multi-scale imaging reveals aberrant connectome organization and elevated dorsal striatal Arc expression in advanced age*. Under revision, preprint available: <https://www.biorxiv.org/content/early/2018/10/03/434191>. *Indicates shared corresponding author.
3. Johnson SA, Turner SM, Lubke KN, Cooper TL, Fertal KE, Bizon JL, Maurer AP, **Burke SN** (2018). Experience-dependent effects of muscimol-induced hippocampal excitation on mnemonic discrimination. Under revision, *Frontiers in Systems Neuroscience*. Preprint available: <https://www.biorxiv.org/content/early/2018/10/29/454744>
4. **Burke SN***, Turner SM#, Desrosiers CL, Johnson SA, Maurer AP* (2018). Perforant path fiber loss results in mnemonic discrimination task deficits in young rats. In press, *Frontiers in Systems Neuroscience*. *Indicates shared corresponding author, #These authors contributed equally.
5. 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. In press, *Frontiers in Aging Neuroscience*.
6. Sheremet A, Kennedy JP, Qin Y, Zhou Y, Lovett SD, **Burke SN**, Maurer AP (2018). Theta-Gamma Cascades and Running Speed. In press, *Journal of Neurophysiology*.
7. Gray DT, Umapathy L, Burke SN, Trouard TP, Barnes CA (2018). Tract-specific white matter correlates of age-related reward devaluation deficits in macaque monkeys. *Journal of Neuroimaging in Psychiatry and Neurology*, 3(2):13-26.
8. Hernandez AR, Reasor JE, Truckenbrod LM, Fertal KE, Maurer AP, **Burke SN** (2018). Differential effects of advanced age on neuronal ensemble activity in hippocampus, perirhinal cortex, and prefrontal cortex. *Neurobiology of Aging*, 70:217-232.
9. Hernandez CM, McQuail JA, Schwabe M, **Burke SN**, Setlow B, Bizon JL (2018). Age-related declines in prefrontal cortical expression of metabotropic glutamate receptors that support working memory. *eNeuro*, 5(3), eCollection 2018 May-Jun.
10. Malem-Shinitzki N, Zhang Y, Gray DT, **Burke SN**, Smith AC, Barnes CA, Ba D (2018). A Separable Two-Dimensional Random Field Model of Binary Response Data from Multi-Day Behavioral Experiments. *Journal of Neuroscience Methods*, 307:175-187.

11. Gaynor LS, Mizell J, Johnson SA, Maurer AP, **Burke SN** (2018). Aging disproportionately affects dual-functions of the perirhinal cortex: discrimination versus association. *Behavioral Neuroscience*, 132(3):138-151.
12. **Burke SN**, Gaynor LS, Barnes CA, Bauer RM, Bizon JL, Roberson RD, Ryan L (2018). Shared Functions of Perirhinal and Parahippocampal Cortices: Implications for Cognitive Aging. *Trends in Neurosciences*, 41(6):349-359.
13. Hernandez AR, Campos KT, Truckenbrod LM, Hernandez CM, Sakarya Y, McQuail JA, Carter CS, Bizon JL, Maurer AP, **Burke SN** (2018). The Antiepileptic Ketogenic Diet Alters Hippocampal Transporter Levels and Reduces Adiposity in Aged Rats. *Journal of Gerontology, Series A Biological Sciences and Medical Sciences*. 73(4):450-458.

Thomas C. Foster, PhD

1. Ivanov, 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 transcriptomic profiles: Subfield vulnerability to age and cognitive impairment. *Front Aging Neurosci* 2018, PMID: 4868850
2. 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* (2018a), 70, 184-193. PMID: 6119103.
3. Kumar, A., Yegla, B., **Foster, T.C.** Redox signaling in neurotransmission and cognition during aging. *Antioxid Redox Signal* (2018b), 18, 1724-1745. PMID: 5962336
4. Barter, J.D. and **Foster, T.C.** Aging in the Brain: New Roles of Epigenetics in Cognitive Decline. *The Neuroscientist*, Published online 6/7/2018.
5. Sartor, G.C., Malvezzi, A.M., Kumar, A., Andrade, N.S., Wiedner, H.J., Vilca, S.J., Janczura, K.J., Bagheri, A., Al-Ali, H., Powell, S.K., Brown, P.T., Volmar, C.H., **Foster, T.C.**, Zeier, Z., and Wahlestedt, C. Enhancement of BDNF expression and memory by HDAC3 inhibition requires BET reader proteins. *Journal of Neuroscience*, in press.
6. Kumar, A. and **Foster, T.C.** Alteration in NMDA Receptor Mediated Glutamatergic Neurotransmission in the Hippocampus During Senescence. *Neurochemical Research* (2018c), in press.

Andrew Maurer, PhD

1. Gaynor LS, Johnson SA, Mizell JM, Campos KT, **Maurer AP**, Bauer RM, Burke SN. Impaired discrimination with intact crossmodal association in aged rats: A dissociation of perirhinal cortical-dependent behaviors. *Behav Neurosci*. 2018 Jun;132(3):138-151. doi: 10.1037/bne0000246. PMID: 29809042
2. Hernandez AR, Reasor JE, Truckenbrod LM, Campos KT, Federico QP, Fertal KE, Lubke KN, Johnson SA, Clark BJ, **Maurer AP**, Burke SN. Dissociable effects of advanced age on prefrontal cortical and medial temporal lobe ensemble activity. *Neurobiol Aging*. 2018 Oct;70:217-232. doi: 10.1016/j.neurobiolaging.2018.06.028. Epub 2018 Jun 30. PMID: 30031931
3. Hernandez AR, Hernandez CM, Campos KT, Truckenbrod LM, Sakarya Y, McQuail JA, Carter CS, Bizon JL, **Maurer AP**, Burke SN. The Antiepileptic Ketogenic Diet Alters Hippocampal Transporter Levels and Reduces Adiposity in Aged Rats. *The journals of gerontology. Series A, Biological sciences and medical sciences*. 2018; 73(4):450-458. *PubMed [journal]* PMID: 29040389 PMID: PMC5861916
4. Nadel L, **Maurer AP**. Recalling Lashley and Reconsolidating Hebb. *Hippocampus*. 2018; *PubMed [journal]* PMID: 30216593
5. Sheremet A, Kennedy JP, Qin Y, Zhou Y, Lovett SD, Burke SN, **Maurer AP**. Theta-Gamma Cascades and Running Speed. *J Neurophysiol*. 2018 Dec 5. doi: 10.1152/jn.00636.2018. [Epub ahead of print] PMID: 30517044
6. Sheremet A, Qin Y, Kennedy JP, Zhou Y, **Maurer AP**. Wave turbulence and energy cascade in the hippocampus. *Front. Syst. Neurosci.* (In Press)
7. Burke SN, Turner SM, Desrosiers CL, Johnson SA, **Maurer AP** Perforant path fiber loss results in mnemonic discrimination task deficits in young rats *Front. Syst. Neurosci.* (In Press)

PUBLICATIONS (OTHER):

Sara N. Burke, PhD

1. Hernandez AR, **Burke SN** (2018). Age-related changes in 'hub' neurons. *Aging*, 10(10): 2551-2552.
2. **Burke SN**, Barnes CA (2018). The Contribution of Recollection, Familiarity and Discrimination to Object Recognition Deficits in Advanced Age. In *Handbook of Object Novelty Recognition*, ed Abdel Ennaceur.
3. **Burke SN** (2018). Award for Distinguished Scientific Early Career Contributions to Psychology: Sara N. Burke. *American Psychologist*.

Thomas C. Foster, PhD

1. Barter, J.D. and **Foster, T.C.** Cellular and Molecular Mechanisms for Age-Related Cognitive Decline. In Heilman and Nadeau (Eds.) *Cognitive Changes and the Aging Brain*

PRESENTATIONS AT SCIENTIFIC MEETINGS:

Jennifer Bizon, PhD

Invited

2018

1. "Neural mechanisms of age-associated alterations in cost-benefit decision making." Winter Conference on Brain Research. Whistler, British Columbia.
2. "Effects of normal aging on spatial memory" Irvine Learning and Memory Conference. Irvine, California.
3. "Effects of age on basolateral amygdala and decision making" Annual Interinstitutional McKnight Brain Research Foundation meeting. University of Alabama, Birmingham, AL.
4. "Neural mechanisms of executive function and decision making in aging" Department of Pharmacology & Therapeutics. Gainesville, Florida, January

Abstracts – Society for Neuroscience Meeting, San Diego, CA (13 in total)

1. A.-R. Wheeler^{1,2}, C. M. Hernandez^{1,2}, C. A. Orsini^{1,3}, T. W. Ten Eyck^{1,2}, C. C. Labiste^{1,2}, B. Setlow^{1,3}, **J. L. Bizon**^{1,2} Female Rats Show Greater Impulsive Choice Than Males in an Intertemporal Choice Task
2. Hernandez, C. M. Hernandez, Iii, K. Campos, L. M. Truckenbrod, Q. P. Federico, B. M. Moon, J. A. McQuail, A. P. Maurer, **J. L. Bizon**, S. N. Burke Nutritional Ketosis Enhances Cognitive Resilience in Young and Aged Rats
3. M. Kreher¹, S. A. Johnson², J.-M. Mizell⁷, D. K. Chetram¹, D. T. Guenther³, S. D. Lovett⁴, B. Setlow⁵, **J. L. Bizon**⁸, S. N. Burke⁴, A. P. Maurer⁶ Contributions of The Perirhinal Cortex to Spatial Delay Discounting
4. C. A. Orsini¹, S. L. Blaes¹, **J. L. Bizon**³, B. Setlow²; Sex Differences in the Relationship Between Risk-Taking Preference And Escalation Of Cocaine Self-Administration in Rats
5. T. W. Ten Eyck¹, C. M. Hernandez^{ii,2}, J. A. Mcquail², M. M. Bruner², S. Ghay², C. C. Labiste², A.-R. Wheeler², B. Setlow³, **J. L. Bizon**²; Altered GABAB Receptor Signaling In Basolateral Amygdala May Contribute to Age- Associated Differences in Intertemporal Choice
6. L. Altidor¹, T. S. Garman¹, S. Ramirez¹, A. M. Crider¹, D. G. Lamb², M. M. Bruner¹, A. M. Finner¹, E. W. Dirr³, F. Delgado³, K. P. Olczak³, A. P. Maurer¹, K. J. Otto³, S. N. Burke¹, B. Setlow², **J. L. Bizon**¹ Targeting GABAergic Mechanisms to Improve Prefrontal Cortical-Mediated Cognitive Flexibility in Novel Touchscreen-Based Reversal Learning Task
7. S. N. Burke¹, A. Crider², K. P. Olczak³, E. W. Dirr³, K. N. Lubke¹, J. Nick¹, B. Mclaurin¹, E. Atkinson¹, K. J. Otto⁴, A. P. Maurer⁵, D. G. Lamb⁷, B. Setlow⁶, **J. L. Bizon**⁸ Acute Vagus Nerve Stimulation Attenuates Novelty-Induced Arc Transcription In Dorsal Ca1
8. S. A. Johnson^{1,4}, S. M. Turner¹, K. N. Lubke¹, K. E. Fertal¹, A. P. Maurer^{1,2}, **J. L. Bizon**^{1,4}, S. N. Burke^{1,4,3} Hippocampal, Perirhinal, And Lateral Entorhinal Contributions to Mnemonic Discrimination in Young And Aged Rats

9. C. M. Hernandez, ⁱⁱⁱ, C. A. Orsini², C. C. Labiste¹, A.-R. Wheeler¹, T. W. Ten Eyck¹, M. M. Bruner¹, S. M. Singhal³, C. J. Frazier³, B. Setlow², **J. L. Bizon**¹ Aged Rats Do Not Use Basolateral Amygdala During Outcome Evaluation in An Intertemporal Choice Task
10. D. G. Lamb^{1,6,2}, T. S. Garman³, S. Ramirez³, A. Crider³, M. M. Bruner³, E. W. Dirr⁴, F. Delgado⁴, K. P. Olczak⁴, A. P. Maurer^{3,2,4,5}, K. J. Otto^{4,2}, S. N. Burke^{3,2}, B. Setlow^{1,2}, **J. L. Bizon**^{3,2} Effects of Vagus Nerve Stimulation on Selective Attention in Brown Norway Rats
11. S. M. Turner¹, S. A. Johnson¹, J. J. Flint¹, K. L. Robertson¹, J. A. Nick¹, S. D. Lovett¹, **J. L. Bizon**², S. N. Burke¹, A. P. Maurer¹ Perforant Path Fiber Loss Results in Mnemonic Similarity Task Deficits in Rats
12. J. A. Mcquail¹, S. A. Johnson¹, M. N. Litenski¹, S. Ghay¹, S. L. Rossi², P. Chakrabarty¹, B. I. Giasson¹, S. N. Burke¹, P. R. Rapp², **J. L. Bizon**¹ Normal Aging Increases Susceptibility to Human Wild Type Tau in Transentorhinal Cortex
13. S. L. Blaes¹, C. A. Orsini¹, H. Holik¹, **J. L. Bizon**³, B. Setlow²; Effects of Inactivation of the Lateral Habenula On Risky Decision Making

Sara N. Burke, PhD

Symposium

April 22, 2018 International Conference on Learning and Memory (International). Rethinking content-based parcellation of the medial temporal lobe. Speakers: Lee Ryan (University of Arizona), **Sara Burke** (University of Florida, Cyriel Pennartz (University of Amsterdam), Kristen Scaplen Kerr (Brown University). **Role: Organizer and co-chair**

Talks

Dec 11, 2018 Clinical Translation Aging Research Seminar, Gainesville, FL. "Neural Network and Metabolic Mechanisms of Cognitive Aging"

Dec 4, 2018 University of California, Irvine Center for Neurobiology of Learning and Memory Colloquium. "Neural Network and Metabolic Mechanisms of Cognitive Aging"

Sep 6, 2018 University of Florida, Department of Neuroscience Seminar, Gainesville, FL. "Linking Cognitive Aging to Cortical Connectivity: Why We Should Ask More of Our Rats"

Feb 19, 2018 University of Texas, Dallas Center for Vital Longevity, Dallas, TX. "A Systems-level Understanding of Cognitive Aging in Pre-clinical Models"

Selected Abstracts

1. Hernandez AR, Hernandez CM, Campos K, Truckenbrod LM, Federico QP, Moon BM, McQuail JA, Maurer AP, Bizon JL, **Burke SN** (2018). Nutritional ketosis enhances cognitive resilience in young and aged rats. *Society for Neuroscience* 48: San Diego, CA.
2. **Burke SN**, Crider A, Olczak KP, Dirr EW, Lubke KN, Nick J, McLaurin B, Atkinson E, Otto KJ, Maurer AP, Lamb DG, Setlow B, Bizon JL (2018). Acute vagus nerve stimulation attenuates novelty-induced arc transcription in dorsal CA1. *Society for Neuroscience* 48: San Diego, CA.
3. Johnson SA, Turner SM, Lubke KN, Fertal KE, Maurer AP, Bizon JL, **Burke SN** (2018). Hippocampal, perirhinal, and lateral entorhinal contributions to mnemonic discrimination in young and aged rats. *Society for Neuroscience* 48: San Diego, CA.
4. McQuail JA, Johnson SA, Litenski MN, Ghay S, Rossi SL, Chakrabarty P, Giasson BI, **Burke SN**, Bizon KL (2018). Normal aging increases susceptibility to human wild type tau in transentorhinal cortex. *Society for Neuroscience* 48: San Diego, CA.

Thomas C. Foster, PhD

Talks

1. miRNA in circulating microvesicles as biomarkers for age-related cognitive decline, Winter Conference of Neural Plasticity Jan 27-Feb 3, 2018, Curacao.
2. Redox regulation of NMDA receptors contributed to age-related impairment of episodic memory, Winter Conference of Neural Plasticity Jan 27-Feb 3, 2018, Curacao.

Posters

1. J. BARTER, A. RANI, A. KUMAR, T. C. FOSTER. "Adulthood infections alters synaptic gene transcription and contributes to age-related memory loss" Soc for Neurosci 2018
2. A. KUMAR, T. C. FOSTER. "Both GluN2A and GluN2B contribute to the induction of the redox-mediated potentiation of NMDA receptor synaptic function at CA3-CA1 hippocampal synapses of aged animals" Soc for Neurosci 2018
3. G. SMITH, A. RANI, A. KUMAR, T.C. FOSTER. "Investigation of age-related impairment in pattern separation employing modified version of water maze beacon task" Soc for Neurosci 2018
4. B. YEGLA, T. FOSTER, A. KUMAR. "Frontal upregulation of serine racemase alters cognitive flexibility in middle age rats" Soc for Neurosci 2018

Andrew Maurer, PhD

1. Multiple posters at SfN. 2018.

PRESENTATIONS AT NON-SCIENTIFIC MEETINGS OR EVENTS:

Thomas C. Foster, PhD

1. Cellular and Molecular Mechanisms for Age-Related Cognitive Decline, for the Emerging Frontiers in Biomedical Research Seminar Series. Rutgers Robert Wood Johnson Medical School 9/25/2018.

AWARDS (OTHER):

Jennifer Bizon, PhD

1. University of Florida Term Professor
2. University of Florida Research Foundation Professor

Sara N. Burke, PhD

1. 2018 McKnight Brain Institute Leadership Award
2. 2018 Exemplary Teaching Award, University of Florida College of Medicine

Thomas C. Foster, PhD

1. NIA R01 AG037984 (PI: Foster) 9/15/2018 to 7/31/2013
Estrogen and cognition over the lifespan
Jolie Barter received an honorable mention award in the judging of the scientific posters at the reception hosted by McKnight Brain Research Foundation (MBRF) in conjunction with the annual meeting of the Society for Neuroscience on November 4, 2018 in San Diego, CA. "Adulthood infections alters synaptic gene transcription and contributes to age-related memory loss".

FACULTY BIOGRAPHICAL SKETCHES: See page 75

TRAINEES:

Jennifer Bizon, PhD

a. Post-doctoral

Dr. Caitlin Orsini

- K99/R00 holder
- Has accepted a tenure track faculty position at University of Texas, Austin

Dr. Joseph McQuail

- K01 application received fundable score

b. Pre-doctoral

Caesar Hernandez (graduate student)

- Bryan Robinson award
- Neuroscience graduate student of the year
- Silver medal in the Medical Guild competition
- Selected as a fellow in National Scholars Program associated with Society for Neuroscience
- Travel fellowship from the International Behavioral Neuroscience Society
- Received PhD December 2018

Shelby Blaes (graduate student)

- McKnight Brain Research Foundation fellowship

c. Other

- Hannah Holik and Lindsay Altidor (undergraduates) received first and second place in poster competition for the North Florida Chapter of the Society for Neuroscience meeting.
- Alexa Rae Wheeler (undergraduate) received a University Scholar's Program award

Sara N. Burke, PhD

a. Post-doctoral

2014-present: Sarah A. Johnson, Ph.D. McKnight Brain Inst. Fellowship and K99 recipient Postdoctoral research associate, University of Florida, McKnight Brain Institute Project: Perceptual discrimination deficits underlying age-related cognitive impairment

2018-present: Abbi R. Hernandez, Ph.D. Postdoctoral research associate, University of Florida, McKnight Brain Institute Project: Metabolic interventions for enhancing cognitive resilience in advanced age

b. Pre-doctoral:

2015-2018: Abbi R. Hernandez, M.S. F31 recipient Graduate Student, University of Florida Interdisciplinary Program in Biomedical Sciences Project: The effects of a ketogenic diet on the bi-directional association of cognitive and physical performance

2017-present: Nicholas DiCola Graduate Student, University of Florida Interdisciplinary Program in Biomedical Sciences Project: Age-related alterations in the hippocampal circuit (co-chair with Maurer)

c. Other:

2014-2018: Sean M. Turner, Undergraduate student, University of Florida Scholar's Program Project: Hippocampal-cortical interactions in mnemonic discrimination in young and aged rats

Thomas C. Foster, PhD

a. Post-doctoral

Brittney Yelga, PhD

Puja Sinha, PhD

b. Pre-doctoral

- (i) **Jolie Barter** (PhD student)
- (ii) **Garret Smith** (MD/PhD student)

- c. **Other**
Ashok Kumar, PhD, Associate Research Professor
Asha Rani (Technical)

Andrew Maurer, PhD

- b. **Pre-doctoral:**
Nick DiCola (co- with Burke)
Jack Kennedy
Dylan Gunther

CLINICAL/TRANSLATIONAL PROGRAMS:

Thomas C. Foster, PhD

- a. **New programs**

A group at the University of Florida has submitted an NIH grant on sepsis and cognitive decline during aging. It was scored at the 30th percentile and will be resubmitted. Much of the preliminary data for the resubmission was generated by the Foster lab and involves age-related and sex-related differences in the brains response to sepsis. A manuscript related to this work will be submitted early next year.

A collaboration with Yenisel Cruz-Almeida on a project entitled "Epigenetic Aging and Chronic Pain 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. Results for the Cruz-Almeida group suggest that a similar clinically-relevant brain aging biomarker is negatively impacted by the complex experience of chronic pain in older adults (Cruz-Almeida et al., in press). Thus, the proposed study focuses on the estimation of "epigenetic age" analyses in blood samples of participants with and without chronic pain to determine whether an epigenetic age biomarker is sensitive to the presence and impact of chronic pain and associations to a "brain age" biomarker. The Foster lab is currently providing measures of the epigenetic clock from blood samples.

We have established an animal colony for aging animals locally. This collaboration with the Pepper Center Metabolism & Translational Sciences Core is designed to assist junior faculty interested in aging research and promote longitudinal studies on age-related cognitive decline. We have created protocols to assess healthspan domains by non-invasive physical/cognitive performance tests and non-invasive technologies (fMRI). under the supervision of ARML faculty. Currently, we a collaboration with several UF faculty (Leeuwenburgh, Esser, Febo) for longitudinal studies to address recommendations by the Cognitive Aging Summit III.

TECHNOLOGY TRANSFER: NA

BUDGET UPDATE: See page 61

Jennifer Bizon, PhD

Current and pending grant support

R01 AG02942 (NIH- NIA)

2014/05/15-2019/05/19

Neural mechanisms of age-related cognitive decline

Principal Investigator: Jennifer L Bizon

The goal of this project is to determine how age-related alterations in GABAergic signaling mechanisms in prefrontal cortex contribute to impairments in working memory, behavioral flexibility and decision making.

RF1AG60778 (NIH-NIA) 2019/09/01-2024/08/31
Decision making and basolateral amygdala dysfunction in aging
Principal Investigator: Jennifer L Bizon (Setlow, Frazier MPIs)
The goal of this project is to determine the neural circuits that mediate alterations in decision making that occur in aging and Alzheimer's disease.

T32 AG061892 (NIH-NIA) 2019/09/01-2024/08/31
Clinical and translational pre-doctoral training in Alzheimer's disease and related dementias
Principal Investigator: Jennifer L Bizon (Lewis MPI)
The goal of this project is to provide training to PhD students in research related to AD and related dementias.

R21AG058240 (NIH-NIA) 2018/03/15-2020/03/01
Interactions of perirhinal tau pathology and aging in cognitive dysfunction
Principal Investigator: Jennifer L Bizon, (Burke MPI)
The goal of this project is to determine the early cognitive consequences of tau pathology in aged perirhinal cortex.

R01 DA036534 (NIH-NIDA) 2015/03/15-2020/03/31
Risk taking and cocaine use: interactions, mechanisms, and therapeutic targets
Co-Investigator: Jennifer L Bizon (Setlow PI)
The goal of this project is to determine neural mechanisms underlying relationships between risk taking behavior and cocaine self-administration.

R01 R01AG049722 (NIH-NIA) 2016/01/05-2021/01/15
The contribution of declines in functional connectivity to cognitive aging
Co-Investigator: Jennifer L Bizon (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.

R01MH109548 (NIH-NIMH) 2016/01/01-2021/10/01
Testing and forecasting hippocampal theta wave propagation in learning and memory
Co-Investigator: Jennifer L Bizon (Maurer PI)
The goal of this project is to investigate how basal forebrain and entorhinal input to hippocampus regulate brain rhythms in behaving animals.

Ed and Ethel Moore Alzheimer's Disease Pilot Grant (FI-DOH) 2017/02/01-2019/02/01
Impact of perirhinal cortical tau pathology on pre-clinical cognitive decline
Principal Investigator: Jennifer L Bizon (Burke MPI)
The goal of this project is to develop a rat model of Alzheimer's disease tau pathology and to explore perceptual discrimination as a behavioral biomarker of disease.

Targeted Neuroplasticity Training Award (DoD) 2017/01/01-2021/01/01
Cognitive augmentation through neuroplasticity
Project Leader: Jennifer L Bizon (Otto PI)
The goal of this project is to explore peripheral nerve stimulation as a means to enhance cognition.

CURRENT MENTORED SUPPORT

K99DA041493 (NIH-NIDA) 2016/03/01 -2020/02/28
Neural circuits and mechanisms underlying maladaptive risk-taking following cocaine self-administration
Principal Investigator: Caitlin A Orsini, **co-Sponsor: Jennifer L Bizon**

K99AG058786 (NIH-NIA) 2018/06/01 -2022/08/31
Hippocampal and dopaminergic mechanisms of novelty detection underlying cognitive decline
Principal Investigator: Sarah Johnson, **co-Sponsor: Jennifer L Bizon**

K01AG061263 (NIH-NIA) Pending
Epigenetic mechanisms of stress and age-related cognitive decline
Principal Investigator: Joe McQuail, **Sponsor: Jennifer L Bizon**
Approved for funding

Sara N. Burke, PhD

01/01/16-11/30/20

1R01AG049722, National Institute on Aging

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.

Role: PI

2017/01/01-2020/12/31

DARPA Targeted Neuroplasticity Training

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.

Role: Co-PI (project leader for Task 1.2)

08/15/16-05/30/18

1R21AG051004

Title: Single-Cell Imaging of Functional Connectivity as a Window into Cognitive Aging

The major goal of this award is to develop novel methods for quantifying functional connectivity between memory-associated brain structures in young and aged rats.

Role: PI

2017/02/01-2019/01/31

Florida Department of Health Ed and Ethel Moore Alzheimer's Disease Research Program

Grant: 7AZ06

Impact of Perirhinal Cortical Tau Pathology on Pre-Clinical Cognitive Decline

Role: co-PI (contact Co-PI Jennifer L., Bizon)

The goal of this proposal is to develop and validate a rat model of human tauopathy.

2016/09/01-2021/06/30

NIH/NIMH R01MH109548 (Maurer, PI)

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.

Role: Co-I

2017/03/31-2022/01/31

NIH/NIA R01AG055544 (Maurer, PI)

Title: Age-associated changes in hippocampal circuits and cognitive function

Role: Co-I

Pending

NIH/NIA R21AG058240 (multiple-PI with Bizon)

Interactions of Perirhinal Tau Pathology and Aging in Cognitive Dysfunction

Impact: 23, percentile: 8%

Pending council review

EDUCATIONAL PROGRAMS FOCUSING ON AGE RELATED MEMORY LOSS:

Jennifer Bizon, PhD

a. Scientific

- Received a new training grant from the National Institute on Aging (see above) which will support up to 5 PhD students whose research is related to cognitive aging and Alzheimer's disease

Sara N. Burke, PhD

Director of the Summer Neuroscience Internship that sponsored students to conduct research in MBI laboratories.

Thomas C. Foster, PhD

a. Scientific

- A T32 grant “Clinical and Translational Pre-doctoral Training in Alzheimer’s Disease and Related Dementias” (Lewis/Bizon PIs) was funded: This grant will fund graduate students interested in Alzheimer’s Disease and Related Dementias and will include training on areas associated with normal aging.
- A T32 grant has been submitted (Manini PI) to support post-doctoral trainees in a program focused on translational research addressing the multi-factorial causes and consequences of age-related decline.

COLLABORATIVE PROGRAMS WITH OTHER MCKNIGHT INSTITUTES, INSTITUTIONS AND RESEARCH PROGRAMS:

Jennifer Bizon, PhD

- Participating in the Inter-Institutional Communications Working Group.

Sara N. Burke, PhD

Member of the ‘Perirhinal Cortex’ working group and published a review for Trends in Neurosciences with faculty from UF (Bizon, Bauer), Arizona (Ryan, Barnes), and Alabama (Roberson). This is serving as a foundation for future grant proposals.

Thomas C. Foster, PhD

We continue to collaborate with other McKnight Brain Research Foundation sponsored institutes to examine genetic and epigenetic mechanisms for brain aging and cognitive decline (Ivanov et al., 2018). Recent work involves ongoing studies of non-polyA mRNA (Huentelman, UA) and quantification of long-noncoding RNA, including from human plasma exosomes (Lubin UAB).

Andrew Maurer, PhD

Pending negotiations on authorship, etc. we may begin a collaboration with Dr. Carol Barnes at the University of Arizona, on oscillations in the young and aged primate brain.

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

Sara N. Burke, PhD

Collaborative R01 with Ben Clark (University of New Mexico) and Kamran Diba (University of Michigan). Pending collaborative grant with Dominic ‘D’Agostino at University of South Florida

Thomas C. Foster, PhD

Regulation of BDNF by HDAC3 and BRD4: Dr. Gregory Charles Sartor (University of Connecticut), Dr. Zane Zeier (University of Miami Miller School of Medicine).

Andrew Maurer, PhD

As part of our recent NIA R01, we are collaborating with Dr. Kamran Diba at the University of Michigan, attempting to understand how neuron-to-neuron communication in the awake, behaving animal changes as a function of aging.

BRIEFLY DESCRIBE PLANS FOR FUTURE RESEARCH AND/OR CLINICAL INITIATIVES:

Jennifer Bizon, PhD

- New R01 submission on the role of the basolateral amygdala in decision making. Target Date: December 16th 2017.
- New R01 submission on effects of cannabis on cognitive aging
- Numerous manuscript submissions, most notably, several using optogenetic silencing of basolateral amygdala to determine its role in cost-benefit decision making and changes to decision making across the lifespan; one regarding the effects of chronic stress on working memory and neural substrates of this aspect of cognition; and one on the role of mGluRs in age-related decline of working memory

Sara N. Burke, PhD

- New R01 or PPG submission on modifiable risk factors and lifestyle interventions to enhance cognitive resilience in advanced age. Target Date: June 5th 2019.
- Numerous manuscript submissions, most notably, several using novel measurements of functional connectivity in the context of cognitive aging.

Thomas C. Foster, PhD

- UF Health Moonshot Proposal: Creating the Healthiest Generation

UF Health moonshot proposal identifies strategic opportunities where UF is uniquely positioned to improve the health and well-being of the next generation. The UF Health Deans and Directors Research Council and the UF College of the Arts have developed a proposal in collaboration with the academic health center's leading research teams, and for which all six UF Health colleges have agreed to participate.

The ultimate goal is to develop approaches and clinical tools for incorporating genomic and other biomarker data, personal lifestyle and community information into clinical decision-making. Theme 2 of the proposal deals with enhancing brain, neuromuscular and mental health for future generations.

- Proposed UF Epigenetics Core for examining the biology of aging.

The core will provide scientific and foundational support for discovery in the area of epigenetics of aging. The goal is to identify the epigenome-transcription interface and its disruption in aging. The aging phenotype is the result of a complex interaction between genetic, epigenetic and environmental factors. Evidence suggests that epigenetic changes (i.e., a set of reversible, heritable changes in gene function or other cell phenotype that occurs without a change in DNA sequence), may affect the aging process through altered transcription and may be one of the central mechanisms by which aging predisposes to many age-related diseases. Epigenetic mechanisms that are central to aging include DNA methylation, histone modifications, and microRNA (miRNA).

- A P01 proposal is planned in collaboration with clinical departments at UF. Our overarching hypothesis is that older adults who survive sepsis are more susceptible to persistent sepsis-induced organ dysfunction and have increasingly morbid outcomes because their host immune response fails to return to homeostasis. This includes progressive kidney, muscle and brain dysfunction driven by persistent myelodyscrasia, inflammation, immune suppression and protein catabolism. Project 4 (Foster/Price Pls) is designed to determine neurological and cognitive predictors of successful recovery of sepsis in older individuals and directly test whether the decreased functional and cognitive recovery seen in some older sepsis survivors is due to persistent systemic inflammation and neuroinflammation.

Andrew Maurer, PhD

- This is the start of my 3rd year as an Assistant Professor with an independent laboratory (which opened in late October of 2016). Current plans are to simply “stay the course”, maintaining our collaborations with Drs. Jen Bizon and Sara Burke. Once we demonstrate that we can maintain a consistent level of success, we will consider expanding the research initiative.

IF APPLICABLE, PLEASE PROVIDE ENDOWMENT INVESTMENT RESULTS FOR THE REPORT PERIOD: See page 69

WERE ANY FUNDS USED FOR A PROHIBITED PURPOSE DURING THE REPORT PERIOD? No

DO YOU RECOMMEND ANY MODIFICATION TO THE PURPOSE OR MANDATES IN THE GIFT AGREEMENT? No

DID ALL ACTIVITIES DURING THE REPORT PERIOD FURTHER THE PURPOSE? Yes

NEGATIVE EVENTS (LOSS OF PERSONNEL, SPACE, BUDGET ETC.): NA

ADDITIONAL COMMENTS: See letter on page 9

SIGNATURE, DATE AND TITLE OF PERSON SUBMITTING THE REPORT:



Thomas C. Foster, PhD

Professor, Department of Neuroscience and Genetics and Genomics Program
Evelyn F. McKnight Chair for Research on Cognitive Aging and Memory

Cognitive Aging and Memory and the Evelyn F. McKnight Chair for Clinical Translational Research in Cognitive Aging

2018 PROGRESS REPORT



December 10, 2018

Dear Trustees of the McKnight Brain Research Foundation:

This progress report for the Center for Cognitive Aging and Memory Clinical Translational Research (CAM) summarizes the activity of center and its faculty for the year ending December 31, 2018. We had another outstanding year, meeting the planned research objectives, with multiple achievements consistent with the mission of the CAM. Changes in the administrative and operational structure of the CAM that were described in last year's report have been completed. In the current year there was significant growth in center, which is summarized along with highlights of research accomplishments and programmatic developments.

With respect to the growth and development, a major accomplishment was the successful recruitment of Dr. Demetrius Maraganore, a senior neurologist from the North Shore Hospital and the University of Chicago. Dr. Maraganore has joined the core faculty of the CAM, along with a primary appointment in the Department of Neurology at the University of Florida. He is receiving partial salary support and start-up funds from CAM reserves that were set aside for this purpose. Dr. Maraganore comes to UF with the mission of conducting research on successful cognitive and brain aging, with a particular interest in developing interventions to promote successful cognitive and brain aging. His research will also focus on the analysis of large datasets from the Florida One initiative to develop predictive algorithms that can be used to identify at-risk individuals and to also tailor interventions according to their individualized profiles. He also is in the process of developing a Brain Wellness Program that will provide assessment and approaches to optimize the cognitive and functional abilities of older adults, I am co-directing this initiative with Dr. Maraganore.

Other areas of growth and development:

- We have recruited and deployed additional study staff as the number of funded projects has increased. We now have 18 study coordinators, along with 7 graduate students, two post-doctoral fellows, and multiple affiliated faculty with whom we collaborate. This expansion has resulted in even greater demand for office and research space, a need which is being addressed with Dr. Todd Golde and the McKnight Brain Institute Executive Committee, and also Dr. Glenn Smith the chairman of the Department of Clinical and Health Psychology.
- Our dedicated research space designed and constructed in the McKnight Brain Institute (MBI) building is being used to near full capacity as we continue to run participants through study protocols for our funded projects.
- The phlebotomy laboratory also continues to be very active with a phlebotomist who draws, processes and stores blood and other biospecimens collected in these studies, including from the Evelyn F. McKnight Brain Aging Registry (MBAR). We are also providing the repository for neuroimaging data obtained from the four MBI sites for this study.

The CAM faculty and trainees have been extremely successful over the past year, including several newly funded studies and many publications. Some activity is highlighted below and additional information is available in their respective biosketches.

- Dr. Adam Woods is now reaching a point where his external funding is such that he will be reducing his effort on his K01 career development award.
 - A U01 grant focusing on the cognitive training and older adults being conducted in conjunction with the University of South Florida and UCSF.
 - Published 20+ manuscripts in the past year.
 - Based on his productivity, Dr. Woods has been proposed for early tenure and promotion.
- Dr. Ron Cohen received two RO1 awards from NIA.
 - One a study examining contributions of the gut microbiome to HIV-Aging interactions on cognition and the brain. In collaboration with Dr. Shirish Barve (MPI), a microbiologist at

- University of Louisville who is leader in the microbiome field.
- Another study is being conducted with another related microbiome study examining alcohol use effects on the microbiome, brain and cognition (Cohen, MPI).
- Dr. Eric Porges has made considerable progress on K01 career development awards study and also has been implementing other intervention studies involving vagal nerve stimulation to enhance cognitive function.
- Dr. John Williamson, received a R21 from NIA to study vagal nerve stimulation effects on cognition in older adults at risk for MCI. He and I are leading efforts to implement a parallel registry to the MBAR in the Gainesville, VA as a part of the Brain Rehabilitation Research Center renewal.
- Dr. Damon Lamb, is working on his career development award from the Veterans Administration conducting a study of age associated changes in the brain's white matter connectivity.
- Dr. Joseph Gullett, a post-doctoral fellow, who I mentor, has published several manuscripts, co-authored a book chapter with me, and has just completed a KL-2 application for funding through the UF Clinical Translational Science Institute to facilitate transition to a research faculty position.
- Dr. Aprinda Indahlastari, mentored by Dr. Woods continues to be productive as well in her publishing of research findings and is also playing a significant role in the execution of the ACT project. She recently received the NYC Neuromodulation and North American Neuromodulation Society Young Investigator award based on work completed in Dr. Woods' lab.
- Graduate students –
 - Four completed their doctoral studies Vaughn Bryant, PhD; Amanda Garcia, PhD; Molly McLaren, PhD and Talia Seider, PhD.
 - Nicole Nissim, a neuroscience doctoral student is close to completing her dissertation under Dr. Woods' guidance.

Progress on existing projects:

- The ACT study is actively collecting data with 154 participants randomized in the past year and a half.
- The MBAR study of successful cognitive aging in people over the age of 85 is also now fully active at the four MBI sites, with approximately 35 participants assessed so far.
- We have now recruited 124 participants for the NIDDK RO1 study "Obesity and Type II diabetes: bariatric surgery effects on brain function and aging. Post-surgery follow-ups are underway.
- We are beginning to complete manuscripts based on analysis of the baseline data in several studies already underway.
- We expanded recruitment for the ARCH II study and also the SHARC U01 (Cohen and Cook, MPIs).
- The R56 grant from NHLBI (Williamson. Cohen), examining the effects of increasing cerebral blood flow on the brain and cognitive function in people with cardiovascular disease, is underway after overcoming many obstacles. We are excited to examine results as they accumulate.
- The McKnight Brain Research Foundation (MBRF) sponsored inter-institute initiatives are making excellent progress and are on track to complete enrollment by the end of 2019. We are planning on submitting an R01 grant proposal to NIA in the spring of 2019 with Dr. Gene Alexander as PI, and the other site leaders as co-PIs.

Thank you for the continuing support of the McKnight Brain Research Foundation. We look forward to continued productivity and scientific achievements in the coming year.

Sincerely,



Ronald Cohen, Ph.D., ABPP, ABCN
 Professor, Clinical and Health Psychology, Neurology, and Psychiatry
 Director, Center for Cognitive Aging and Memory Clinical Translational Research (CAM)
 Evelyn McKnight Chair for Clinical Translation in Cognitive Aging

Active Federal Funding as PI

PI	Project Number	Project Title	NIH Institute/ Federal Department	FY	FY Total Cost
Cohen,Ronald A	R01DK099334	OBESITY AND TYPE-2 DIABETES: BARIATRIC SURGERY EFFECTS ON BRAIN FUNCTION	NIDDK	2018	\$ 779,748
Cohen,Ronald A RC1 PI	P01 AA019072	ALCOHOL AND HIV: BIOHAVIORAL INTERACTIONS AND INTERVENTIONS	NIAAA	2018	\$ 110,695
Cook,Robert L/Cohen,Ronald A	U01AA020797	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	NIAAA	2018	\$ 861,518
Cohen,Ronald A	AA019072	ALCOHOL AND HIV-ASSOCIATED BRAIN DYSFUNCTION	NIAAA	2018	\$ 322,174
Cohen,Ronald A	DK020595	PILOT AND FEASIBILITY PROGRAM	NIDDK	2018	\$ 461,658
Barve,Shirish S/Cohen, Ronald A	1R01AG061065	ROLE OF GUT MICROBIAL DYSBIOSIS AND AGING ON HIV-ASSOCIATED NEUROCOGNITIVE AND BRAIN DYSFUNCTION	NIA	2018	\$ 779,748
Woods,Adam J/ Cohen, Ronald A	1R01AG054077	AUGMENTING COGNITIVE TRAINING IN OLDER ADULTS - THE ACT GRANT	NIH	2018	\$ 1,119,975
Woods,Adam J	1K01AG050707	NEUROMODULATION OF COGNITION IN OLDER ADULTS	NIA	2018	\$ 123,417
Ding,Mingzhou/Woods, Adam J	MH112206	STIMULATING THETA OSCILLATIONS TO ENHANCE WORKING MEMORY	NIMH	2018	\$ 216,877
Porges,Eric S Carter	K01AA025306	COGNITIVE AND FUNCTIONAL DEFICITS ASSOCIATED WITH REDUCED CORTICAL GABA IN HIV-INFECTED HEAVY DRINKERS	NIAAA	2018	\$ 160,729
Lamb,Damon	HR0011-17-2-0019	BRAIN CHANGES UNDERLYING EMOTIONAL AND EXECUTIVE ALTERATIONS IN TBI	DOD	2017	\$ 10,149
Williamson, John B	R21AG054876	TREATMENT OF MILD COGNITIVE IMPAIRMENT WITH TRANSCUTANEOUS VAGAL NERVE STIMULATION	NIA	2018	\$ 190,625

SUMMARY OF SCIENTIFIC ACHIEVEMENTS SINCE LAST REPORT:

Ronald A. Cohen, PhD

1. The ACT R01 grant from NIA, a multi-site MBI study to examine the augmenting effects of tDCS brain stimulation on cognitive training in the elderly (Cohen, Woods, Marskike, MPis) is now operating at near full capacity with recruitment that consistent with targeted enrollment. In addition to quarterly Data Safety Management Board meetings (with Dr. Wagster and other board members), we hold regular laboratory meetings to discuss progress. A manuscript that describes this randomized clinical trial was published (Woods, et., 2018). We are analyzing baseline data to address scientific questions related to cognitive and brain aging that will lead to the first set of publications.
2. The McKnight Brain Aging Registry (MBAR), an inter-institute study of successful cognitive and brain aging in people over 85 years is proceeding according to plan. We have collected large quantities of cognitive, neuroimaging and laboratory data from across the four institutes. Approximately half of intended sample has been recruited and assessed and preliminary analyses have been initiated. Two initial findings were presented this year at the Society for Neuroscience meeting and are being prepared for publication.
3. U01 grant to study of the effects of reducing alcohol consumption among HIV-infected people in the context of aging received IRB approval and recruitment is now underway in Miami. (Cohen, Cook, MPis);
4. Continuation of several ongoing R01 projects and a R56 study that focus on risk factors affecting cognitive aging. (e.g., WISE study that examines bariatric surgery induced weight loss effects on the brain and cognition). Other NIH supported projects include ARCH, HIV-ETOH 30-day challenge, HIV-ETOH Microbiome study, Marijuana effects of cognition in older adults (MAPLE). The R56 has recruited heart failure patients undergoing cardiac resynchronization to improve cardiac output is wrapping up with cognitive, neuroimaging and vascular indices being analyzed.
5. ROGUE R01 – funded by NIA: Study to examine HIV-aging interactions on the microbiome and effects on the brain and cognition.
6. Publications related to studies chemotherapy effects for breast cancer in older women (CAM-Nursing-Cancer Institute initiative). This year a third manuscript focusing on effects of chemotherapy and breast cancer itself on fatigue was accepted for publication.
7. Multiple manuscripts were published related to my lines of research as listed subsequently.
8. Special edition of *Frontiers in Aging Neuroscience* that focuses on neuroimaging for the study and assessment of cognitive and brain aging was completed and published this year. Dr. Cohen is the primary editor, Drs. Alexander, Visscher, Wright, and Woods (Co-editors). A list of the manuscripts in this special edition is included in the full report.
9. Mentoring of career development awards for several faculty continues (Woods, Porges, Lamb, Cruz, and Terry). Each has made exceptional progress in their research. Currently, working Dr. Joseph Gullett, a CAM post-doctoral fellow on development of a K01 career development award which we hope will lead to funding supporting a faculty position in CAM for him through the Department of Clinical and Health Psychology. I am also working with the Department of Neurology in the recruitment of a senior neuropsychological researcher who has multiple R01 grants. This individual would work in collaboration with Drs. Maraganore and myself on studies of cognitive and brain aging, and brain wellness.
10. Dr. Maraganore and I have met on an ongoing basis since his arrival at UF in September to facilitate his development of a brain wellness program in Neurology at UF. We also have focused on developing a R01 to examine the effects of the microbiome on cognitive and brain aging in successful agers and also adults with MCI.
11. Collaboration with Gainesville VA Brain Rehabilitation Research Center (BRRC) renewal. I serve on the BRRC executive board and scientific committees. As a central theme of the renewal, the BRRC is developing a registry of neuroimaging and cognitive data that is harmonized with the MBAR registry under my guidance. The goal is to leverage the large VA population of aging veterans to examine brain and cognitive aging, along with the effects of earlier traumatic brain injury, PTSD, and stroke.
12. Drs. DeKosky, Mitchell, Woods, and I have collaborated on the development of pilot study to examine whether intermittent hypoxia therapy has beneficial effects on cognition, specifically neural plasticity, in older adults.

Damon Geoffrey Lamb, PhD

Continued to advance research program through executing research funded by the DARPA, NIH, and VA. This included several proposals to investigate safe, non-invasive forms of vagal nerve stimulation in an aging human population as well as individuals with PTSD, who are at high risk of age-related diseases and disorders. I am also developing new MRI techniques to evaluate diseases of aging and normal age-related decline.

Demetrius M. Maraganore, PhD

I am the Principal Investigator (PI) of the Florida Health Ed and Ethel Moore Alzheimer's Disease Research Program application entitled "Utilizing Data from the Electronic Medical Record to Predict Alzheimer's and Dementia Risk". This was awarded on December 13, 2018. That grant aims to develop an Alzheimer's prediction model using data routinely captured by the University of Florida (UF) electronic medical record (EMR), to replicate the model using EMR data shared by the OneFlorida Clinical Research Consortium, to implement the replicated model into the UF EMR using clinical decision support (CDS) tools, and to share the replicated model and CDS tools with OneFlorida Clinical Research Consortium sites. The long-term goal is to create a Florida statewide Alzheimer's prediction and prevention initiative. I am also the PI of the Agency for Healthcare Research and Quality grant R01HS024057 entitled "Quality Improvement and Practice Based Research in Neurology Using the EMR". I supervised the building of structured clinical documentation support (SCDS) and CDS toolkits within the EMR, for the evaluation and management of patients with 11 different neurological indications (including memory disorders and brain health). These toolkits support the clinical practices of neurologists and are also used to support clinical research (including in cognitive decline, mild cognitive impairment, dementia, and Alzheimer's disease). The EMR toolkits that my team built are being shared with 15+ academic departments across the nation, and in return the participating sites are sharing deidentified electronically captured data into a registry, with the aims of quality improvement and practice-based research in neurology using the EMR. One of the projects includes an EMR-based pragmatic trial comparing the effectiveness of three memory and cognitive enhancing drugs in mild cognitive impairment. Regarding brain health (primary prevention of aging related cognitive decline, dementias, including Alzheimer's disease), as the past Chair of Neurology at NorthShore University HealthSystem in Evanston, IL, I developed and led the NorthShore Center for Brain Health. My team and I targeted populations at risk for dementia through community outreach and continuing medical education of physicians. The Center provided outpatient consultations that included risk assessments (of genetic and modifiable factors), personalized interventions (lifestyle, behavioral, and medical), and annual surveillance (early disease detection). In two years, more than 550 patients were evaluated and managed. This was one of the first brain health clinics in the United States. In the Center, my team and I also conducted clinical research, including point of care electronic data capture via SCDS and CDS tools built into the EMR. We developed a preliminary Alzheimer's prediction model using data routinely captured by the EMR. At the University of Florida, I am building and directing a similar Brain Health Clinic (that will evaluate and manage persons at high risk for dementia identified by the prediction model to be refined, replicated, implemented into the EMR as clinical decision support, and disseminated to OneFlorida Clinical Research Consortium practices via the recently awarded Ed and Ethel Moore grant).

Eric Porges, PhD

1. Initiation of NIH funded study (PI) data collection.
 - Study 1. Cognitive flexibility in the context of HIV and Alcohol
 - Study 2. Transcutaneous vagal nerve stimulation in MCI.
2. Development and testing of method for concurrent edited Magnetic Resonance Spectroscopy measurement of GABA, Glutathione and Alcohol, in humans.
3. Collaboration with ARML to apply Magnetic Resonance Spectroscopy in aging rodent models.

John B. Williamson, PhD

Since the last reporting period, I have made progress on several scientific fronts. I recently accepted a position within the Center for OCD and Anxiety Related Disorders (COARD) in the Department of Psychiatry. Further, Dr. Damon Lamb, from my lab group, also accepted a tenure track position in the COARD. In addition, I was asked to assume a leadership role within the Brain Rehabilitation Research Center as the lead of the Emotion Function Initiative. Together, these changes support our research mission emphasizing the role of chronic stress and mood disruption on the brain and behavioral outcomes. These shifts have already fostered several new initiatives.

I am co-lead on a BRRC wide center project in which we have updated and re-vamped our Center's registry. In the past, the registry was for patients with stroke and was used as a recruitment tool for many studies involving stroke in the group. However, we have now added traumatic brain injury, post-traumatic stress disorder, and, shortly, combat exposed healthy individuals to the registry. We have also added a longitudinal assessment cohort of these groups as well as blood, neuroimaging, and neuropsychological assessments. Dr. Ron Cohen is part of this process and we are intending to use this in a manner that is in concert with the ACTIVE and MBAR aging studies to address differences associated with military experience that modify aging trajectories.

Supporting this move to chronic TBI mechanistic assessment, we recently received DOD funding for a consortium project including the University of Pittsburgh, SUNY Downstate, Baylor, and UF. This project will begin enrolling participants in 2019 and is designed to develop precision medicine data for negative outcomes associated with TBI.

Further, we have multiple clinical trials underway furthering the development of our neurostimulation line of investigation of transcutaneous vagal nerve stimulation. These studies are also in parallel to mechanistic work initiated by our team funded by DARPA (targeted neuroplasticity training grant). Last September, funding for our tVNS and amnesic MCI project started (NIH R21) and we have been steadily enrolling participants with a target completion time of September 2019. Parallel to this, we have acquired promising data demonstrating sleep architecture modification associated with tVNS in veterans with PTSD.

In addition, in our R56 funded heart failure research line, we have added a secondary collaborator site, Mayo Jacksonville, to improve patient access and enable future funding in that regard.

Adam Joshua Woods, PhD

Since last report, I have acquired additional funding for my research on novel non-invasive interventions for remediating cognitive aging. In addition to existing funds for a multisite R01 randomized clinical trial across three of the McKnight Brain Institutes (The ACT study, n=360, \$5.8 million), a K01 performing a dose response companion study to my R01 (Stimulated Brain, n=80, \$612K), two R21s (1 PI, 1 Co-I) and an RF1 (Co-I), I was recently awarded funding in an MRBF pilot (MPI), U01 (site PI), R37 (Co-I) and VA Merit Grant (Co-I). My research program currently has been awarded over \$10 million dollars to find and implement novel non-invasive methods for intervening on cognitive aging and the prevention of dementia. Collectively, this body of work represents the CAM's efforts to pioneer novel non-invasive interventions for combating cognitive aging in older adults. The MBRF pilot investigates a novel form of non-invasive photobiomodulation for enhancing mitochondrial function and cognition in older adults. The U01 investigates the value of cognitive training in halting functional decline in people with mild cognitive impairment. The R37 investigates the efficacy of transcranial direct current stimulation and mindfulness-based stress reduction in alleviating chronic knee pain in older adults. The VA Merit grant extends our R21 project to a large Phase II clinical trial investigating the benefits of transcranial direct current stimulation paired with complex walking for enhancing executive function and mobility in older adults. My lab has grown to 21 lab members and continues to expand with funding success. <https://woodslab.phphp.ufl.edu>

PUBLICATIONS IN PEER REVIEWED JOURNALS:

Ronald A. Cohen, PhD

1. Burke SE, Babu Henry Samuel I, Zhao Q, et al. Task-Based Cognitive Fatigability for Older Adults and Validation of Mental Fatigability Subscore of Pittsburgh Fatigability Scale. *Front Aging Neurosci.* 2018;10:327.
2. **Cohen RA**, Gullett JM, Porges EC, et al. Heavy Alcohol Use and Age Effects on HIV-Associated Neurocognitive Function. *Alcohol Clin Exp Res.* 2018.

3. Cohen RA, Siegel S, Gullett JM, et al. Neural response to working memory demand predicts neurocognitive deficits in HIV. *J Neurovirol.* 2018;24(3):291-304.
4. Gullett JM, Lamb DG, Porges E, et al. The Impact of Alcohol Use on Frontal White Matter in HIV. *Alcohol Clin Exp Res.* 2018;42(9):1640-1649.
5. Monnig MA, Kahler CW, Cioe PA, et al. Markers of Microbial Translocation and Immune Activation Predict Cognitive Processing Speed in Heavy-Drinking Men Living with HIV. *Microorganisms.* 2017;5(4).
6. O'Shea DM, Dotson VM, Woods AJ, et al. Depressive Symptom Dimensions and Their Association with Hippocampal and Entorhinal Cortex Volumes in Community Dwelling Older Adults. *Front Aging Neurosci.* 2018;10:40.
7. O'Shea DM, Fieo R, Woods A, Williamson J, Porges E, **Cohen R.** Discrepancies between crystallized and fluid ability are associated with frequency of social and physical engagement in community dwelling older adults. *J Clin Exp Neuropsychol.* 2018;40(10):963-970.
8. O'Shea DM, Langer K, Woods AJ, et al. Educational Attainment Moderates the Association Between Hippocampal Volumes and Memory Performances in Healthy Older Adults. *Front Aging Neurosci.* 2018;10:361.
9. Porges EC, Woods AJ, Edden RA, et al. Frontal Gamma-Aminobutyric Acid Concentrations Are Associated With Cognitive Performance in Older Adults. *Biol Psychiatry Cogn Neurosci Neuroimaging.* 2017;2(1):38-44.
10. 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;8:239.
11. Rani A, O'Shea A, Ianov L, **Cohen RA**, Woods AJ, Foster TC. miRNA in Circulating Microvesicles as Biomarkers for Age-Related Cognitive Decline. *Front Aging Neurosci.* 2017;9:323.
12. Szymkowicz SM, Dotson VM, McLaren ME, et al. Precuneus abnormalities in middle-aged to older adults with depressive symptoms: An analysis of BDI-II symptom dimensions. *Psychiatry Res Neuroimaging.* 2017;268:9-14.
13. Szymkowicz SM, Woods AJ, Dotson VM, et al. Associations between subclinical depressive symptoms and reduced brain volume in middle-aged to older adults. *Aging Ment Health.* 2018:1-12.
14. Thompson PM, Andreassen OA, Arias-Vasquez A, et al. ENIGMA and the individual: Predi
15. White TL, Monnig MA, Walsh EG, et al. Psychostimulant drug effects on glutamate, Glx, and creatine in the anterior cingulate cortex and subjective response in healthy humans. *Neuropsychopharmacology.* 2018;43(7):1498-1509.
16. 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.* 2018;65:19-32. cting factors that affect the brain in 35 countries worldwide. *Neuroimage.* 2017;145(Pt B):389-408.

Damon Geoffrey Lamb, PhD

1. White TL, Monnig MA, Walsh EG, Nitenson AZ, Harris AD, Cohen RA, Porges EC, Woods AJ, **Lamb DG**, Boyd CA, Fekir S. Psychostimulant drug effects on glutamate, Glx, and creatine in the anterior cingulate cortex and subjective response in healthy humans. *Neuropsychopharmacology.* 2018;43(7):1498-509. doi: 10.1038/s41386-018-0027-7. **PubMed PMID: 29511334; PMCID: PMC5983539.**
2. Williamson JB, **Lamb DG**, Burtis DB, Haque S, E MZ, Kesayan T, Harciarek M, Heilman KM. Right hemispatial ipsilesional neglect with chronic right hemisphere strokes. *J Clin Exp Neuropsychol.* 2018;40(4):347-56. doi: 10.1080/13803395.2017.1347606. **PubMed PMID: 28812421.**
3. Rodriguez JA, Jr., **Lamb DG**, Salazar L, Correa LN, Mosquera DM, Schwartz ZJ, Cohen RA, Falchook AD, Heilman KM. Background distraction during vertical solid and character line bisections. *J Clin Exp Neuropsychol.* 2018;40(9):887-94. Epub 2018/04/05. doi: 10.1080/13803395.2018.1444735. **PubMed PMID: 29614901.**
4. **Lamb DG**, Balavage KT, Williamson JB, Knight LA, Heilman KM. The Influence of Focused and Sustained Spatial Attention on the Allocation of Spatial Attention. *J Int Neuropsychol Soc.* 2018:1-7. Epub 2018/11/30. doi: 10.1017/S1355617718000802. **PubMed PMID: 30486914.**

- Mosquera DM, Lamb DG, Garcia AM, Rodriguez JA, Correa LN, Salazar L, Schwartz ZJ, Cohen RA, Falchook AD, Heilman KM. Asymmetrical distractibility of global and focal visuospatial attention during segmental and total compound line bisections. *Neuropsychology*. 2018;32(7):843-9. Epub 2018/07/10. doi: 10.1037/neu0000455. PubMed PMID: 29985016.
- Cohen RA, Gullett JM, Porges EC, Woods AJ, Lamb DG, Bryant VE, McAdams M, Tashima K, Cook R, Bryant K, Monnig M, Kahler CW, Monti PM. Age Effects on HIV-Associated Neurocognitive Function. *Alcohol Clin Exp Res*. 2018. Epub 2018/10/30. doi: 10.1111/acer.13915. PubMed PMID: 30371953.
- Gullett JM, Lamb DG, Porges E, Woods AJ, Rieke J, Thompson P, Jahanshad N, Nir TM, Tashima K, Cohen RA. The Impact of Alcohol Use on Frontal White Matter in HIV. *Alcohol Clin Exp Res*. 2018;42(9):1640-9. Epub 2018/06/30. doi: 10.1111/acer.13823. PubMed PMID: 29957870; PMCID: PMC6120768.

Demetrius M. Maraganore, PhD

- Design and implementation of pragmatic clinical trials using the electronic medical record and an adaptive design.
Simon KC, Tideman S, Hillman L, Lai R, Jathar R, Ji Y, Bergman-Bock S, Castle J, Franada T, Freedom T, Marcus R, Mark A, Meyers S, Rubin S, Semenov I, Yucus C, Pham A, Garduno L, Szela M, Frigerio R, Maraganore DM. *JAMIA Open*. 2018 Jul;1(1):99-106. doi: 10.1093/jamiaopen/ooy017. Epub 2018 Jun 11. PMID: 30386852
- Long-term risk of depressive and anxiety symptoms after early bilateral oophorectomy.
Rocca WA, Grossardt BR, Geda YE, Gostout BS, Bower JH, Maraganore DM, de Andrade M, Melton LJ 3rd. *Menopause*. 2018 Nov;25(11):1275-1285. doi: 10.1097/GME.0000000000001229. PMID: 30358723
- Use of an Electronic Medical Record to Track Adherence to the Mediterranean Diet in a US Neurology Clinical Practice.
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Eric Porges, PhD

- Szymkowicz, S. M., Woods, A. J., Dotson, V. M., Porges, E. C., Nissim, N. R., O'Shea, A., ... Ebner, N. C. (2018). Associations between subclinical depressive symptoms and reduced brain volume in middle-aged to older adults. *Aging & Mental Health*, 1–12.
- Clark, D. J., Chatterjee, S. A., McGuirk, T. E., Porges, E. C., Fox, E. J., & Balasubramanian, C. K. (2018). Sympathetic nervous system activity measured by skin conductance quantifies the challenge of walking adaptability tasks after stroke. *Gait & Posture*, 60, 148–153.
- O'Shea, D. M., Dotson, V. M., Woods, A. J., Porges, E. C., Williamson, J. B., O'Shea, A., & Cohen, R. (2018). Depressive Symptom Dimensions and Their Association with Hippocampal and Entorhinal Cortex Volumes in Community Dwelling Older Adults. *Frontiers in Aging Neuroscience*, 10, 40.

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5. Wang, Y., Fridberg, D. J., Leeman, R. F., Cook, R. L., & Porges, E. C. (2018). Wrist-Worn Alcohol Biosensors: Strengths, Limitations, and Future Directions. *Alcohol*.
6. Chatterjee, S. A., Daly, J. J., Porges, E. C., Fox, E. J., Rose, D. K., McGuirk, T. E., ... Clark, D. J. (2018). Mobility Function and Recovery After Stroke. *Journal of Neurologic Physical Therapy*, 42(4), 1.
7. Cohen, R. A., Gullett, J. M., Porges, E. C., Woods, A. J., Lamb, D. G., Bryant, V. E., ... Monti, P. M. (2018). Age Effects on HIV-Associated Neurocognitive Function. *Alcoholism: Clinical and Experimental Research*.
8. O'Shea, D. M., Langer, K., Woods, A. J., Porges, E. C., Williamson, J. B., O'Shea, A., & Cohen, R. A. (2018). Educational Attainment Moderates the Association Between Hippocampal Volumes and Memory Performances in Healthy Older Adults. *Frontiers in Aging Neuroscience*, 10, 361.
9. Cohen, R. A., Siegel, S., Gullett, J. M., Porges, E., Woods, A. J., Huang, H., ... Ding, M.-Z. (2018). Neural response to working memory demand predicts neurocognitive deficits in HIV. *Journal of NeuroVirology*, 24(3), 291–304.
10. O'Shea, D. M., Fieo, R., Woods, A., Williamson, J., Porges, E., & Cohen, R. (2018). Discrepancies between crystallized and fluid ability are associated with frequency of social and physical engagement in community dwelling older adults. *Journal of Clinical and Experimental Neuropsychology*, 40(10), 963–970.

John B. Williamson, PhD

1. **Williamson, JB**, Drago, V, Harciarek, M, Falchook, AD, Wargovich, BA, Heilman, KM. (2018). Chronological effects of emotional valence on the self-selected retrieval of autobiographical memories. *Cognitive and Behavioral Neurology*, In press.
2. O'Shea D, Langer, K., Woods, AJ, Porges, E, **Williamson, JB**, O'Shea, A, Cohen, R. (2018) Educational attainment moderates the associated between hippocampal volumes and memory performances in health older adults. *Frontiers in Aging Neuroscience*.
3. Lamb, DG, Balavage, KT, **Williamson, JB**, Knight, LA, Heilman, KM. (2018) The influence of focused spatial attention and habitation of the allocation of spatial attention. *Journal of the International Neuropsychological Society*, In Press.
4. Mankowska, A., Heilman, K.M., **Williamson, J.B.**, Harciarek, M. (2018) Age related changes in the allocation of vertical attention. *Journal of the International Psychological Society*, In Press.
5. Makowska, A., Harciarek, M., **Williamson, J.B.**, Heilman, K.M. (2018) The influence of rightward and leftward spatial deviations on spatial attention on emotional picture recognition. *Journal of Clinical and Experimental Neuropsychology*, 1-12.
6. O'Shea, D., Fieo, R., Woods, A., **Williamson, J.B.**, Porges, E., Cohen, R. (2018) Discrepancies between crystallized and fluid ability are associated with frequency of social and physical engagement in community dwelling adults. *Journal of Clinical and Experimental Neuropsychology*, In Press.
7. O'Shea, D., Dotson, V., Woods, A., Porges, E., **Williamson, J.**, O'Shea, A., Cohen, R. (2018). Depressive symptom dimensions and their association with hippocampal and entorhinal cortex volumes in community dwelling older adults. *Frontiers in Aging Neuroscience*.
8. ****Williamson, J. B.**, Lamb, D. G., Burtis, D. B., Haque, S., Zilli, E. M., Kesayan, T., ... Heilman, K. M. (2018). Right hemispatial ipsilesional neglect with chronic right hemisphere strokes. *J Clin Exp Neuropsychol*, 1-10. doi:10.1080/13803395.2017.1347606
9. Morris, M.K., Bowers, D., **Williamson, J.B.**, Heilman, K.M. (2017). Alterations of emotional reactivity following right temporal lobectomy. *Neurocase*, 1-7.
10. Manikoska, A., Heilman, K.M., **Williamson, J.B.**, Biedunkiewicz, B., Debska-Slizien, A., Harciarek, M. (2017). Leftward bias of visual attention in patients with End-Stage Renal Disease receiving Dialysis: A neglected phenomenon. *Cognitive and Behavioral Neurology*, 30, 176-181.

Adam Joshua Woods, PhD

1. Indahlastari A, Albizu A, Nissim N, Traeger K, O'Shea A, **Woods AJ**. Methods to monitor accurate and consistent electrode placements in conventional transcranial electrical stimulation. *Brain Stimulation*. Accepted October 2018. Impact Factor: 6.078.
2. Cohen R, Gullet J, Porges E, **Woods AJ**, Bryant V, Mcadams M, Tashima K, Cook R, Bryant K, Monnig M, Kahler C, Monti P. Heavy alcohol use and age effects on HIV-associated neurocognitive function. *Alcoholism: Clinical and Experimental Research*. Accepted October 2018. Impact Factor: 2.716.
3. O'Shea D, Langer K, **Woods AJ**, Porges E, Williamson J, O'Shea A, Cohen R. (2018). Educational attainment moderates the association between hippocampal volumes and memory performance in healthy older adults. *Frontiers in Aging Neuroscience*. 10: 361. Impact Factor: 4.504.
4. Soyata A, Aksu S, **Woods AJ**, Iscen P, Sacar K, Karamursel S. Effects of transcranial direct current stimulation on decision making and cognitive flexibility in gambling disorder. *European Archives of Psychiatry and Clinical Neuroscience*. Accepted October 2018. Journal Impact Factor: 3.617.
5. Gedoth N, Esmaeilpour Z, Adair D, Chelette K, Dmochowski D, **Woods AJ**, Kappenman E, Parra L, Bikson M. (2019). Inherent physiological artifacts in EEG during tDCS. *NeuroImage*. 185: 408-424. Impact Factor: 5.835.
6. Wanigatunga A, Gill T, Marsh A, Hsu F, Yaghjyan L, **Woods AJ**, Glynn N, King A, Newton R, Fielding R, Pahor M, Manini T. (2018). Effect of hospitalizations on physical activity patterns in mobility-limited older adults. *Journal of the American Geriatric Society*. 49(11): 2167-2175. Impact Factor: 4.155.
7. Ahn H, Suchting R, **Woods AJ**, Miao H, Green C, Cho R, Choi E, Fillingim R. (2018). Bayesian analysis of the effect of transcranial direct current stimulation on experimental pain sensitivity in older adults with knee osteoarthritis: randomized sham-controlled pilot clinical study. *Journal of Pain Research*. 11: 2071-2082. Impact Factor: 2.645.
8. Pope C, Stavrinou D, Vance D, **Woods AJ**, Bell T, Ball K, Fazeli P. (2018). A pilot investigation on the effects of combination transcranial direct current stimulation and speed of processing cognitive remediation therapy on simulated driving behavior in older adults with HIV. *Transportation Research Part F: Traffic Psychology and Behavior*. 58: 1061-1073. Impact Factor: 1.935.
9. Gomes-Osman J, Indahlastari A, Freid PJ, Rice J, Cabral D, Nissim N, Aksu S, McLaren M, **Woods AJ**. (2018). Non-invasive brain stimulation: probing intracortical circuits and improving cognition in the aging brain. *Frontiers in Aging Neuroscience*, 10: 177. Impact Factor: 4.504.
10. Gullett J, Lamb D, Porges E, **Woods AJ**, Rieke J, Thompson P, Jahanshad N, Nir T, Tashima K, Cohen R. (2018). The impact of alcohol use on frontal white matter in HIV. *Alcoholism: Clinical and Experimental Research*. 1-12. 42(9): 1640-1649. Impact Factor: 2.716.
11. Thomas C, Datta A, **Woods AJ**. (2018). Effect of aging on cortical current flow due to transcranial direct current stimulation: considerations for safety. *IEEE EMBC*. 3084-3087. Impact Factor: 0.50.
12. O'Shea D, Fieo R, **Woods AJ**, Williamson J, Porges EC, Cohen R. (2018). Frequency of social and cognitive engagement is associated with discrepancies between crystallized and fluid ability in community dwelling adults. *Journal of Clinical and Experimental Neuropsychology*. 40(10): 963-970. Impact Factor: 1.839.
13. White TL, Monnig MA, Walsh EG, Nitenson AZ, Harris AD, Cohen RA, Porges EC, **Woods AJ**, Lamb D, Boyd C, Fekir S. (2018). Psychostimulant drug effects on glutamate, Glx, and creatine in the anterior cingulate cortex and subjective response in healthy humans. *Neuropsychopharmacology*. 43(7): 1498-1509. Impact Factor: 6.403.
14. O'Shea D, Dotson V, **Woods AJ**, Porges E, Williamson J, O'Shea A, Cohen R. (2018). Depressive symptom dimensions and their association with hippocampal and entorhinal cortex volumes in community dwelling older adults. *Frontiers in Aging Neuroscience*, 10: 40. Impact Factor: 4.504.
15. Szymkowicz SM, **Woods AJ**, Dotson V, Porges EC, Nissim N, O'Shea A, Cohen R, Ebner N. Association between subclinical depressive symptoms and reduced brain volume in middle-aged to older adults. *Aging and Mental Health*. Accepted January 2017. Impact Factor: 2.65.
16. Bikson M, Brunoni AR, Charvet LE, Clark V, Cohen LG, Deng Z, Dmochowski J, Edwards D, Frohlich F, Kappenman E, Lim KO, Loo C, Mantovani A, McMullen D, Parra LC, Pearson M, Richardson JD, Rumsey JM, Pejman S, Sommers D, Unal G, Wassermann EM, **Woods AJ**, Lisanby H. (2018). Rigor and reproducibility in research with transcranial electrical stimulation: An NIMH-sponsored workshop. *Brain Stimulation*. 11(3): 465-480. Impact Factor: 6.078.

17. Cohen R, Siegel S, Porges E, Tashima K, **Woods AJ**, Ding MZ. (2018). Neural response to working memory demand predicts neurocognitive deficits in HIV. *Journal of NeuroVirology*. 24(3): 291-304. Impact Factor: 3.206.
18. **Woods AJ**, Cohen R, Marsiske M, Alexander G, Czaja S, Wu S. (2018). Augmenting cognitive training in older adults (The ACT Study): Design and methods of a Phase III tDCS and cognitive training trial. *Contemporary Clinical Trials*. 65: 19-32. Impact Factor: 2.095.

PUBLICATIONS (OTHER):

Ronald A. Cohen, PhD

1. **Cohen, RA**. *Encyclopedia of Clinical Neuropsychology* (2018), Springer, New York (20 Chapters)
2. **Cohen, RA**, Smith, M, Marsiske, M. Neuropsychology of Aging. In *Handbook of Geriatric Neurology*. (DeKosky, ed.), in press
3. **Cohen, RA**, Porges, E, Gullett, J. *Neuroimaging of Brain Aging*. In *Cognitive Changes in the Aging Brain* (Heilman and Nadeau, eds), in press.

Eric Porges, PhD

1. **Porges E.C.** Pre-Pulse Inhibition. *Encyclopedia of Clinical Neuropsychology*. 2018. New York, NY: Springer Science
2. **Porges E.C.** Attentional Blink. *Encyclopedia of Clinical Neuropsychology*. 2018. New York, NY: Springer Science
3. **Porges E.C.** Backwards Masking. *Encyclopedia of Clinical Neuropsychology*. 2018. New York, NY: Springer Science
4. **Porges E.C.** Priming. *Encyclopedia of Clinical Neuropsychology*. 2018. New York, NY: Springer Science
5. Lamb D.G.; **Porges E.C.** Flanker Task. *Encyclopedia of Clinical Neuropsychology*. 2018. New York, NY: Springer Science

PRESENTATIONS AT SCIENTIFIC MEETINGS:

Ronald A. Cohen, PhD

1. International Neuropsychological Society, Washington, DC. (2018), Cognitive and Brain Aging (3 hr workshop).
2. Florida Society for Neurology. Orlando, FL (2018). NeuroHIV: Clinical manifestations and management issues
3. Society for Obesity: Nashville, Tenn 11-15-18. Weight loss and cognition
4. ARCH annual summer meeting: Brown University, Research Component 1 update
5. SHARC annual meeting: Miami, Florida

Damon Geoffrey Lamb, PhD

1. **D. G. Lamb**, T. S. Garman, S. Ramirez, A. Crider, M. M. Bruner, E. W. Dirr, F. Delgado, K. P. Olczak, A. P. Maurer, K. J. Otto, S. N. Burke, B. Setlow, J. L. Bizon. *Effects of vagus nerve stimulation on selective attention in brown Norway rats*. Society for Neuroscience Annual Meeting, San Diego, CA, 2018
2. S. N. Burke, A. Crider, K. P. Olczak, E. W. Dirr, K. N. Lubke, J. Nick, B. Mclaurin, E. Atkinson, K. J. Otto, A. P. Maurer, **D. G. Lamb**, B. Setlow, J. L. Bizon. *Acute vagus nerve stimulation attenuates novelty-induced arc transcription in dorsal CA1*. Society for Neuroscience Annual Meeting, San Diego, CA, 2018
3. L. Altidor, T. S. Garman, S. Ramirez, A. M. Crider, **D. G. Lamb**, M. M. Bruner, A. M. Finner, E. W. Dirr, F. Delgado, K. P. Olczak, A. P. Maurer, K. J. Otto, S. N. Burke, B. Setlow, J. L. Bizon. *Targeting GABAergic mechanisms to improve prefrontal cortical-mediated cognitive flexibility in a novel touchscreen-based reversal learning task*. Society for Neuroscience Annual Meeting, San Diego, CA, 2018

12. **Woods AJ.** *Lecture.* Transcranial Direct Current Stimulation: Safety. International Neuroergonomics Conference. Philadelphia, PA. June 27, 2018.
13. Gradone A, Szymkowicz S(g), McLaren M(g), **Woods AJ**, O'Shea A, Dotson V. Interrelationships between depressive symptoms, memory, and prefrontal surface area in middle-aged to older adults. *Poster* presented at the Cognitive Aging Conference. Atlanta, GA, USA, May 5, 2018.
14. Michalak H, McLaren M(g), Szymkowicz S(g), **Woods AJ**, O'Shea A, Dotson V. Depressive symptom dimensions are associated with cerebellar volumes independent of memory performance. *Poster* presented at the Cognitive Aging Conference. Atlanta, GA, USA, May 5, 2018.
15. McLaren M(g), O'Shea A, Porges E, Cohen R, **Woods AJ.** *Poster.* Frontal structural neural correlates of processing speed performance in older adults. Poster presented at the Cognitive Aging Conference. Atlanta, GA, USA, May 4, 2018.
16. Nissim N(g), O'Shea A, Richards L, Telles R, Porges E, Cohen R, **Woods AJ.** *Poster.* Effects of bilateral frontal tDCS on the working memory network: an fMRI-tDCS study in healthy older adults. Poster presented at the Cognitive Aging Conference. Atlanta, GA, USA, May 4, 2018.
17. **Woods AJ.** *Symposium.* Augmenting Cognitive Training in Older Adults: a Phase III tDCS trial. International Learning and Memory Conference. Huntington Beach, CA, USA, April 20, 2018.
18. McLaren M(g), O'Shea A, Porges E, Cohen R, **Woods AJ.** *Poster.* Frontal structural neural correlates of processing speed performance in older adults. Poster presented at the 46th annual International Neuropsychological Society. Washington, DC, USA, March 17, 2018.
19. **Woods AJ.** *Symposium.* Continuum of Care from Wearables to Non-Invasive Neuromodulation: Clinical Applications of tDCS in the Aging Population. North American Neuromodulation Society, Las Vegas, NV, USA, January 11, 2018.
20. **Woods AJ.** *Lecture.* Hands-On tDCS. North American Neuromodulation Society, Las Vegas, NV, USA, January 11, 2018.

PRESENTATIONS AT PUBLIC (NON-SCIENTIFIC) MEETINGS OR EVENTS:

Demetrius M. Maraganore, PhD

1. September 12, 2018: "From Brain Disorders to Brain Health: Primary Prevention of Cognitive Decline and Dementia". The Volusia County Medical Society Meeting, Daytona Beach, FL

John B. Williamson, PhD

1. **Invited speaker, VA Sleep Seminar Series** **2018**
 **PTSD, TBI, hyperarousal features and sleep disruption

AWARDS (OTHER):

Ronald A. Cohen, PhD

1. Distinguished Professor Award, Department of Clinical and Health Psychology

Funded Research

1. COHEN, R. P01 AA019072 Monti (PI) 09/01/15 - 05/31/20 1.20 CM NIAAA 110,695
 Alcohol and HIV: Biobehavioral Interactions and Intervention
 One of two primary R01 projects in the Brown University HIV-Alcohol center grant, this study focuses on the interactive effects of HIV and alcohol use on metabolic-vascular disturbances underlying brain dysfunction. We are longitudinally assessing HIV infected and seronegative controls who are stratified by alcohol use into three groups (heavy, moderate, none use) over a 36-month period. The study examines MRI-based neuroimaging biomarkers of brain dysfunction including diffusion tensor imaging (DTI), morphometry, and magnetic resonance spectroscopy (MRS) to measure cerebral metabolite abnormalities. Dr.

Cohen is the principal investigator of this R01 project overseeing all aspects of the study.

Role: Co-Investigator

2. R56 HL127175-01 (Williamson, PI) 09/01/15-08/30/20 1.8 CM NHLBI \$31,989
The effects of heart failure and cardiac resynchronization on the brain and cognition
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
3. U24 AA022002 Cook (PI) 09/01/2013-08/31/2017 .36 CM NIAAA \$6,313
Southern HIV Alcohol Research Consortium (SHARC) Admin and Research Support Cure. The objective of this proposal is to establish the administrative structure and to provide research support for the SHARC, a collaboration that links several universities and investigators with a common goal of supporting new research related to HIV and alcohol consumption.
Role: Co-I
4. 2U01AA010797-06 (Cook, PI; Cohen MPI) 09/01/2016-08/30/2021 1.8CM NIAAA \$4,718,864
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. This proposed U01 study will 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. We will conduct state-of-the-art neuroimaging, cognitive, and behavioral assessments at each time point and then continue to track long-term drinking and HIV outcomes in our companion Cohort (U24). The Specific Aims of this proposal are: 1) to demonstrate improved cognitive performance and brain function (fMRI) after 4-weeks of CM-induced alcohol reduction among HIV+ adults, followed by worsening of these effects 1-year later if heavy drinking resumes; 2) to demonstrate that cerebral metabolic (MRS) and neuroinflammatory (DTI-free water) markers will also improve with CM-induced alcohol reduction and worsen if drinking resumes post-CM; and 3) Determine whether perceived benefits and challenges to drinking reduction identified during motivational interviewing (MI) predict drinking reductions or relapse one-year post-CM. We will also determine whether changes in cerebral pathophysiology (MRS, DTI-FW) correspond with changes in cognition, brain function (fMRI) and serum inflammatory and liver biomarkers.
Role: MPI
5. AA022002 Cohen (MPI) 09/01/2013-08/31/2017 .36 CM NIAAA \$6,313
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 Southern HIV Alcohol Research Consortium (SHARC) Admin and Research Support Cure. The objective of this proposal is to establish the administrative structure and to provide research support for the SHARC, a collaboration that links several universities and investigators with a common goal of supporting new research related to HIV and alcohol consumption.
Role: MPI
6. 1R01DK099334 06/25/2014-05/31/2019 3.60 CM NIH \$1,826,328
Obesity and type-2 diabetes: Bariatric surgery effects of brain function
The proposed prospective longitudinal study will examine whether cerebral metabolic and vascular dysfunction, including glucose/insulin disturbances (co-morbid diabetes) underlie obesity-associated cognitive dysfunction, and whether significant weight loss and diabetes remission following bariatric surgery reduces these disturbances.
Role: PI
7. NIH 1U54 EB020403 Thompson (PI) 07/01/2014-06/30/2018 .24 CM \$180,000
ENIGMA Center for Worldwide Medicine, Imaging & Genomics
ENIGMA is not a project; it is a scientific movement of rapidly and constantly interacting collaborations that support each other. ENIGMA cohorts boost each other's power with gigantic datasets, and the tools and expertise to maximally exploit each other's data, performing some of the world's largest disease studies, beyond what any one site could perform on its own.
Role: Co-I Sub Award PI
8. NIH/NIA 1R01AG054077-01 (Woods/Cohen) 7/1/2016-6/30/2021 1.2 cal months \$21,538
Augmenting Cognitive Training in Older Adults – The ACT Grant
This randomized clinical trial examines the effect of augmenting cognitive training with transcranial direct current stimulation 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.

9. NIA K01AG050707-A1 (Woods, PI) 07/01/2016-06/30/21 .0 cal months \$0
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.
Role: Mentor

Damon Geoffrey Lamb, PhD

1. MBI grant supplement (\$10,000) for equipment and training to supplement IK2 grant.
2. IK2RX002490 (\$965,534, 5yrs) Brain changes underlying emotional and executive alterations in TBI

Eric Porges, PhD

1. K01 AA025306-01A1, NIH/NIAAA Porges, Eric (PI) 08/01/17-01/31/22
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. To ensure an independent career post award, two critical areas of training will be addressed: 1) Behavioral and biological consequences of alcohol use in the context of HIV and 2) the development of expertise in the measurement of GABA, the principal inhibitory neurotransmitter, using Magnetic Resonance Spectroscopy (MRS). The PI is a cognitive neuroscientist with a strong research background in aging, cognition, experimental design, autonomic measurement, and magnetic resonance imaging (fMRI & MRI). Role: PI

John B. Williamson, PhD

1. NIH R21AG054876 \$275,000 2017 – 2019
Treatment of mild cognitive impairment with transcutaneous vagal nerve stimulation.
PI: Williamson
2. VA 0217BRRC-04 \$60,000 2017 – 2018
Department of Veterans Affairs Brain Rehabilitation Research Center Pilot Award:
Transcutaneous vagal nerve stimulation modulation of sleep quality and emotion in mild TBI and PTSD
PI: Williamson
3. NIH 1R56HL127175-01 \$544,000 2016-2018
Brain and cognition effects of cardio resynchronization therapy in heart failure. The goal of this funding is to characterize brain changes as a result of improved cardiac output in heart failure including hemodynamic, task dependent regional brain activation and brain metabolic changes associated with improved cognitive performance and brain health.
PI: Williamson
4. 1 LK2RX000707-01 CDA-2 (VA-K) \$898,188 2012-2018
White matter changes and mild TBI: Emotional and autonomic consequences. Funded by the Department of Veterans Affairs:
Williamson, Principal Investigator
PI: Williamson

Pending Submissions

1. NIH R01/Merit Review ~1.1 million to 2.5 million 2019 – 2023
Transcutaneous vagal nerve stimulation modulation of sleep quality and emotion in PTSD
Status: Follow-up to currently funded BRRC pilot (currently active collecting pilot data)

Adam Joshua Woods, PhD

1. **NIA U01AG062368 (Edwards; PI) 09/30/18-05/31/20 \$614,914**
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
2. **McKnight Brain Research Foundation (Woods/Bowers, MPIs) 05/1/18-04/31/20 \$120,000**
McKnight Brain Research Foundation
CAM-CTRP Pilot Study: 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
3. **NIA R37AG033906 (Fillingim; PI) 05/01/19-04/31/24 \$6,144,138**
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 two site phase II clinical trial.
Role: Co-I
4. **VA Merit Review (Clark; PI) 04/01/2019-03/31/23 \$1,100,000**
VA Rehabilitation Research and Development Service
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

FACULTY BIOGRAPHICAL SKETCHES/CVs: See page 77

TRAINEES

Ronald A. Cohen, PhD

- a. **Post-doctoral**
 1. Joseph Gullett, PhD
 2. Ellen Terry, PhD
- b. **Pre-doctoral**
 1. Amanda Garcia, PhD (Graduated)
 2. Talia Seider, PhD (Graduated)
 3. Vaughn Bryant, MS

4. Nicole Nissan, MS
- c. **Other: Faculty mentoring: K awards, etc.**
 1. Adam Woods, PhD
 2. Eric Porges, PhD
 3. Robert Fieo, PhD
 4. Yenisel Cruz-Almeda, PhD
 5. Natalie Ebner, PhD
 6. David Clark, PhD
 7. Lisa Delmonico, PhD
 8. Ellen Terry, PhD
 9. Joseph Gullett, PhD
 10. David Clark, PhD
 11. Damon Lamb, PhD

Eric Porges, PhD

- a. **Post-doctoral**
 1. Joseph M. Gullett, PhD
- b. **Pre-doctoral**
 1. Destin Shortell
 2. Kathleen Hupfield
- c. **Other**
 1. Gennel Samson (undergraduate)

John B. Williamson, PhD

- a. **Post-doctoral**
 1. Sudeshna Chatterjee, PhD
- b. **Pre-doctoral**
 1. Amy Tran, BS
 2. Ryan Pynosky, BS
 3. Heather Bouchard, BS
 4. Tyron Slack
 5. Aaron Colverson, PhD
 6. Vaughn Bryant, PhD

Adam Joshua Woods, PhD

- a. **Post-doctoral**
 1. Aprinda Indahlastari, PhD
- b. **Pre-doctoral**
 1. Nicole Nissim, MS

2. Emanuel Boutzoukas
3. Hanna Hausman
4. Jessica Kraft, MA
5. Nicole Evangelista

c. Other

1. Kathleen Frost (undergrad)
2. Cindy Hernandez (undergrad)
3. Klea Agollari (undergrad)

CLINICAL/TRANSLATIONAL PROGRAMS

Ronald A. Cohen, PhD

a. New programs:

1. VA Brain Rehabilitation Research Center Renewal
2. Brain Wellness Program (Maganore)

b. Update on existing clinical studies

1. ACT study in progress (see above)
2. MBAR project is underway. We are collecting data (see above)
3. MBAR database now in place
4. ACTIVE studies: Manuscripts continue to be written and published, including findings from the Talia Seider (Seeing Brain) and Amanda Garcia (Talking Brain) dissertations.
5. CAM-ARML pilot studies being completed
6. HIV-alcohol-aging studies continuing to recruit. Publishing findings
7. Study of bariatric surgery effects on brain function making excellent progress. We have over 110 participants. Publishing findings
8. Heart failure project to examine effects of increasing cardiac output on cerebral perfusion and brain function in older adults underway.
9. MUSE – Marijuana effects on HIV and aging: In progress
10. Microbiome study of HIV-Alcohol effects: In progress
11. Studies linked to all career development awards initiated

Demetrius M. Maraganore, PhD

b. Update on existing clinical studies:

1. At the University of Florida, I am building and directing a Brain Health Clinic (that will evaluate and manage persons at high risk for dementia identified by the prediction model to be refined, replicated, implemented into the EMR as clinical decision support, and disseminated to OneFlorida Clinical Research Consortium practices via the recently awarded Ed and Ethel Moore grant).

Eric Porges, PhD

b. Update on existing clinical studies:

1. R5 K01 AA025306-01A1, NIH/NIAAA

Porges, Eric (PI)

08/01/17-01/31/22

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. To ensure an independent career post award, two critical areas of training will be addressed: 1) Behavioral and biological consequences of alcohol use in the context of HIV and 2) the development of expertise in the measurement of GABA, the principal inhibitory neurotransmitter, using Magnetic Resonance Spectroscopy (MRS). The PI is a cognitive neuroscientist with a strong research background in aging, cognition, experimental design, autonomic measurement, and magnetic resonance imaging (fMRI & MRI).

Role: PI

- **Update: study is underway, preliminary analysis are pending.**

2. NIH R21AG054876(Williamson; PI) 06/01/17-5/31/19

The goal of this study was to collect pilot data investigating the ability of transcutaneous vagal nerve stimulation (tVNS) to impact MCI symptoms.

Role: Co-I

- **Update: study is underway, preliminary analysis are pending.**

3. U01AA020797, NIA/NIAAA

Ronald, Cohen & Cook, Robert (Co-PI)

09/01/16-08/31/21

Continuous monitoring with wearable alcohol biosensors (SCRAM) to confirm effects of experimentally induced reductions in alcohol consumption in HIV-infected high risk drinkers on the brain and cognition. This study examines the degree to which reductions in alcohol use via contingency management leads to improvements in cognitive and brain functioning.

Role: Co-I

- **Data collection ongoing**

4. Brain Rehabilitation Research Center Pilot, VA

Williamson, John (PI)

2017-2018

External autonomic nervous system (ANS) modulation for the treatment of sleep in PTSD.

The goal of this study is to collect pilot data investigating the ability of transcutaneous vagal nerve stimulation (tVNS) to alleviate anxiety and sleep related PTSD symptoms.

Role: Co-I

- **Data collection underway, preliminary analysis have been generated and used to support VA Merit (R01 equivalent) application. Initial submission well scored, resubmission underway.**

John B. Williamson, PhD

b. Update on existing clinical studies

I have two clinical trials active. One is a BRRC funded pilot on the role of tVNS in the modification of sleep quality in Veterans with PTSD. We have enrolled ~15 people with a target n of 20 in a cross-over design polysomnography study in which we are measuring sleep architecture, changes in emotional state, and cognitive performance effects of tVNS.

The second clinical trial is funded by NIH via an R21 and is designed to assess the impact of tVNS on cognitive performance in patients with amnesic MCI. The team includes Drs. Porges, Lamb, DeKosky and I. We have enrolled ~20 people with a target sample size of 60.

Adam Joshua Woods, PhD

a. New programs

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.

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. In October, our team submitted data from this effort for an NIA R01. Data collection in the pilot are ongoing.

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 will start in April of 2019, but notice of funding has already been received. 300 participants at the University of Florida and University of Alabama at Birmingham will participate.

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 will start in April of 2019, but notice have funding has already been received.

b. Update on existing clinical studies

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. 147 participants have been randomized to date.

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 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. This study is currently in its second year. Based on this project, we have a new VA Merit grant extending this work into a larger population.

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 second 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 in its second year with over 45 participants recruited.

TECHNOLOGY TRANSFER:

Ronald A. Cohen, PhD

- a. Patents applications
Porges, Lamb, Williamson received a patent for their TVNS stimulation system.

Damon Geoffrey Lamb, PhD

- a. Patents applications
Pending: 15/535965 docket 450-N0013US and PCT/US15/65524 – System and method for monitoring and controlling nervous system behavior using autonomic features

Eric Porges, PhD

- a. Patents applications
US Patent Application for: SYSTEM AND METHOD FOR MONITORING AND CONTROLLING NERVOUS SYSTEM BEHAVIOR USING AUTONOMIC FEATURES
Inventors: Williamson, Lamb & Porges
USAN 15/535.965; filed 6/14/2017 O/Ref. No. 10457-331US1; UF#15256

John B. Williamson, PhD

- a. Patents applications
We have a patent currently pending
- b. Revenue generated from technology
We are in the process of starting a spinoff company via UF's tech transfer program.

BUDGET UPDATE: See page 61

Demetrius M. Maraganore, PhD

- c. Extramural funding
"Quality Improvement and Practice Based Research in Neurology Using the EMR," Principal Investigator, \$1,205,979 from the Agency for Healthcare Research and Quality (1R01HS024057) July 1, 2015 – April 40, 2020

"Utilizing Data from the Electronic Medical Record to Predict Alzheimer's and Dementia Risk," Principal Investigator, \$237,500 from Florida Health Ed and Ethel Moore Program (9AZ14) December 2018-December 2020

EDUCATIONAL PROGRAMS FOCUSING ON AGE-RELATED MEMORY LOSS:

Eric Porges, PhD

- a. Scientific
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.

COLLABORATIVE PROGRAMS WITH OTHER MCKNIGHT INSTITUTES, INSTITUTIONS AND RESEARCH PROGRAMS

Ronald A. Cohen, PhD

The CAM-CTRP has continued to make considerable progress in fulfilling the mission of the center and meeting our objectives from last year, including the extension of collaboration with investigators in the UF ARML program, other UF departments, and across the other McKnight institutes. These objectives are listed below along with...

Clinical translation: We have continued to emphasize: 1. translation of pre-clinical research on cognitive aging in humans to clinical applications; and 2. integrating basic neuroscience findings coming from the AMRL faculty into the human realm with a focus on clinical translation and developing new clinical outcomes and biomarkers for cognitive aging and also novel interventions. Several initiatives are underway related to the first of these objectives:

1. Collaboration with Dr. Bizon and her group to develop agents to enhance cognitive and behavioral function in the elderly;
2. Studies bridging high field in vitro and in vivo MR methods in laboratory animals with human MRI and MRS approaches to study neuroinflammation, blood-brain-barrier function, and epigenetic mechanisms contributing to age-associated cognitive decline (Febo, DeKosky, Woods, Cohen);
3. Genetic and epigenetic analyses of blood from the CAM ACTIVE brain study of older adults (Foster, Woods, Cohen).
4. The initiation of the ACT grant represents a major accomplishment related to clinical translation in humans. Other clinical translation accomplishments, include the WISE study, Papaya study and a number of other projects. The status of these initiatives are outlined later in this report.
5. Collaboration with UF ADRC to harmonize data for successful agers with the ADRC database for comparative analyses
7. Collaboration with Mt. Sinai and UF researchers on analysis of PET beta-amyloid relative to resting state fMRI and structural brain data from ADRC.

Damon Geoffrey Lamb, PhD

Initiated expanded ARML & CAM-CTRP collaboration through local events to foster cross-fertilization of research groups.

Eric Porges, PhD

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

Collaborative project has been initiated with ARML at the UF to apply Magnetic resonance spectroscopy measures used in our aging research to rodent models of aging. In collaboration with Drs. Burke and Febo we have done initial analysis, revealing increased Myo-inositol levels in aged rodents, this measure has been associated with neuroinflammation. We plan to extend this collaboration to look at Dr. Burke's rodents fed a ketogenic diet.

John B. Williamson, PhD

Center for OCD and Anxiety Related Disorders

Center for Cognitive Aging and Memory

Adam Joshua Woods, PhD

MBRF Cognitive Aging and Memory Intervention Core – The CAMI Core first round RFA produced 2 funded studies. These studies are ongoing across MBI sites. The core is in the process of soliciting a second round of LOIs for interest in a second round RFA.

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.

A new study investigating the effects of tDCS on chronic knee pain is now funded through the NIA with collaboration across UF and UAB.

Our funded MBRF pilot across University of Florida and University of Arizona is currently underway.

COLLABORATIONS ACROSS UF AND MCKNIGHT INSTITUTES:

Ronald A. Cohen, PhD

CAM-CTRP has a number of collaborations that meet these objectives. These include:

1. CTSI investigators in epidemiology, biostatistics, and health outcomes (e.g., SHARC U-grant, ARCH-2);
2. Veterans Administration Hospital Brain Rehabilitation Research Center investigators (multiple projects including TBI and aging, heart failure, and HIV);
3. biomedical engineering and nanotechnology (closed end feedback brain stimulation grant with Jack Judy, PhD);
4. cardiology (cardiac resynchronization for heart failure)
5. Epidemiology and Infectious Medicine (SHARC, ARCH-2)
6. ADRC collaboration
7. Collaboration with DeKosky (neurology) and Mitchell (Physical Therapy) on Intermittent Hypoxia Therapy

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

Ronald A. Cohen, PhD

1. ARCH project: Involves Brown University and UF collaboration
2. SHARC: University of Miami, FIU collaboration with UF
3. ENERGISE study: Multi-site study of anti-inflammatory drug treatment effects in the elderly. Study involves: UF, Tufts, Yale, Pittsburgh, etc.

Demetrius M. Maraganore, PhD

Agency for Healthcare Research and Quality (AHRQ); Maraganore (PI); 05/01/15-04/30/20

Quality Improvement and Practice Based Research in Neurology Using the EMR

Aim 1: We will create a national network for quality improvement and practice based patient-centered outcomes research in Neurology using the electronic medical record (EMR) to make health care safer and to improve healthcare efficiency, in keeping with the mission and priority areas of the Agency for Healthcare Research and Quality. Aim 2: We will conduct pragmatic trials using the EMR and subgroup-based adaptive design tools that determine which treatments are most effective for specific patients, individualizing medicine at the point of care.

Eric Porges, PhD

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

In collaborative multisite study with Dept. of Radiology at Johns Hopkins University to establish site to site variation in GABA 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.

John B. Williamson, PhD

1. Alzheimer's Disease Research center.
2. Brain Rehabilitation Research Center, TBI and PTSD programs, cognitive and emotion initiatives.

Adam Joshua Woods, PhD

Dr. Woods has ongoing collaborations in his areas of expertise in tDCS and neuroinflammation brain imaging at University of Arkansas for Medical Sciences, (UAMS); University of Alabama at Birmingham (UAB), 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.

BRIEFLY DESCRIBE PLANS FOR FUTURE RESEARCH AND/OR CLINICAL INITIATIVES:

Ronald A. Cohen, PhD

1. Continued expansion and development of current lines of research
2. Clinical translational studies testing effects of novel drugs for enhancing cognitive function in the elderly
3. Longitudinal studies of the MBAR cohort.
4. Obtain R01 funding for current heart failure research
5. Apply for funding to conduct neuroimaging studies of chemotherapy and cancer effects on brain function in women with breast cancer.
6. Facilitate current work on pain effects in cognitive and brain aging in collaboration with Dr. Cruz and her collaborators.
7. Collaborate with other CAM investigators on their lines of research, including tDCS and vagal nerve stimulation methods.

Damon Geoffrey Lamb, PhD

Longitudinal studies of non-invasive intervention for aMCI populations, continue work on stress & anxiety related disorders which can lead to 'accelerated aging.'

Demetrius M. Maraganore, PhD

I am the Principal Investigator (PI) of the Florida Health Ed and Ethel Moore Alzheimer's Disease Research Program application entitled "Utilizing Data from the Electronic Medical Record to Predict Alzheimer's and Dementia Risk". This was awarded on December 13, 2018. That grant aims to develop an Alzheimer's prediction model using data routinely captured by the University of Florida (UF) electronic medical record (EMR), to replicate the model using EMR data shared by the OneFlorida Clinical Research Consortium, to implement the replicated model into the UF EMR using clinical decision support (CDS) tools, and to share the replicated model and CDS tools with OneFlorida Clinical Research Consortium sites. The long-term goal is to create a Florida statewide Alzheimer's prediction and prevention initiative. I am also the PI of the Agency for Healthcare Research and Quality grant R01HS024057 entitled "Quality Improvement and Practice Based Research in Neurology Using the EMR". I supervised the building of structured clinical documentation support (SCDS) and CDS toolkits within the EMR, for the evaluation and management of patients with 11 different neurological indications (including memory disorders and brain health). These

toolkits support the clinical practices of neurologists and are also used to support clinical research (including in cognitive decline, mild cognitive impairment, dementia, and Alzheimer's disease). The EMR toolkits that my team built are being shared with 15+ academic departments across the nation, and in return the participating sites are sharing deidentified electronically captured data into a registry, with the aims of quality improvement and practice-based research in neurology using the EMR. One of the projects includes an EMR-based pragmatic trial comparing the effectiveness of three memory and cognitive enhancing drugs in mild cognitive impairment. Regarding brain health (primary prevention of aging related cognitive decline, dementias, including Alzheimer's disease), as the past Chair of Neurology at NorthShore University HealthSystem in Evanston, IL, I developed and led the NorthShore Center for Brain Health. My team and I targeted populations at risk for dementia through community outreach and continuing medical education of physicians. The Center provided outpatient consultations that included risk assessments (of genetic and modifiable factors), personalized interventions (lifestyle, behavioral, and medical), and annual surveillance (early disease detection). In two years, more than 550 patients were evaluated and managed. This was one of the first brain health clinics in the United States. In the Center, my team and I also conducted clinical research, including point of care electronic data capture via SCDS and CDS tools built into the EMR. We developed a preliminary Alzheimer's prediction model using data routinely captured by the EMR. At the University of Florida, I am building and directing a similar Brain Health Clinic (that will evaluate and manage persons at high risk for dementia identified by the prediction model to be refined, replicated, implemented into the EMR as clinical decision support, and disseminated to OneFlorida Clinical Research Consortium practices via the recently awarded Ed and Ethel Moore grant).

Eric Porges, PhD

My near term plans will include multiple branches.

1. The extension of my work with GABA MRS in older adults, and accelerated aging populations including HIV+ and Heavy Drinkers. Here we are exploring the relationship and role of GABA as indexed non-invasively using MRS to multiple domains of cognitive function, with an emphasis on cognitive flexibility. Relevant to this, I was recently awarded a K01 by NIAAA/NIH to investigate the relationship of GABA to cognitive flexibility. I am CO-I on studies investigating the relationship between GABA and motor function, GABA and pain and, GABA and social cognition. In the near future we plan to target GABAergic influences on these important domains via pharmacological intervention.
2. We are developing transcutaneous vagal nerve stimulation (tVNS) applications for the modulation of cognitive function. To enable this, we were recently awarded a NIAAA/NIH R21 to explore the capacity of tVNS to improve cognitive function in older adults, including those with MCI. An R01 submission based on this work is forthcoming.
3. Dr. David Clark, Dr. Steven DeKosky and I have recently submitted an R01 and Dr. Clark and I have a VA Merit (R01 equivalent), both to be resubmitted. Both projects use ambulatory autonomic measurement to predict falls in older adults related to cognitive load, anxiety and their interaction. The primary objective is to develop a clinical assessment to predict falls. A secondary goal, is to leverage the small, non-intrusive nature of the ambulatory sensors into a device that could be worn outside of a clinical environment (e.g. home) to predict fall risk and alert the individual or care taker during period when fall risk increases.
4. As an extension of my Magnetic resonance spectroscopy work we have been developing methods that allow for the dynamic characterization of changes to Glutathione (endogenous antioxidant, responsive to oxidative stress) in the brain in response to acute experimental interventions. Our initial application of this is in response to alcohol administration in a control population. We have begun the IRB and regulatory process that will allow us to apply this protocol to older adults as well as other populations with increased vulnerability to oxidative stress. IRB dependent, data collection should begin in the spring.

John B. Williamson, PhD

I have a clinical trial that was scored well on its initial submission to the VA which is now pending review of the resubmission. If that goes well, that will start in 2019. The R21 project results should be analyzable in late 2019 if recruiting continues going well. That will determine if we submit an R01 follow-up for our memory enhancing effects. I have another line of clinical trial studies for which Dr. Carol Mathews and I will be applying for funds in January. Further, we recently received funding on two consortium projects, one in microbiome relationship to cognition in patients with HIV funded by NIH and aging and another, funded by the DOD to understand mechanisms of behavioral decline associated with traumatic brain injury. Further, the consortium group that we started last year, the DOD funded Brain Heart Consortium, will be publishing a position paper in early 2019. We will be following that up with chronic stress and aging project proposals.

Adam Joshua Woods, PhD

Dr. Woods currently has multiple grants under review and several in preparation. Each of these grants represents the investigation and application of novel non-invasive interventions for cognitive aging. He will continue to pursue external funding, but with current grant success is nearing an upper limit regarding new projects that can be run directly out of his large laboratory (n=21). As such, he will be working in the coming year to facilitate his junior faculty and post-doctoral fellows toward success in some of these funding endeavors, with the hope of expanding the overall bandwidth of the CAM for cognitive aging interventions and grooming a new cadre of interventional cognitive neuroscientists focused on cognitive aging. In addition, due to the size of his lab, Dr. Woods is currently striving to find creative space solutions that will allow his large dynamic lab group to work in a unified space. The lab is currently spread across 3 locations across campus, which undermines efficiency and limits overall potential for productivity. In addition, Dr. Woods is strongly interested in approaches that will allow the University of Florida to capitalize on the many world-firsts achieved by UF faculty in the area of neuromodulation. Working toward a central mechanism for synergizing these investigators could not only push forward the use of varied neuromodulation methods for aging research, but make significant impacts in numerous age-related diseases/disorders. Over the coming years, Dr. Woods will be working toward realizing this goal.

IF APPLICABLE, PLEASE PROVIDE ENDOWMENT INVESTMENT RESULTS FOR THE REPORT PERIOD: See page 69

WERE ANY FUNDS USED FOR A PROHIBITED PURPOSE DURING THE REPORT PERIOD? No

DO YOU RECOMMEND ANY MODIFICATION TO THE PURPOSE OR MANDATES IN THE GIFT AGREEMENT? No

DID ALL ACTIVITIES DURING THE REPORT PERIOD FURTHER THE PURPOSE? Yes

NEGATIVE EVENTS (LOSS OF PERSONNEL, SPACE, BUDGET ETC.): NA

ADDITIONAL COMMENTS: See letter on page 31

SIGNATURE, DATE AND TITLE OF PERSON SUBMITTING THE REPORT:



Ronald A. Cohen, PhD, ABPP, ABCN
Professor, Aging, Neurology, and Psychiatry
Director, CAM-CTRP, and Evelyn McKnight Endowed Chair
for Clinical Translation in Cognitive Aging Program



William G. Luttge Lectureship in Neuroscience



December 5, 2018

Dear McKnight Brain Research Foundation Trustees,

On March 15, 2018 the 6th Annual William G. Luttge Lectureship in Neuroscience was held with Dr. Michela Gallagher as the lectureship speaker. Dr. Gallagher's lecture titled "Contributions of neurocognitive aging to risk or resilience" was delivered to a full audience in the DeWeese Auditorium at the McKnight Brain Institute. Dr. Gallagher is working in the field of memory and cognitive aging, and is currently the Krieger-Eisenhower Professor of Psychological and Brain Sciences & Neuroscience at The Johns Hopkins University.

Dr. Gallagher received her PhD in Physiological Psychology from the University of Vermont. She is Director of the Neurogenetics and Behavior Center at The Johns Hopkins University. Among her many scientific accomplishments, Dr. Gallagher has conducted pioneering work on individual differences in cognitive aging. Her work in this area has directly led to translational programs targeting hippocampal overactivity as a basis for memory impairment in older adults and patients with amnesic MCI. She was a faculty member at The University of North Carolina at Chapel Hill for 20 years before joining the faculty at The Johns Hopkins University in 1997, where she has served in many capacities including as Department Chair, Vice Provost for Academic Affairs, and Interim Dean for the Krieger School of Arts and Sciences. She has published more than 250 research articles and book chapters on topics ranging from fundamental mechanisms of associative learning to the molecular basis of mnemonic decline and resilience in aging. Her work in these areas has been recognized with numerous awards including an Ellison Medical Foundation Senior Scientist Award, the D.O. Hebb Distinguished Scientific Contribution Award from the American Psychological Association, the Gantt Medal from the Pavlovian Society and the Mika Salpeter Lifetime Achievement Award from the Society for Neuroscience.

Members of the Luttge Lectureship Committee are:

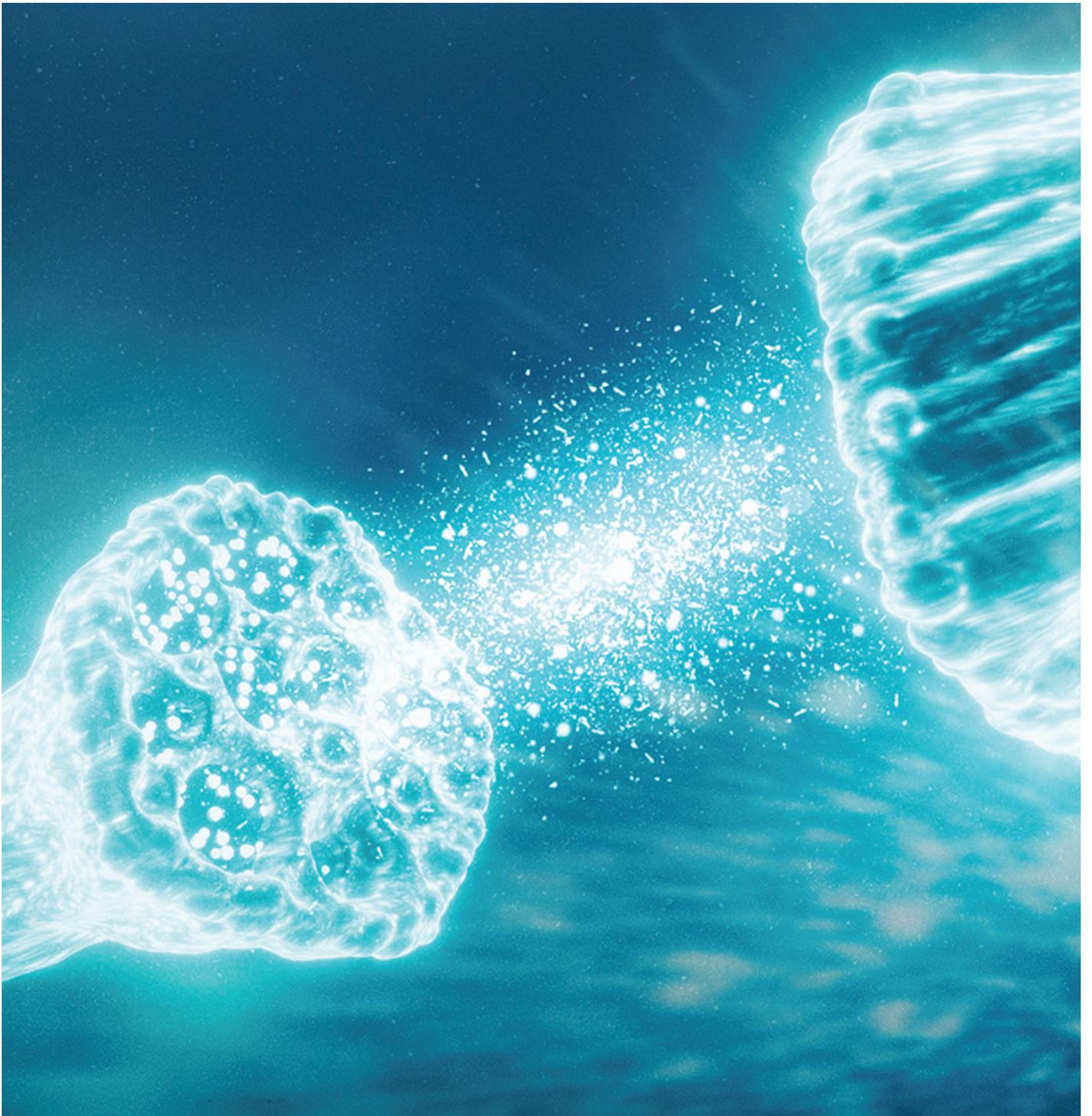
- Steven T. DeKosky, MD, Deputy Director of the Evelyn F. and William L. McKnight Brain Institute at UF; Rene Aerts/ Virginia J. Cosper Professor of Alzheimer's Research; Associate Director, Florida Alzheimer's Disease Research Center; and Professor of Neurology
- Lucia Notterpek, PhD, Chair and Professor of the Department of Neuroscience
- Tom C. Foster, PhD, Professor of Neuroscience, and Evelyn F. McKnight Chair for Research on Age-related Memory Loss
- David R. Borchelt, PhD, Professor of Neuroscience, Director of the Santa Fe Health Alzheimer's Disease Research Center, and Director of CTRND
- Sara Jo Nixon, PhD, Professor of Psychiatry, Addiction Research Division Chief, and Director of the Neurocognitive Laboratory
- Jennifer Bizon, PhD, Professor of Neuroscience

The committee is now organizing the 7th Annual William G. Luttge Lectureship which will be held on Monday, March 11, 2019 with Dr. George Koob as speaker. The lectureship will be held at the beginning of National Brain Awareness Week. Dr. Koob is the Director of the National Institute on Alcohol Abuse and Alcoholism. Dr. Koob has a distinguished research program focused on understanding the neuropharmacological mechanisms of substance use disorders.

Sincerely,


Lucia Notterpek, Ph.D.
Chair and Professor
Department of Neuroscience

Program Financials



Age-related Memory Loss Program

Financial Summary January 1 to December 31, 2018

Foundation Spendable Account	Amount
Endowment income transferred in:	
Mar 31, 2018	\$ 260,322
Jun 30, 2018	260,322
Sept 30, 2018	260,322
Dec 31, 2018	262,078
Total endowment income transferred in	1,043,046
Additional funds from MBRF	-
Total funds available	1,043,046
Transferred to UF Peoplesoft spendable accounts	1,041,290 ^(a)
Net change in foundation spendable account	1,756
Beginning balance, Jan. 1, 2018	260,322
Ending balance, Dec. 31, 2018	\$ 262,078

UF PeopleSoft Accounts	Amount
Received from foundation spendable account	\$ 1,041,290 ^(a)
Other funds received	-
Total funds available	1,041,290
Transferred out:	
Dr. Maurer startup and project support	-
Drs. Ebner&Cruz-Almeida project support	30,000
Total transferred out	30,000 ^(b)
Expenditures:	
ARML faculty salaries	162,038
Travel and other	1,452
Total expenditures	163,490
Total transfers out and expenditures	193,490
Net change in UF Peoplesoft accounts	847,800
Beginning balance, Jan. 1, 2018	645,913
Ending balance, Dec. 31, 2018	\$ 1,493,713
Due to CAM	651,684 ^(c)
Total funds available to ARML, Dec. 31, 2018	\$ 1,104,107

^(a) Transfers from foundation spendable account to Peoplesoft account in 2018.

^(b) \$74,000 is owed to Dr. Maurer and scheduled to be transferred in Jan. 2019.

^(c) Accumulation of the CAM portion of the endowment interest income (50%), per the 2009 Gift Agreement Amendment. Scheduled to be transferred in 2019.

McKnight Endowed Chair for Brain Research in Memory Loss Tom Foster, PhD

Financial Summary January 1 to December 31, 2018

Foundation Spendable Account	Amount
Endowment income transferred in:	
March 31, 2018	34,953
June 30, 2018	34,953
Sept 30, 2018	34,953
Dec 31, 2018	35,189
Total endowment income transferred in	140,050
Transferred to UF Peoplesoft spendable accounts	139,814 ^(a)
Net change in foundation spendable account	236
Beginning balance, January 1, 2018	34,953
Ending balance, Dec. 31, 2018	\$ 35,189
UF PeopleSoft Accounts	
	Amount
Received from foundation spendable account	\$ 139,814 ^(a)
Transfers and Expenditures:	
Transfers	-
Faculty and research staff salaries	77,415 ^(b)
Research equipment, supplies, and services	197,717
Travel and other	7,978
Total transfers and expenditures	283,109
Net change in UF Peoplesoft accounts	(143,295)
Beginning balance, January 1, 2018	520,905
Ending balance, Dec. 31, 2018	\$ 377,610
Total funds avail. to McKnight ARML Chair, Dec. 31, 2018	\$ 412,799

^(a)Transfers from foundation spendable account to Peoplesoft account in 2018.

^(b)Please note that this figure was erroneously reported for 2017 as \$46,746. The correct figure is \$68,035.

Cognitive Aging & Memory

Financial Summary January 1 to December 31, 2018

UF PeopleSoft Accounts	Amount
Received from McKnight Brain Research Grant	\$ - ^(a)
Program expenditures and commitments:	
Faculty, Research Staff & Staff Earnings	277,474
Graduate Assistant & Student Assistant Earnings	24,022
Research equipment, supplies, and services	35,779
Tuition Waivers	10,770
Publications	8,731
Travel and other	1,918
Total program expenditures and commitments	<u>358,694</u>
Net change in UF Peoplesoft accounts	<u>(358,694)</u>
Beginning balance, Jan. 1, 2018	<u>935,928</u>
Ending balance, Dec. 31, 2018	<u>\$ 577,234</u>
Due from McKnight Brain Research Grant	<u>651,684</u> ^(a)
Total funds available to CAM-CTRP, Dec. 31, 2018	<u>\$ 1,228,918</u>

^(a) Accumulation of the CAM portion of the endowment interest income (50%), per the 2009 Gift Agreement Amendment. Scheduled to be transferred in 2019.

McKnight Endowed Chair for Clinical Translational Research in Cognitive Aging Ron Cohen, PhD

Financial Summary July 1 to December 31, 2018

Foundation Spendable Account	Amount
Endowment income transferred in:	
March 31, 2018	34,938
June 30, 2018	34,938
Sept 30, 2018	34,938
Dec 31, 2018	35,174
Total endowment income transferred in	139,989
Transferred to UF Peoplesoft spendable accounts	139,754 ^(a)
Net change in foundation spendable account	235
Beginning balance, January 1, 2018	34,938
Ending balance, Dec. 31, 2018	\$ 35,174
UF PeopleSoft Accounts	Amount
Received from foundation spendable account	\$ 139,754
Expenditures:	
Faculty and research staff salaries	136,398
Research equipment, supplies, and services	-
Travel and other	-
Total expenditures	136,398
Net change in UF Peoplesoft accounts	3,355
Beginning balance, January 1, 2018	61,202
Ending balance, Dec. 31, 2018	\$ 64,557
Total funds avail. to McKnight CAM Chair, Dec. 31, 2018	\$ 99,731

^(a)Transfers from foundation spendable account to Peoplesoft account in 2018.

Dr. William G. Luttge Lectureship in Neuroscience

Financial Summary January 1 to December 31, 2018

Endowment account balance, Dec. 31, 2018 \$ 282,690

Spendable account activity	Amount
Endowment income transfers, 4 quarters ending Dec. 31, 2018	9,645
Less UF Foundation gift overhead fees	<u>1</u>
Total funds available	9,644
Expenses for March 2018 lectureship	<u>5,551</u>
Net change in spendable funds	4,092
Beginning balance, January 1, 2018	<u>67,482</u>
Ending balance, December 31, 2018	<u><u>\$ 71,574</u></u>

McKnight Brain Research Grant Fund Report

with related accounts
Balances through December 31, 2018

Evelyn F. McKnight Brain Research Grant	Market Value Balance of Endowment	Fiscal Year Ending	Annual Endowment Transfers from Principal	Total Expenses / Net Transfers	Additional Investment Revenue ¹	Ending Spendable Fund Balance
	F008057		F008058			
F008057 / 58	\$ 12,967,682	2000	\$ -	\$ -	\$ -	\$ -
	\$ 12,967,682	2001	\$ 648,384	\$ -	\$ 7,264	\$ 655,648
	\$ 13,157,047	2002	\$ 657,852	\$ (37,840)	\$ 315,280	\$ 1,590,940
	\$ 20,249,996	2003	\$ 651,801	\$ (1,139,621)	\$ 89,549	\$ 1,192,669
	\$ 25,363,355	2004	\$ 729,335	\$ (944,138)	\$ 266,063	\$ 1,243,930
	\$ 26,681,575	2005	\$ 843,131	\$ (502,502)	\$ 174,351	\$ 1,758,910
	\$ 29,091,810	2006	\$ 881,347	\$ (250,000)	\$ 52,383	\$ 2,442,639
	\$ 33,148,130	2007	\$ 1,056,031	\$ (500,000)	\$ 73,172	\$ 3,071,843
	\$ 32,666,165	2008	\$ 1,172,824	\$ (350,003)	\$ 66,972	\$ 3,961,636
	\$ 25,549,465	2009	\$ 1,086,475	\$ (1,300,000)	\$ (479,678)	\$ 3,268,433
	\$ 26,893,099	2010	\$ 941,689	\$ (1,864,217)	\$ 67	\$ 2,345,972
	\$ 30,185,328	2011	\$ 971,846	\$ (2,413,940)	\$ -	\$ 903,877
	\$ 28,834,098	2012	\$ 1,026,301	\$ (1,017,551)	\$ -	\$ 912,627
	\$ 29,845,891	2013	\$ 1,028,384	\$ (1,415,244)	\$ -	\$ 525,767
	\$ 32,801,128	2014	\$ 1,063,533	\$ (920,824)	\$ -	\$ 668,477
	\$ 32,738,048	2015	\$ 1,117,603	\$ (1,596,541)	\$ 169,626	\$ 359,165
	\$ 28,270,285	2016	\$ 1,071,895	\$ (1,231,863)	\$ 167,343	\$ 366,540
	\$ 27,773,120	2017	\$ 1,041,290	\$ (1,147,507)	\$ -	\$ 260,322
	\$ 30,479,220	2018	\$ 1,041,290	\$ (1,041,290)	\$ -	\$ 260,322
	\$ 30,570,658	2019	\$ 522,401	\$ (520,645)	\$ -	\$ 262,078
Life-to-date Totals			\$ 17,553,411	\$ (18,193,725)	\$ 902,392	

CAM	Fiscal Year Ending	Transferred from F008058 (1/2 of MBRF Grant Income)	Total Expenses / Net Transfers	Additional Investment Revenue	Ending Spendable Fund Balance
		F016327			
F016327	2010	\$ 1,634,217	\$ (200,000)	\$ -	\$ 1,434,217
	2011	\$ 941,689	\$ -	\$ -	\$ 2,375,906
	2012	\$ -	\$ -	\$ -	\$ 2,375,906
	2013	\$ 784,804	\$ (400,000)	\$ -	\$ 2,760,710
	2014	\$ 652,756	\$ (1,000,000)	\$ -	\$ 2,413,466
	2015		\$ (2,413,466)	\$ -	\$ -
Life-to-date Totals		\$ 4,013,466	\$ (4,013,466)	\$ -	

AMENDED GIFT AGREEMENT - reconciliation		Fiscal Year Ending	Endowment Transfers from Principal	1/2 allocated to CAM	Actual transfers to CAM ²	Still due to CAM
Initial Transfer	9/17/2009	2010		\$ (1,634,217)	\$ 1,634,217	\$ -
		2010	\$ 941,689	\$ (470,845)	\$ -	\$ 470,845
		2011	\$ 971,846	\$ (485,923)	\$ 941,689	\$ 15,078
		2012	\$ 1,026,301	\$ (513,151)	\$ -	\$ 528,229
		2013	\$ 1,028,384	\$ (514,192)	\$ 784,804	\$ 257,617
		2014	\$ 1,063,533	\$ (531,767)	\$ 652,756	\$ 136,628
		2015	\$ 1,117,603	\$ (558,802)	\$ 415,567	\$ 279,735
		2016	\$ 1,071,895	\$ (535,947)	\$ 684,727	\$ 130,956
		2017	\$ 1,041,290	\$ (520,645)	\$ -	\$ 651,600
		2018	\$ 1,041,290	\$ (520,645)	\$ 781,762	\$ 390,483
		2019	\$ 522,401	\$ (261,200)	\$ -	\$ 651,684
Life-to-date Totals			\$ 9,826,232	\$ (6,547,332)	\$ 5,895,522	

¹Distributions from investment income were limited and variable from 2003-2009, resulting in additional revenues (/losses) from the reinvested endowment income. Additional revenues starting in 2015 are reimbursements from MBRF for Epigenetics Core expenses.

²Earnings from the endowment transfer to the MBI Peoplesoft account and MBI then transfers half to the CAM-CTRP.

Evelyn F. McKnight Chair Endowments

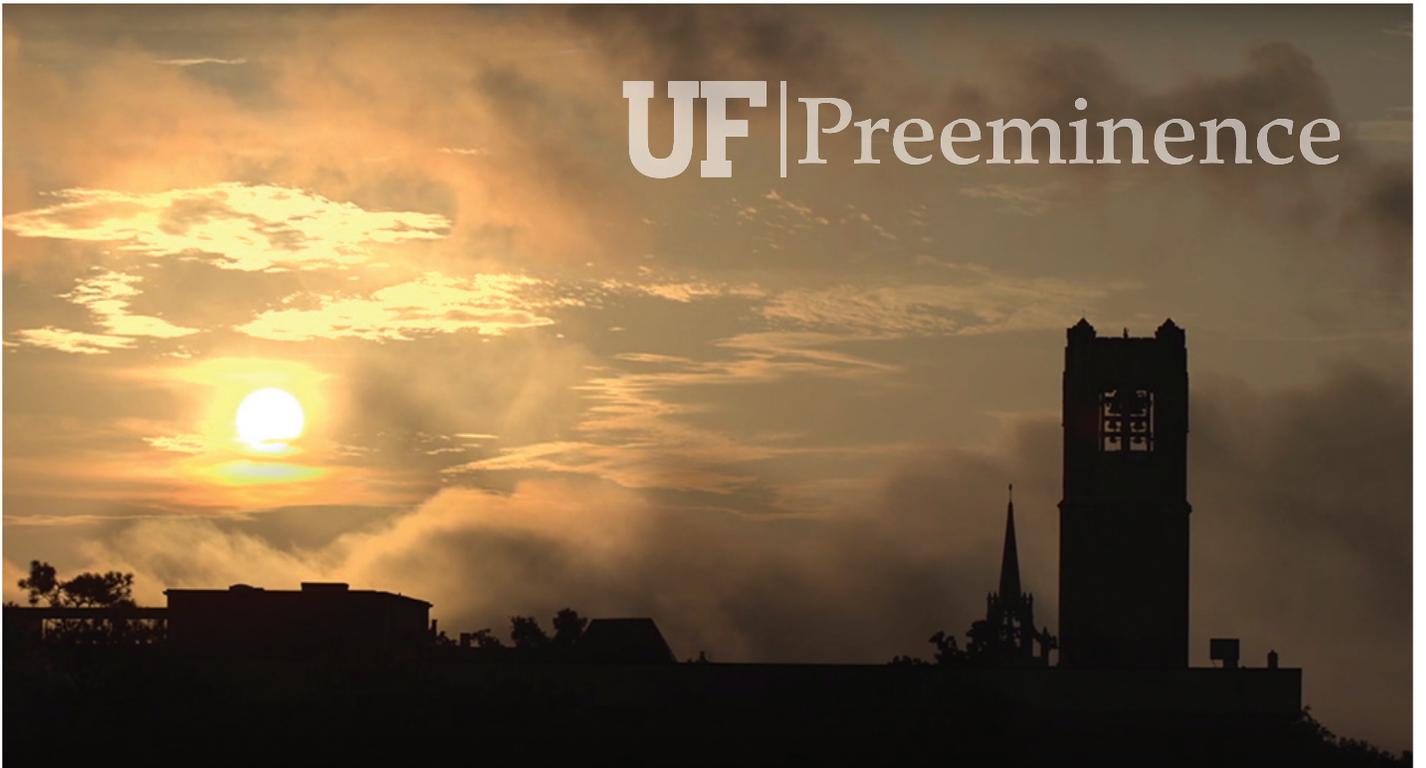
Balances through December 31, 2018

Evelyn F. McKnight Chair for Brain Research in Memory Loss	Market Value Balance of Endowment	Fiscal Year Ending	Annual Endowment Transfers from Principal	Total Expenses / Net Transfers	Additional Investment Revenue	Ending Spendable Fund Balance
	F007889			F007890		
F007889 / 90	\$ 1,988,345	2000	\$ 3,438	\$ (9,625)	\$ -	\$ (6,188)
	\$ 1,988,345	2001	\$ 99,417	\$ -	\$ (62)	\$ 93,167
	\$ 2,017,380	2002	\$ 100,869	\$ (7,810)	\$ (1,258)	\$ 184,968
	\$ 3,447,965	2003	\$ 125,768	\$ (52,502)	\$ 237,079	\$ 495,313
	\$ 3,866,391	2004	\$ 124,127	\$ (7,810)	\$ 14,191	\$ 625,820
	\$ 4,068,286	2005	\$ 127,813	\$ -	\$ 4,602	\$ 758,235
	\$ 4,435,787	2006	\$ 134,384	\$ (150,000)	\$ 19,578	\$ 762,197
	\$ 5,054,277	2007	\$ 161,019	\$ (150,000)	\$ 19,448	\$ 792,663
	\$ 4,980,774	2008	\$ 178,827	\$ (200,000)	\$ 14,387	\$ 785,877
	\$ 3,895,655	2009	\$ 165,660	\$ (450,000)	\$ (38,922)	\$ 462,615
	\$ 4,100,525	2010	\$ 143,584	\$ (499,000)	\$ 739	\$ 107,938
	\$ 4,602,508	2011	\$ 148,182	\$ -	\$ -	\$ 256,121
	\$ 4,396,479	2012	\$ 156,485	\$ (200,000)	\$ -	\$ 212,606
	\$ 4,550,752	2013	\$ 156,803	\$ (126,670)	\$ -	\$ 242,739
	\$ 5,001,352	2014	\$ 162,162	\$ (250,000)	\$ -	\$ 154,901
	\$ 5,006,025	2015	\$ 170,407	\$ (282,515)	\$ -	\$ 42,793
	\$ 3,795,851	2016	\$ 143,923	\$ (151,549)	\$ -	\$ 35,167
	\$ 3,729,097	2017	\$ 139,814	\$ (140,027)	\$ -	\$ 34,954
	\$ 4,092,445	2018	\$ 139,814	\$ (139,814)	\$ -	\$ 34,954
\$ 4,104,722	2019	\$ 70,143	\$ (69,907)	\$ -	\$ 35,189	
Life-to-date Totals			\$ 2,652,638	\$ (2,887,230)	\$ 269,781	

Evelyn F. McKnight Chair for Clinical Transl. Research in Cognitive Aging	Market Value Balance of Endowment	Fiscal Year Ending	Annual Endowment Transfers from Principal	Total Expenses / Net Transfers	Additional Investment Revenue	Ending Spendable Fund Balance
	F020105			F020106		
F020105 / 06	\$ 3,794,210	2016	\$ 143,861	\$ (108,709)	\$ -	\$ 35,152
	\$ 3,727,485	2017	\$ 139,754	\$ (139,967)	\$ -	\$ 34,938
	\$ 4,090,675	2018	\$ 139,754	\$ (139,754)	\$ -	\$ 34,938
	\$ 4,102,948	2019	\$ 70,112	\$ (69,877)	\$ -	\$ 35,174
Life-to-date Totals			\$ 493,481	\$ (458,307)	\$ -	

UF Foundation Endowment Reports

UF | Preeminence



FUND IMPACT REPORT

Evelyn F. McKnight Chair for Brain Research in Memory Loss

Book Value as of 9/30/18	\$3,995,676.90
Market Value as of 9/30/18	\$4,139,911.38
Projected Spendable Income for 2018/19	\$140,756.99

Endowment Management

Endowment assets are invested through the University of Florida Investment Corporation (UFICO), created in 2004 to manage UF's investment portfolios. UFICO is headed by a Chief Investments Officer who reports to a volunteer Board of Directors and to the President of the University of Florida.

FUND IMPACT REPORT

Evelyn F. McKnight Cognitive Aging and Memory Research Fund

Book Value as of 9/30/18	\$25,967,781.35
Market Value as of 9/30/18	\$30,832,736.18
Projected Spendable Income for 2018/19	\$1,048,313.03

Endowment Management

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FUND IMPACT REPORT

William G. Luttge Lectureship in Neuroscience

Book Value as of 9/30/18	\$250,300.00
Market Value as of 9/30/18	\$285,113.42
Projected Spendable Income for 2018/19	\$9,693.86

Endowment Management

Endowment assets are invested through the University of Florida Investment Corporation (UFICO), created in 2004 to manage UF's investment portfolios. UFICO is headed by a Chief Investments Officer who reports to a volunteer Board of Directors and to the President of the University of Florida.



FUND IMPACT REPORT

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

Book Value as of 9/30/18	\$4,000,000.00
Market Value as of 9/30/18	\$4,138,121.55
Projected Spendable Income for 2018/19	\$140,696.13

Endowment Management

Endowment assets are invested through the University of Florida Investment Corporation (UFICO), created in 2004 to manage UF's investment portfolios. UFICO is headed by a Chief Investments Officer who reports to a volunteer Board of Directors and to the President of the University of Florida.

FUND IMPACT REPORT

McKnight Brain Research Foundation

Evelyn F. McKnight Chair for Brain Research in Memory Loss (007889) Spendable Fund Transfers since endowment inception

FY 2018/2019	\$34,953 (09/30/18 YTD)
FY 2017/2018	\$139,814
FY 2016/2017	\$139,814
FY 2015/2016	\$143,923
FY 2014/2015	\$170,407
FY 2013/2014	\$162,162
FY 2012/2013	\$156,803
FY 2011/2012	\$156,485
FY 2010/2011	\$148,182
FY 2009/2010	\$143,584
FY 2008/2009	\$165,660
FY 2007/2008	\$178,827
FY 2006/2007	\$161,019
FY 2005/2006	\$134,384
FY 2004/2005	\$127,813
FY 2003/2004	\$124,127
FY 2002/2003	\$125,768
FY 2001/2002	\$100,869
FY 2000/2001	\$99,417
FY 1999/2000	\$3,438
TOTAL	\$2,617,449

FUND IMPACT REPORT

McKnight Brain Research Foundation**Evelyn F. McKnight Cognitive Aging and Memory Research (008057)
Spensible Fund Transfers since endowment inception**

FY 2018/2019	\$260,322 (09/30/18 YTD)
FY 2017/2018	\$1,041,290
FY 2016/2017	\$1,041,290
FY 2015/2016	\$1,071,895
FY 2014/2015	\$1,117,603
FY 2013/2014	\$1,063,533
FY 2012/2013	\$1,028,384
FY 2011/2012	\$1,026,301
FY 2010/2011	\$971,846
FY 2009/2010	\$941,689
FY 2008/2009	\$1,086,475
FY 2007/2008	\$1,172,824
FY 2006/2007	\$1,056,031
FY 2005/2006	\$881,347
FY 2004/2005	\$843,131
FY 2003/2004	\$729,335
FY 2002/2003	\$651,801
FY 2001/2002	\$657,852
FY 2000/2001	\$648,384
TOTAL	\$17,291,333

FUND IMPACT REPORT**McKnight Brain Research Foundation****William G. Luttge Lectureship in Neuroscience (018093)
Spendable Fund Transfers since endowment inception**

FY 2018/2019	\$2,407 (09/30/18 YTD)
FY 2017/2018	\$9,628
FY 2016/2017	\$9,627
FY 2015/2016	\$9,909
FY 2014/2015	\$9,386
FY 2013/2014	\$9,074
FY 2012/2013	\$6,754
TOTAL	\$56,785

**Evelyn F. McKnight Chair for Clinical Translational Research
in Cognitive Aging (020105)
Spendable Fund Transfers since endowment inception**

FY 2018/2019	\$34,938 (09/30/18 YTD)
FY 2017/2018	\$139,854
FY 2016/2017	\$139,754
FY 2015/2016	\$143,861
TOTAL	\$458,407

UF Foundation – Endowment Pool

Endowment Pool

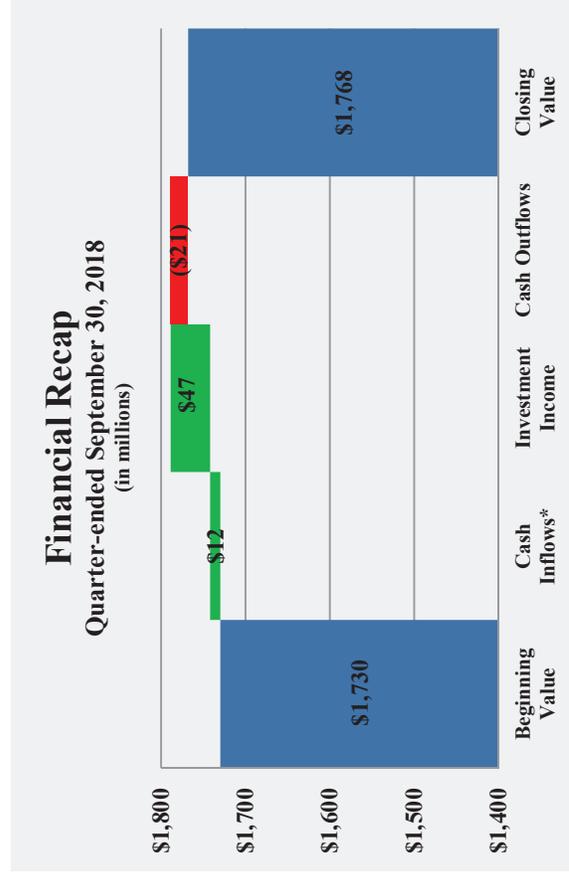
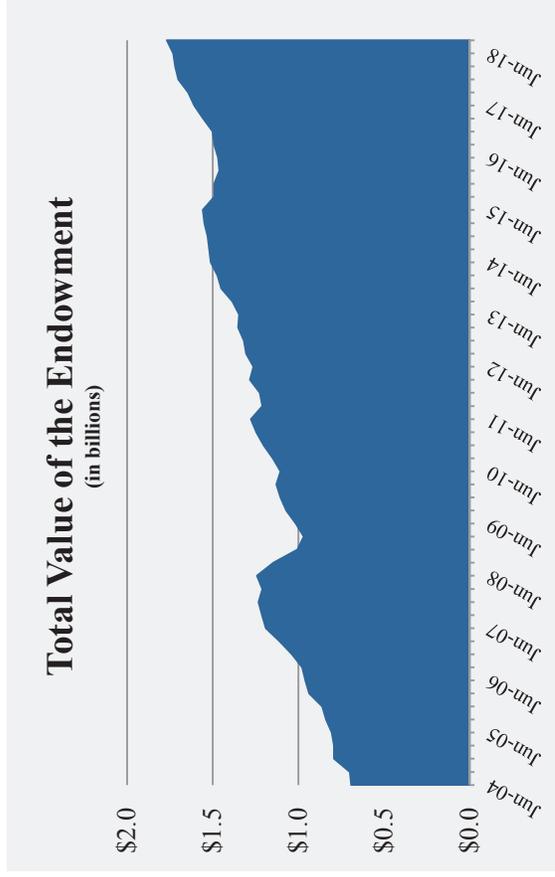
Since the founding of the University of Florida (UF) in 1853, generous alumni, corporations, foundations, parents and friends have contributed financial resources to assist UF in achieving its long-term mission of providing a superb education for undergraduates while maintaining excellent graduate programs and professional schools. As a result, UF’s total endowment market value is among the largest public university endowments in the United States.

The UF endowment assets reside with the University of Florida Foundation (UF Foundation). The UF Foundation is a private, not-for-profit, 501(c)(3) direct support organization of the University that raises and manages all gift money for the benefit of the University of Florida. The management of the Endowment Pool is designed to accomplish two goals:

- Provide a total return from assets invested that will preserve or increase the purchasing power of the endowment capital, and;
- Generate the maximum current spendable income stream to support activities of funds held for colleges and units of the University.

Endowments are an irreplaceable source of quality, stability, productivity and creativity for the University of Florida. The thoughtful individuals and organizations who create endowments provide security and confidence for our students and faculty, now and in the future. As such, the UF Foundation invests gift assets to protect the ability of the endowment to provide, in perpetuity, an income stream sufficient to support the University activity designated by the donor, and to ensure the proceeds thereof are used in accordance with their designation.

For the first quarter of the 2019 fiscal year, the Endowment Pool started with a balance of \$1.73 billion. During the quarter, there was \$12 million of cash inflows to the Endowment Pool thanks to the generous support of donors. Endowment investments generated net income of \$47 million during the quarter and there was \$21 million of cash paid out during the quarter in support of the University of Florida and its programs. The quarter ended with an Endowment Pool balance of \$1.77 billion.



* The timing of cash inflows does not always correspond with the timing of endowment gifts.

UF Foundation – Endowment Pool

Investment Objectives

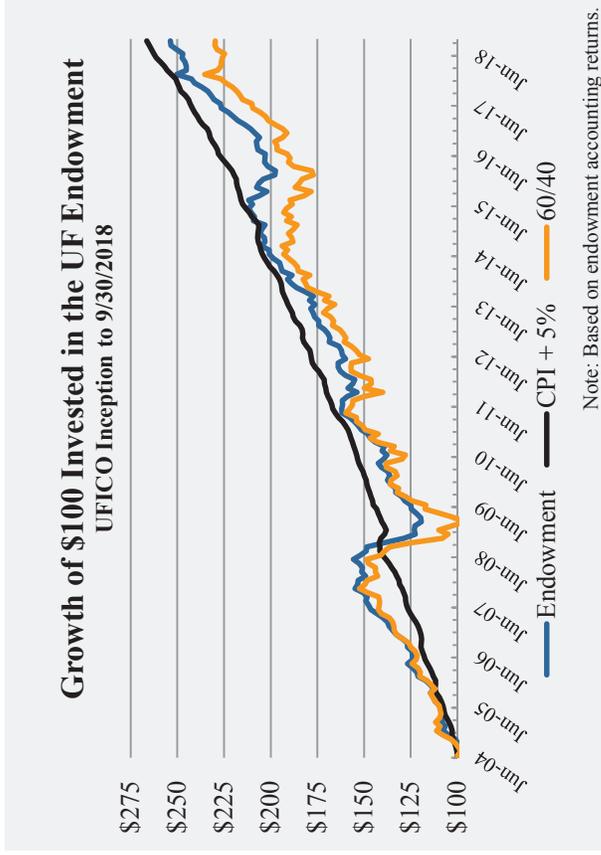
Since the inception of the University of Florida Investment Corporation (UFICO) in June 2004, the investment of the Endowment Pool has been managed by UFICO. Through UFICO’s management of the Endowment Pool, the UF Foundation seeks to achieve an annualized real rate of return of at least 5% net of fees to preserve and enhance the purchasing power of the endowment. Returns are measured over the long-term as the Endowment Pool is able to tolerate variability in the short and intermediate-term given its long investment horizon.

To measure performance results, investment returns are compared against the following benchmarks:

Benchmark	Purpose
CPI + 5%	The consumer price index plus the average gross spending rate for the endowment. This is a long-term growth benchmark that seeks to measure the purchasing power of the endowment over time.
60/40	Comprised of 60% - MSCI All Country World Index and 40% - Barclays Global Aggregate Bond Index, this benchmark represents the investible alternative for the endowment.

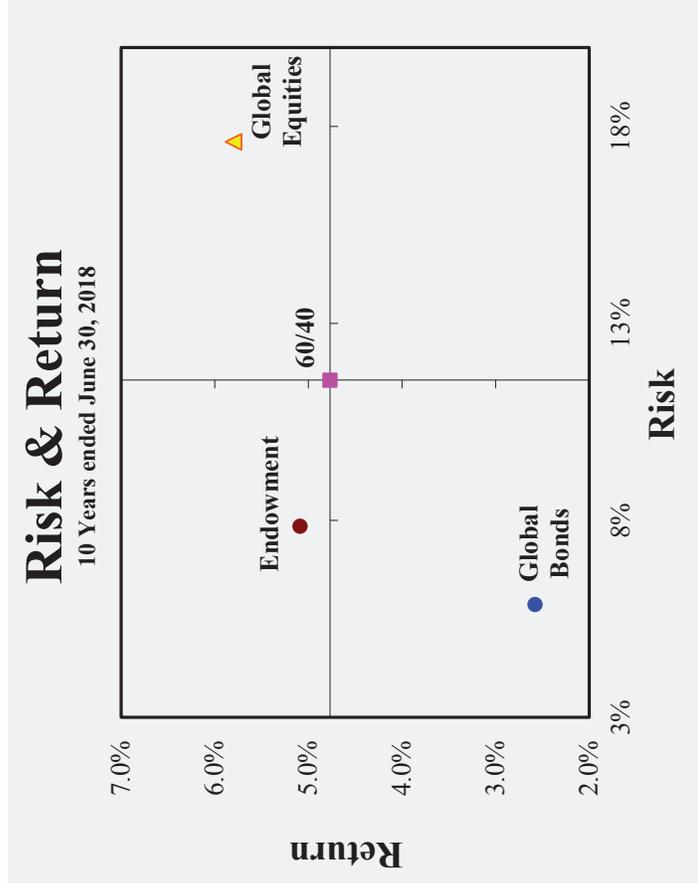
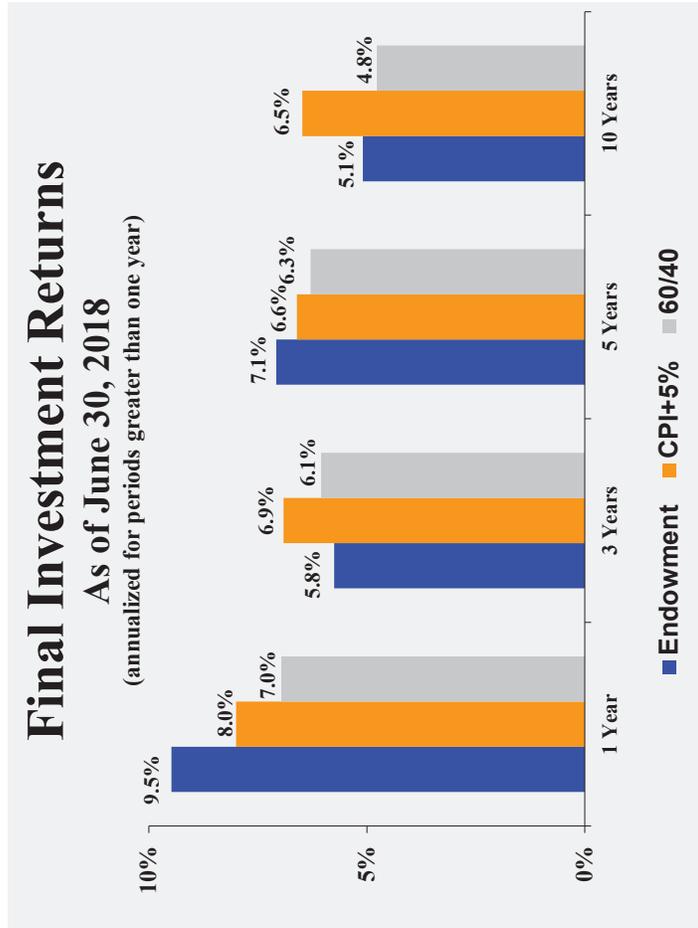
UFICO manages the Endowment Pool based on the objectives for the endowed assets as established by the Finance Committee of the UF Foundation Board of Directors. UFICO has constructed a long-term strategic asset allocation for the endowment portfolio based on the prioritization of these requirements including:

- **Positive Real Returns** – Intergenerational equity and maintaining the real purchasing power of the assets
- **Liquidity** – Retaining the ability to fund endowment obligations in all market conditions
- **Good Stewardship** – Maximizing *risk adjusted* returns
- **Growth** – Increasing the endowment’s ability to support the University



Strategic Asset Allocation As of 9/30/2018			
Strategy	Asset Classes	Target Allocation	Actual Allocation
Growth	Public Equities	82.5%	81.7%
	Hedged Strategies		
	Private Equity		
Real Assets	Natural Resources	7.5%	8.7%
	Real Estate		
Liquidity	Fixed Income Cash	10%	9.6%

UF Foundation – Endowment Pool



Faculty Biographical Sketches



Jennifer L. Bizon, PhD

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 of Neuroscience and Psychiatry

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 cognition and that contribute to cognitive decline in aging and disease. Using rodent models, my laboratory employs an integrative approach that combines sensitive behavioral assessments with cellular, molecular, optogenetic and pharmacological methodologies. We have uncovered disruptions in both glutamatergic and GABAergic signaling in the aged brain that contribute to impairments in cognitive flexibility, memory and decision making. In a second line of work, we have demonstrated age-associated alterations in impulsive and risky choice in aged rats that parallel those observed in humans (Simon et al., 2010, Hernandez et al, 2017) and are now employing optogenetic tools to dissect the neural circuits that govern changes to decision making in aging and Alzheimer's disease (Orsini et al., 2017, Hernandez et al., under review). In a third line of work, we have identified deficits in olfactory discrimination abilities in aged rats that strongly predict impairments in hippocampal-dependent memory function (LaSarge et al., 2007, Yoder et al., 2017). We hypothesize that these perceptual discrimination deficits reflect impaired function of the transentorhinal subregion of perirhinal cortex (area 35), a brain region heavily implicated in the encoding of stimulus representations that are used to form new memories. We are currently probing the neural mechanisms in rat models of aging and Alzheimer's disease that could contribute to loss of cognition supported by this brain region and are investigating the impact of risk factors such as chronic stress. 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 can target these mechanisms to improve cognitive health and life quality in older adults.

B. Positions & 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-	Professor of Neuroscience and Psychiatry, 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	Member, NSF Modulatory Brain Systems Review Panel
2011-2015	Director, Neuroscience Graduate Program, University of Florida College of Medicine
2012	<i>Ad hoc</i> member, NIH Chronic Dysfunction and Integrative Neurodegeneration
2013	<i>Ad hoc</i> member, NIH Sensory and Motor Neuroscience, Cognition and Perception Fellowship Study Section (F02B)
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	<i>Ad hoc</i> 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
2017 -	Associate Chair, Department of Neuroscience, University of Florida

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
2011-2016	Exemplary Teaching Award, College of Medicine, University of Florida
2017-present	Term Professor, University of Florida
2018-present	Research Foundation Professor, University of Florida

C. Contributions to Science

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

Publications December 2017-Present

- Hernandez CM, Orsini CA, Labiste CC, Wheeler AR, Ten Eyck TW, Bruner MM, Sahagian JJ, Harden SW, Frazier CJ, Setlow B, **Bizon JL**. The changing role of the basolateral amygdala during intertemporal choice in aging. Under Review.
- Blaes SL, Orsini CA, Holik HM, Stubbs TD, Ferguson SN, Heshmati SC, Bruner MM, Wall SC, Febo M, Bruijnzeel AW, **Bizon JL**, Setlow B. (2018) Enhancing effects of acute exposure to cannabis smoke on working memory performance. *Neurobiol Learning and Memory* pii: S1074-7427(18)30277-6. doi: 10.1016/j.nlm.2018.12.001.
- Orsini CA, Hernandez CM, **Bizon JL**, Setlow B. (2018) Deconstructing value-based decision making via temporally selective manipulation of neural activity: insights from rodent models. *Cogn Affect Behav Neurosci*. Epub ahead of print.
- Blaes SL, Orsini CA, Mitchell M, Bezhold SM, Spurrell MS, **Bizon JL**, Setlow B (2018) Monoaminergic modulation of decision making under risk of punishment in a rat model. *Behavioural Pharmacology*. 29(8):745-761.
- Hernandez CM, McQuail JA, Schwabe M, Burke SN, Setlow B, **Bizon JL** (2018) Age-related declines in prefrontal cortical expression of metabotropic glutamate receptors that support working memory. *eNeuro* 28:5(3) pii: ENEURO.0164-18.2018.
- McQuail JA, Krause EG, Setlow B, Scheur DA, **Bizon JL** (2018) Stress-induced corticosterone secretion covaries with working memory in aging. *Neurobiology of Aging* 71:156-160.
- Orsini CA, Heshmati SC, Garman TS, Wall SC, **Bizon JL**, Setlow B (2018) Contributions of medial prefrontal cortex to decision making involving risk of punishment. *Neuropharmacology* 139:205-216.
- Burke SN, Gaynor LS, Barnes CA, Bauer RM, **Bizon JL**, Roberson ED, Ryan L. Shared functions of perirhinal and parahippocampal cortices: implications for cognitive aging. *Trends in Neuroscience*. 41(6):349-359.
- 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(48): 11537-11548.

Abstracts for 2018 Society of Neuroscience Meeting in San Diego, CA

- A.-R. Wheeler^{1,2}, C. M. Hernandez^{1,2}, C. A. Orsini^{1,3}, T. W. Ten Eyck^{1,2}, C. C. Labiste^{1,2}, B. Setlow^{1,3}, **J. L. Bizon**^{1,2} Female Rats Show Greater Impulsive Choice Than Males in an Intertemporal Choice Task
- Hernandez, C. M. Hernandez, Iii, K. Campos, L. M. Truckenbrod, Q. P. Federico, B. M. Moon, J. A. McQuail, A. P. Maurer, **J. L. Bizon**, S. N. Burke Nutritional Ketosis Enhances Cognitive Resilience in Young and Aged Rats

3. M. Kreher¹, S. A. Johnson², J.-M. Mizell⁷, D. K. Chetram¹, D. T. Guenther³, S. D. Lovett⁴, B. Setlow⁵, **J. L. Bizon**⁸, S. N. Burke⁴, A. P. Maurer⁶ Contributions of The Perirhinal Cortex to Spatial Delay Discounting
4. C. A. Orsini¹, S. L. Blaes¹, **J. L. Bizon**³, B. Setlow²; Sex Differences in the Relationship Between Risk-Taking Preference And Escalation Of Cocaine Self-Administration in Rats
5. T. W. Ten Eyck¹, C. M. Hernandez, Iii², J. A. Mcquail², M. M. Bruner², S. Ghay², C. C. Labiste², A.-R. Wheeler², B. Setlow³, **J. L. Bizon**²; Altered GABAB Receptor Signaling In Basolateral Amygdala May Contribute to Age- Associated Differences in Intertemporal Choice
6. L. Altidor¹, T. S. Garman¹, S. Ramirez¹, A. M. Crider¹, D. G. Lamb², M. M. Bruner¹, A. M. Finner¹, E. W. Dirr³, F. Delgado³, K. P. Olczak³, A. P. Maurer¹, K. J. Otto³, S. N. Burke¹, B. Setlow², **J. L. Bizon**¹ Targeting GABAergic Mechanisms to Improve Prefrontal Cortical-Mediated Cognitive Flexibility in Novel Touchscreen-Based Reversal Learning Task
7. S. N. Burke¹, A. Crider², K. P. Olczak³, E. W. Dirr³, K. N. Lubke¹, J. Nick¹, B. Mclaurin¹, E. Atkinson¹, K. J. Otto⁴, A. P. Maurer⁵, D. G. Lamb⁷, B. Setlow⁶, **J. L. Bizon**⁸ Acute Vagus Nerve Stimulation Attenuates Novelty-Induced Arc Transcription In Dorsal Ca1
8. S. A. Johnson^{1,4}, S. M. Turner¹, K. N. Lubke¹, K. E. Fertal¹, A. P. Maurer^{1,2}, **J. L. Bizon**^{1,4}, S. N. Burke^{1,4,3} Hippocampal, Perirhinal, And Lateral Entorhinal Contributions to Mnemonic Discrimination in Young And Aged Rats
9. C. M. Hernandez, Iii¹, C. A. Orsini², C. C. Labiste¹, A.-R. Wheeler¹, T. W. Ten Eyck¹, M. M. Bruner¹, S. M. Singhal³, C. J. Frazier³, B. Setlow², **J. L. Bizon**¹ Aged Rats Do Not Use Basolateral Amygdala During Outcome Evaluation in An Intertemporal Choice Task
10. D. G. Lamb^{1,6,2}, T. S. Garman³, S. Ramirez³, A. Crider³, M. M. Bruner³, E. W. Dirr⁴, F. Delgado⁴, K. P. Olczak⁴, A. P. Maurer^{3,2,4,5}, K. J. Otto^{4,2}, S. N. Burke^{3,2}, B. Setlow^{1,2}, **J. L. Bizon**^{3,2} Effects of Vagus Nerve Stimulation on Selective Attention in Brown Norway Rats
11. S. M. Turner¹, S. A. Johnson¹, J. J. Flint¹, K. L. Robertson¹, J. A. Nick¹, S. D. Lovett¹, **J. L. Bizon**², S. N. Burke¹, A. P. Maurer¹ Perforant Path Fiber Loss Results in Mnemonic Similarity Task Deficits in Rats
12. J. A. Mcquail¹, S. A. Johnson¹, M. N. Litenski¹, S. Ghay¹, S. L. Rossi², P. Chakrabarty¹, B. I. Giasson¹, S. N. Burke¹, P. R. Rapp², **J. L. Bizon**¹ Normal Aging Increases Susceptibility to Human Wild Type Tau in Transentorhinal Cortex
13. S. L. Blaes¹, C. A. Orsini¹, H. Holik¹, **J. L. Bizon**³, B. Setlow²; Effects of Inactivation of the Lateral Habenula On Risky Decision Making

D. Current Research Support

R01 AG02942 (NIH- NIA)

2014/05/15-2019/05/19

Neural mechanisms of age-related cognitive decline

Principal Investigator: Jennifer L Bizon

The goal of this project is to determine how age-related alterations in GABAergic signaling mechanisms in prefrontal cortex contribute to impairments in working memory, behavioral flexibility and decision making.

RF1AG60778 (NIH-NIA)

2019/09/01-2024/08/31

Decision making and basolateral amygdala dysfunction in aging

Principal Investigator: Jennifer L Bizon (Setlow, Frazier MPIs)

The goal of this project is to determine the neural circuits that mediate alterations in decision making that occur in aging and Alzheimer's disease.

T32 AG061892 (NIH-NIA)

2019/09/01-2024/08/31

Clinical and translational pre-doctoral training in Alzheimer's disease and related dementias

Principal Investigator: Jennifer L Bizon (Lewis MPI)

The goal of this project is to provide training to PhD students in research related to AD and related dementias.

R21AG058240 (NIH-NIA)

2018/03/15-2020/03/01

Interactions of perirhinal tau pathology and aging in cognitive dysfunction

Principal Investigator: Jennifer L Bizon, (Burke MPI)

The goal of this project is to determine the early cognitive consequences of tau pathology in aged perirhinal cortex.

R01 DA036534 (NIH-NIDA)

2015/03/15-2020/03/31

Risk taking and cocaine use: interactions, mechanisms, and therapeutic targets

Co-Investigator: Jennifer L Bizon (Setlow PI)

The goal of this project is to determine neural mechanisms underlying relationships between risk taking behavior and cocaine self-administration.

R01 R01AG049722 (NIH-NIA) 2016/01/05-2021/01/15

The contribution of declines in functional connectivity to cognitive aging

Co-Investigator: Jennifer L Bizon (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.

R01MH109548 (NIH-NIMH) 2016/01/01-2021/10/01

Testing and forecasting hippocampal theta wave propagation in learning and memory

Co-Investigator: Jennifer L Bizon (Maurer PI)

The goal of this project is to investigate how basal forebrain and entorhinal input to hippocampus regulate brain rhythms in behaving animals.

Ed and Ethel Moore Alzheimer's Disease Pilot Grant (FL-DOH) 2017/02/01-2019/02/01

Impact of perirhinal cortical tau pathology on pre-clinical cognitive decline

Principal Investigator: Jennifer L Bizon (Burke MPI)

The goal of this project is to develop a rat model of Alzheimer's disease tau pathology and to explore perceptual discrimination as a behavioral biomarker of disease.

Targeted Neuroplasticity Training Award (DoD) 2017/01/01-2021/01/01

Cognitive augmentation through neuroplasticity

Project Leader: Jennifer L. Bizon (Otto PI)

The goal of this project is to explore peripheral nerve stimulation as a means to enhance cognition.

Current Mentored Support

K99DA041493 (NIH-NIDA) 2016/03/01-2020/02/28

Neural circuits and mechanisms underlying maladaptive risk-taking following cocaine self-administration

Principal Investigator: Caitlin A Orsini, **co-Sponsor: Jennifer L Bizon**

K99AG058786 (NIH-NIA) 2018/06/01-2022/08/31

Hippocampal and dopaminergic mechanisms of novelty detection underlying cognitive decline

Principal Investigator: Sarah Johnson, **co-Sponsor: Jennifer L Bizon**

K01AG061263 (NIH-NIA) Pending

Epigenetic mechanisms of stress and age-related cognitive decline

Principal Investigator: Joe McQuail, **Sponsor: Jennifer L. Bizon**

Approved for funding

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: 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 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

My NIH/NIA funded research program is broadly focused on improving health outcomes in the elderly by determining the biological mechanisms that are responsible for the cognitive decline that occurs in later stages of life. Even in the absence of pathology, a large proportion of elderly people experience memory decline that interferes with their quality of life. Thus, understanding the neurobiology of memory impairments in advanced age is paramount both improving health outcomes in the elderly as well as distinguishing normal aging from dementia. A significant barrier to uncovering the neurobiology of age-related cognitive decline is that memory processes are distributed throughout the brain and a fundamental gap exists in our understanding of how different brain structures interact over the lifespan. The long-term goal of my laboratory is to determine the alterations in network-level interactions that underlie cognitive impairment in advanced age and dementia, and how this interacts with neurometabolism. Current projects are focused on uncovering mechanisms of age-related impairments in sensory discrimination across modalities, identifying age-associated changes in medial temporal lobe-prefrontal functional connectivity that contribute to memory deficits, and testing whether diet can globally improve neural network function in old animals. To answer these questions, my lab integrates neurophysiology and anatomy with behavioral analysis in order to determine the extent that age-related memory impairments manifest from dysfunction in inter-regional communication. Our rationale is that by elucidating how aging influences systems-level dynamics, we will be better positioned to develop interventions that broadly improve cognition.

B. Positions and Honors

Positions & 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 - Assistant Professor, Department of Neuroscience, University of Florida, Gainesville, FL

Other Experience and Professional Memberships

2002 - Member, Society for Neuroscience
 2008 - 2009 Mentor and small group leader, Undergraduate Biology Research Program, University of Arizona
 2010 - 2012 Membership Enhancement Plan Working Group, Society for Neuroscience
 2010 - 2011 Mentor, University of Arizona Assurance Program
 2014 - Mentor, HHMI Science for Life
 2014 - Member, North Central Florida Chapter of the Society for Neuroscience
 2014 - Mentor, University of Florida Scholar Award

- 2015 - Judge for speaker competition, Junior Science, Engineering and Humanities Symposium
- 2015 - Member Faculty for Undergraduate Neuroscience
- 2015 - Director of the UF Summer Neuroscience Internship Program

Honors

- 2018 McKnight Brain Institute Leadership Award

C. Contribution to Science

1. Gaynor LS, Curiel RE, Penate A, Rosselli M, **Burke SN**, Wicklund M, Loewenstein DA, Bauer RM (2018). Visual Object Discrimination Impairment as an early predictor of Mild Cognitive Impairment and Alzheimer's disease. Under revision, *Journal of the International Neuropsychological Society*.
2. Colon-Perez LM, Turner SM, Lubke KN, Febo M*, **Burke SN*** (2018). Multi-scale imaging reveals aberrant connectome organization and elevated dorsal striatal Arc expression in advanced age. Under revision, preprint available: <https://www.biorxiv.org/content/early/2018/10/03/434191>. *Indicates shared corresponding author.
3. Johnson SA, Turner SM, Lubke KN, Cooper TL, Fertal KE, Bizon JL, Maurer AP, **Burke SN** (2018). Experience-dependent effects of muscimol-induced hippocampal excitation on mnemonic discrimination. Under revision, *Frontiers in Systems Neuroscience*. Preprint available: <https://www.biorxiv.org/content/early/2018/10/29/454744>
4. **Burke SN*#**, Turner SM#, Desrosiers CL, Johnson SA, Maurer AP* (2018). Perforant path fiber loss results in mnemonic discrimination task deficits in young rats. In press, *Frontiers in Systems Neuroscience*. *Indicates shared corresponding author, #These authors contributed equally.
5. 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. In press, *Frontiers in Aging Neuroscience*.
6. Sheremet A, Kennedy JP, Qin Y, Zhou Y, Lovett SD, **Burke SN**, Maurer AP (2018). Theta-Gamma Cascades and Running Speed. In press, *Journal of Neurophysiology*.
7. Gray DT, Umapathy L, **Burke SN**, Trouard TP, Barnes CA (2018). Tract-specific white matter correlates of age-related reward devaluation deficits in macaque monkeys. *Journal of Neuroimaging in Psychiatry and Neurology*, 3(2):13-26.
8. Hernandez AR, Reasor JE, Truckenbrod LM, Fertal KE, Maurer AP, **Burke SN** (2018). Differential effects of advanced age on neuronal ensemble activity in hippocampus, perirhinal cortex, and prefrontal cortex. *Neurobiology of Aging*, 70:217-232.
9. Hernandez CM, McQuail JA, Schwabe M, **Burke SN**, Setlow B, Bizon JL (2018). Age-related declines in prefrontal cortical expression of metabotropic glutamate receptors that support working memory. *eNeuro*, 5(3), eCollection 2018 May-Jun.
10. Malem-Shinitzki N, Zhang Y, Gray DT, **Burke SN**, Smith AC, Barnes CA, Ba D (2018). A Separable Two-Dimensional Random Field Model of Binary Response Data from Multi-Day Behavioral Experiments. *Journal of Neuroscience Methods*, 307:175-187.
11. Gaynor LS, Mizell J, Johnson SA, Maurer AP, **Burke SN** (2018). Aging disproportionately affects dual-functions of the perirhinal cortex: discrimination versus association. *Behavioral Neuroscience*, 132(3):138-151.
12. **Burke SN**, Gaynor LS, Barnes CA, Bauer RM, Bizon JL, Roberson RD, Ryan L (2018). Shared Functions of Perirhinal and Parahippocampal Cortices: Implications for Cognitive Aging. *Trends in Neurosciences*, 41(6):349-359.
13. Hernandez AR, Campos KT, Truckenbrod LM, Hernandez CM, Sakarya Y, McQuail JA, Carter CS, Bizon JL, Maurer AP, **Burke SN** (2018). The Antiepileptic Ketogenic Diet Alters Hippocampal Transporter Levels and Reduces Adiposity in Aged Rats. *Journal of Gerontology, Series A Biological Sciences and Medical Sciences*. 73(4):450-458.

Other Publications and Book Chapters

1. Hernandez AR, **Burke SN** (2018). Age-related changes in 'hub' neurons. *Aging*, 10(10): 2551-2552.
2. **Burke SN**, Barnes CA (2018). The Contribution of Recollection, Familiarity and Discrimination to Object Recognition Deficits in Advanced Age. In *Handbook of Object Novelty Recognition*, ed Abdel Ennaceur.
3. **Burke SN** (2018). Award for Distinguished Scientific Early Career Contributions to Psychology: Sara N. Burke. *American Psychologist*.
4. McQuail JA, Johnson SA, **Burke SN**, Bizon JL (in press). Rat Models of Cognitive Aging. In *Conn's Handbook of Models for Human Aging*, CH 17, ed Jeffrey Ram.

5. Foster TC, **Burke SN** (in press). Animal Models of Cognitive Aging and Circuit-Specific Vulnerability. In *Geriatric Neurology*, eds DeKosky and Asthana.

First Author and Other Selected Abstracts

1. Hernandez AR, Hernandez CM, Campos K, Truckenbrod LM, Federico QP, Moon BM, McQuail, JA, Maurer AP, Bizon JL, **Burke SN** (2018). Nutritional ketosis enhances cognitive resilience in young and aged rats. *Society for Neuroscience 48: San Diego, CA*.
2. **Burke SN**, Crider A, Olczak KP, Dirr EW, Lubke KN, Nick J, McLaurin B, Atkinson E, Otto KJ, Maurer AP, Lamb DG, Setlow B, Bizon JL (2018). Acute vagus nerve stimulation attenuates novelty-induced arc transcription in dorsal CA1. *Society for Neuroscience 48: San Diego, CA*.
3. Johnson SA, Turner SM, Lubke KN, Fertal KE, Maurer AP, Bizon JL, **Burke SN** (2018). Hippocampal, perirhinal, and lateral entorhinal contributions to mnemonic discrimination in young and aged rats. *Society for Neuroscience 48: San Diego, CA*.
4. McQuail JA, Johnson SA, Litenski MN, Ghay S, Rossi SL, Chakrabarty P, Giasson BI, **Burke SN**, Bizon KL (2018). Normal aging increases susceptibility to human wild type tau in transentorhinal cortex. *Society for Neuroscience 48: San Diego, CA*.

Invited Talks

- Dec 11, 2018 Clinical Translation Aging Research Seminar, Gainesville, FL. "Neural Network and Metabolic Mechanisms of Cognitive Aging"
- Dec 4, 2018 University of California, Irvine Center for Neurobiology of Learning and Memory Colloquium. "Neural Network and Metabolic Mechanisms of Cognitive Aging"
- Sep 6, 2018 University of Florida, Department of Neuroscience Seminar, Gainesville, FL. "Linking Cognitive Aging to Cortical Connectivity: Why We Should Ask More of Our Rats"
- Feb 19, 2018 University of Texas, Dallas Center for Vital Longevity, Dallas, TX. "A Systems-level Understanding of Cognitive Aging in Pre-clinical Models"

Conference Symposium Organized

- April 22, 2018 International Conference on Learning and Memory (International). Rethinking content-based parcellation of the medial temporal lobe. Speakers: Lee Ryan (University of Arizona), **Sara Burke** (University of Florida, Cyriel Pennartz (University of Amsterdam), Kristen Scaplen Kerr (Brown University). Role: Organizer and co-chair

Complete List of Published Work in My Bibliography:

<http://www.ncbi.nlm.nih.gov/myncbi/sara.burke.1/bibliography/47433007/public/?sort=date&direction=ascending>

D. Research Support

Ongoing Research Support

01/01/16-11/30/20

1R01AG049722, National Institute on Aging

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.

Role: PI

2017/01/01-2020/12/31

DARPA Targeted Neuroplasticity Training

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.

Role: co-PI (project leader for Task 1.2)

03/15/2018 - 02/29/2020

NIH/NIA R21AG058240 (multiple-PI with Bizon)

The goal of this award is to determine in the interaction between tau pathology, age, and declines in stimulus discrimination. Interactions of Perirhinal Tau Pathology and Aging in Cognitive Dysfunction

Role: m-PI

08/15/16-05/30/19 (NCE)

1R21AG051004

Title: Single-Cell Imaging of Functional Connectivity as a Window into Cognitive Aging

The major goal of this award is to develop novel methods for quantifying functional connectivity between memory-associated brain structures in young and aged rats.

Role: PI

2017/02/01-2019/01/31

Florida Department of Health Ed and Ethel Moore Alzheimer's Disease Research Program

Grant: 7AZ06

Impact of Perirhinal Cortical Tau Pathology on Pre-Clinical Cognitive Decline

Role: co-PI (contact co-PI Jennifer L., Bizon)

The goal of this proposal is to develop and validate a rat model of human tauopathy.

2013/10/01-2018/09/30

0011249, McKnight Brain Research Foundation

Neural system dysfunction and cognitive aging

This goal of this award is to provide institutional support in order to establish a rigorous research program aimed and determining the neurobiological basis of cognitive impairments in the elderly and to identify potential therapeutic strategies.

Role: PI

2016/09/01-2021/06/30

NIH/NIMH R01MH109548 (Maurer, PI)

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.

Role: co-I

2017/03/31-2022/01/31

NIH/NIA R01AG055544 (Maurer, PI)

Title: Age-associated changes in hippocampal circuits and cognitive function

The goal of this award is to elucidate if age-related alterations in hippocampal activity patterns reflect synaptic dysfunction or adaptive compensation.

Role: co-I

07/01/2018-06/30/2023

NIH/ NIA 1R01AG060778-01, PI: Bizon

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.

Role: co-I

2018/04/01-2020/04/01

K99AG058786 NIH Pathway to Independence Award (Johnson, PI)

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 prepared to transition to research independence.

Role: Mentor

Pending

NIH/ NIA R01AG060977

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.

Pending council review, percentile: 3%

Role: PI

Ronald A. Cohen, PhD

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 rcohen1

POSITION TITLE: Professor

EDUCATION/TRAINING

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	Clinical Psychology, Neuropsychology
UCLA Neuropsychiatric Institute, Westwood, CA	Resident	07/1982	Clinical Psychology Internship
University of Florida, Gainesville, FL	Postdoctoral Fellow	09/1983	Neuropsychology

A. Personal Statement

Dr. Cohen is director of the University of Florida Center for Cognitive Aging and Memory Clinical Translational Research (CAM). He is a professor of Clinical and Health Psychology with joint appointments in the departments of Clinical and Health Psychology, Neurology, Psychiatry. Dr. Cohen also is the Evelyn McKnight Chair for Cognitive and Memory Clinical Translational Research at UF. The CAM is a multidisciplinary research program focused on factors that influence cognitive aging that will integrate neurocognitive, neuroimaging, and laboratory biomarker methods. A primary goal of this center is clinical translational in nature with a focus on translating neuroscience findings from the laboratory to clinical application for both improvement assessment and intervention. He has extensive background in neuroimaging and the neuroscience of attention-executive functions, and strong record of research involving the use of functional and structural neuroimaging methods in studies of age-associated brain disorders and neurodegenerative brain disorders. He has published over 250 peer-reviewed articles, and numerous book chapters on topics of relevance to this project. Besides co-editing several books on topics related to areas of clinical neuropsychological research, Dr. Cohen authored "Neuropsychology of Attention" in 1993 which was the first book on this topic in the field, which was recently updated and published as a second edition this year. He authored a book "Brain Imaging in Behavioral Medicine and Clinical Neuroscience", which will be the first to address the use of neuroimaging methods for studying various problems in clinical neuroscience and to lead the current project. Specifically, Dr. Cohen's CAM laboratory has been conducting human studies employing multimodal neuroimaging in conjunction with MRS to examine pathophysiological changes occurring in normal and pathological brain aging, and also secondary to risk factors including obesity, diabetes, heart disease, viral infections (e.g., HIV), and neurodegenerative disease such as AD. He has assembled an outstanding team of researchers with specific areas of expertise that will enable the success of the CAM.

B. Positions and Honors

Positions and Employment

1983 - 1990 Assistant Professor, Department of Neurology, University of Massachusetts Medical School

1990 - 1993 Associate Professor, Department of Neurology, University of Massachusetts Medical School

1993 - 1996 Assistant Professor, Department of Psychiatry-Human Behavior, Brown University

1993 - 2008 Director of Neuropsychology, The Miriam Hospital, Warren Alpert School of Medicine, Brown University

2004 - 2012 Professor, Department of Psychiatry - Human Behavior, Brown University

2004 - 2012 Professor, Brain Sciences Program, Brown University

2012 - 2016 Professor, Departments of Aging, Neurology and Psychiatry, University of Florida

2016 - Professor, Departments of Clinical and Health Psychology, Neurology and Psychiatry, University of Florida

2012 - Director, Center for Cognitive Aging and Memory, University of Florida

Other Experience and Professional Memberships

1983 - Member, International Neuropsychological Society

Honors

2012 Endowment in Support of the Center for Cognitive Aging and Memory, McKnight Brain Research Foundation

2015 Evelyn McKnight Chair, Cognitive Aging and Memory

C. Contribution 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 coinfecting 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 with out 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 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.
- 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. Szabo AJ, Alosco ML, Miller LA, McGeary JE, Poppas A, **Cohen RA**, Gunstad J. Brain-derived neurotrophic factor Val66Met polymorphism and cognitive function in persons with cardiovascular disease. *Psychogeriatrics.* 2013 Dec;13(4):206-12. **PubMed PMID: 24289461; PubMed Central PMCID: PMC3847660.**
 - c. **Cohen RA**, Seider TR, Navia B. HIV effects on age-associated neurocognitive dysfunction: premature cognitive aging or neurodegenerative disease? *Alzheimers Res Ther.* 2015;7(1):37. **PubMed PMID: 25848401; PubMed Central PMCID: PMC4386102.**
 - d. Hawkins MA, Alosco ML, Spitznagel MB, Strain G, Devlin M, **Cohen R**, Crosby RD, Mitchell JE, Gunstad J. The Association Between Reduced Inflammation and Cognitive Gains After Bariatric Surgery. *Psychosom Med.* 2015 Jul-Aug;77(6):688-96. **PubMed PMID: 25478707; PubMed Central PMCID: PMC4456339.**

D. Research Support

Ongoing Research Support

1R01DK09933401A1 (Ronald Cohen, PI)	\$349,225	6/25/2014 – 05/31/2019	3.6 CM
National Institute of Health NIDDK			
Obesity and Type-2 Diabetes: Bariatric Surgery Effects on Brain Function			
The study will delineate mechanism underlying the effects of chronic obesity on brain functioning and determine if cognitive benefits of bariatric surgery and weight loss contribute to enhanced cerebral metabolic or hemodynamic function assessed using multimodal neuroimaging methods.			
R21AG053736-01A1 (Clark; PI)	\$14,219	06/01/2017 -05/31/2019	.36 CM
National Institute of Health NIA			
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.			
1R01AG054077-01 (Woods/Cohen, PI's)	\$21,546	09/1/2016-04/30/2021	1.2 CM
National Institute of Health			
Augmenting Cognitive Training in Older Adults – The ACT Grant			
This randomized clinical trial examines the effect of augmenting cognitive training with transcranial direct current stimulation 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.			
R01DA042069 (Cook, PI)	\$20,093	08/15/2017 – 03/31/2022	.60 CM
National Institute of Health NIDA			
Health outcomes and cognitive effects of marijuana use in people living with HIV/AIDS. The overarching goals of this study are to obtain evidence regarding the influence of marijuana on major health outcomes and behavior in PLWH in order to help guide clinical recommendations and identify risk factors for consequences.			
U01AA026225 – (Barve, Cohen, Cook PI's)	\$24,369	09/22/2017 – 08/31/2018	.96 CM
National Institute of Health NIAAA			
This U01 project contains to components, one which involves a collaboration between Florida investigators from UF, UM, and FIU who are part of the SHARC and Dr. Barve and his group at the University of Louisville. This study examines the impact of abnormalities in the gut microbiome associated with HIV and heavy ETOH use. Stool samples collected at the Miami site from participants enrolled in U01AA020797 are sent to Dr. Barve's laboratory and biomarkers are derived. These biomarkers are examined relative to cognitive, neuroimaging, and clinical measures collected at three time points. Dr. Cohen's laboratory is responsible for the analysis of cognitive and neuroimaging data, and resulting manuscripts.			
R21AG054876 – (Williamson, PI)	\$7,362	09/01/2017 – 05/31/2019	.12 CM
National Institute of Health NIA			
Treatment of mild cognitive impairment with transcutaneous vagal nerve stimulation. This study examines whether cognitive and brain functioning in MCI can be improved via vagal stimulation applied in conjunction with cognitive training.			
U01AA020797 (Cook, Cohen, MPIs)	\$63,200	09/01/2016 – 06/30/2021	1.4 CM
National Institute of Health NIAAA			
Effects of experimentally-induced reduction alcohol use on cognitive and brain function in HIV-infected adults. This U01 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. Electronic alcohol monitors are worn to verify actual alcohol consumption on a continuous basis. Participants 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.			
2 P01 AA019072 (Monti, PI)	\$110,695	9/01/2015-05/31/2020	1.2 CM
National Institute of Health NIAAA			
Alcohol and HIV: Biobehavioral Interactions and Intervention			
The goals of this program project are to study the effects of alcohol use on HIV disease progression, the effects of interventions to reduce alcohol use in HIV-infected populations, and the effects of alcohol on sexual decision making. The project also fosters multidisciplinary collaborations and training in research on alcohol and HIV and dissemination of research findings to clinicians			

treating addictions and HIV. Research Component 1 (Cohen, PI) is a continuation of the study being conducted in the parent ARCH, but will now examine the effects of reducing alcohol consumption via a motivational interviewing approach in HIV-infected heavy drinkers, with a specific focus on changes in cognitive performance, functional brain response on fMRI, and cerebral metabolite abnormalities (MRS).

1R21HL140492-01 (Salmoirago-Blotcher, PI) \$10,733 5/25/2018 – 04/30/2020 .60CM
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.

Barve, **Cohen**, Cook **PI's** \$174,641 annual 10/01/2018 – 09/30/2023 1.8 CM

R01AG061065 – NIA: Microbiome study of HIV and aging

The Role of Gut Microbial Dysbiosis and Aging on HIV-associated neurocognitive and brain dysfunction

This study extends our current research on neuroHIV and the contribution of the gut-liver-brain axis to neurocognitive and brain abnormalities. In this project we will recruit HIV+ and HIV- adults ranging in age from young adulthood to advanced age. The project examines 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.

Steven T. DeKosky, MD, PhD

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	Grad. 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

I have worked in Alzheimer's disease (AD) and related disorders for over 30 years, studying 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. I began clinical studies in cognitive, behavioral, neuroimaging and therapeutic interventions to translate my bench research studies, correlating imaging and cognition, trials of new medications including First in Man studies in the Pitt Alzheimer Center, and large scale (>3,000 Ss) long term (>6 years) multicenter dementia prevention trials using Ginkgo biloba; I was PI of the GEM trial. I was founding co-director (1985-1990; U. Kentucky) then director (1994-2008; Pittsburgh) of Alzheimer's Disease Research Centers (ADRCs) and serve as chair of 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 for the NIA regarding aging and dementia. I served on the NCCAM (now NCCIH) Council was a member of the NIH Council of Councils (overseeing the Common Fund). I maintained an NIH-funded wet lab for over 30 years, and was chair of the Pitt Department of Neurology for 8 years. 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, and my return to research via a sabbatical year at Penn (bioethics) and Pitt (in the PET labs) has facilitated my re-entry into research and research administration. My knowledge of the multiple dimensions of neurodegenerative diseases, of ADRCs, and extensive experience with PET and clinical trials puts me in an excellent position to work on this grant proposal.

Ikonomovic, MD, Uryu, K, Abrahamson, EE, Ciallella, JR, Trojanowski, JQ, Lee, V M-Y, Clark, RS, Marion, DW, Wisniewski, SR, and **DeKosky, ST** Alzheimer's pathology in human temporal cortex surgically excised after severe brain injury *Experimental Neurology* 190:192-203, 2004

Mintun, MA, LaRossa, GN, Sheline, YI, Dence, CS, Lee, SY, Mach, RH, Klunk, WE, Mathis, CA, **DeKosky, ST**, and Morris, JC [11C] PIB in a nondemented population: Potential antecedent marker of Alzheimer disease. *Neurology* 67:446-452, 2006.

B. Positions and Honors

Positions and Employment

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 of Neurology, Neuroscience and Aging and Geriatric Research, University 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-present 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 for the 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

1968-1969 Predoctoral Fellowship, Center for Neurobiological Sciences, Univ. Florida College of Medicine
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 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

C. Contribution to Science

Science (chosen from >450 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, 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, Knopman, DS, Reeder, TM, Shetter, AG, Senter, HJ, Markesbery, WR, and the Intraventricular 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, Ikonomic, 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.

Ikonomic, MD, Klunk, WE, Abrahamson, EE, Wu, 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 A β in mild cognitive impairment: An example of brain reserve. *Journal of Neuroscience* 29:14770-14778, 2009. PMID: 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.

Ikonomic, MD, Klunk, WE, Abrahamson, EE, Mathis, CA, Price, JC, Tsopelas, ND, Lopresti, BJ, Ziolk, 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. PMID: PMC2408940

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* 8:389-398, 2012. PMID: 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. PMID: PMC3662268

Curiel, R E, Loewenstein, DA, Rosselli, M, Penate, A, Greig-Custo, MT Bauer, RM, ... Duara, R. (2018). Semantic intrusions and failure to recover from semantic interference in mild cognitive impairment: Relationship to amyloid and cortical thickness. *Current Alzheimer Research*. <https://doi.org/10.2174/1567205015666180427122746>

3. Experimental Brain Trauma:

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

DeKosky, S.T., Goss, J.R., Miller, P.D., Styren, S.D., Kochanek, P.M., and Marion, D. Up-regulation of nerve growth factor following cortical trauma. *Experimental Neurology* 130:173-177, 1994.

DeKosky, S.T., Taffe, K.M., Abrahamson, E.A., Dixon, C.E., Kochanek, P.M., and Ikonomic, M.D. 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, E.E., Ikonomic, M.D., Ciallella, J.R., Hope, C.E., Paljug, W.R.,

Isanski, B.A., Flood, D.G., Clark, R.S.B., and **DeKosky, S.T.** Caspase inhibition therapy abolishes brain trauma-induced increases in A β peptide: Implications for clinical outcome. *Experimental Neurology* 197:437-450, 2006.

Abrahamson, E. E., Ikonovic, M.D., Dixon, D.E. and **DeKosky, S.T.** Simvastatin therapy prevents brain trauma-induced elevations in β -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 β and A β 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 Ikonovic, MD Association of increased cortical soluble A β 42 levels with diffuse plaques after severe brain injury in humans *Archives of Neurology* 64:541-544, 2007.

DeKosky, ST, Ikonovic, 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, Ikonovic, MD and Gandy, S. Acute and chronic traumatic encephalopathies: Pathogenesis and biomarkers. *Nature Reviews Neurology* 9:192-200, 2013. PMID: 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. PMID: 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. PMID: PMC2823569.

Curjel, 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>

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

Ongoing Research Support

P50 AG047266 Golde (Director & Project Leader)

05/31/2020

University of Florida and Mt. Sinai Medical Center AD Research Center

Major goals. The UF-MSMC ADRC will be focused on several 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: Associate Director (Assoc. PL, Administrative Core)

529-13-0046-00001 Texas Health & human Serv.-HRSA, Shenkman (PI)

03/01/2015-08/31/2019

Texas External Quality Review Organization Vendor and Quality Vendor

The major goals are to assess a program in which dual eligible (Medicare and Medicaid) patients are provided with resources to improve health and fitness using flexible methods and objective follow-up of health and health care resource utilization.

Role: Co-Investigator

- R01 AG054077**, Woods (PI) 09/01/2016-4/30/2021
 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.
Role: Co-Investigator
- R21 AG054876**, Williamson (PI) 09/01/2017-08/31/2019
 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).
Role: Co-Investigator
- Completed Research Support**
- RF1 AG051593** Catalano (PI) 09/15/2016-06/30/2018
 "Phase 1 safety trial for CT1812, a novel small molecule therapeutic targeting a synaptic receptor for Abeta oligomers"
 This study assesses safety & pharmacokinetics of oral doses of CT1812 in a Phase I trial in healthy volunteers.
Role: Clinical Advisor
- RF1 AG054176** Catalano (PI) 08/15/2016-07/31/2018
 "Phase 1b first-in-patient safety trial for CT1812, a novel Alzheimer's synaptic protection therapeutic"
 This study assesses safety and pharmacokinetics of oral doses of CT1812 in a Phase 1b trial in early AD.
Role: Clinical Advisor
- 6AZ05** FL Dept. of Health Ed & Ethel Moore Alzheimer's, Cottler (PI) 02/23/2016-01/31/2018
 Linking Older Adults from the Community in Florida to Memory Screening and Related Health Research
 This project determines best ways to screen and direct subjects to a Memory Clinic and research studies.
Role: Co-Investigator
- 1P01 AG025204** Klunk (PI) 06/15/2011-04/30/2015
 In Vivo PIB PET Amyloid Imaging: Normals, MCI & Dementia
 The aim of this proposal is to define amyloid deposition in early (and pre-clinical) phases of AD and assess PIB as a surrogate marker of efficacy for anti-amyloid therapies.
Role: Site PI
- P50 AG005133** Lopez (PI) 04/01/2010-03/31/2015
 ADRC Core B: UVA Satellite Clinic
 The Satellite Clinic will perform clinical and research evaluations and study entry & annual follow up with rural African American subjects with dementia & normal cognition in the Satellite Clinic at the University of Virginia.
Role: Site PI
- P01 AG14449** Mufson (PI) 09/01/2007-03/31/2013
 Neurobiology and Cognitive Impairment of the Elderly
 This proposal seeks to determine what specific system impairment is reasonable for the earliest manifestations
Role: PL Project 4

Thomas C. Foster, PhD

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 of brain aging and age-related cognitive decline and neurodegenerative disease of aging. My long-term goal is the amelioration of memory deficits associated with aging and Alzheimer's disease. 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. I have been continuously funded through NIH as a principle investigator since 1992 and my work includes over 100 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 electrophysiological methods for examining synaptic function and protocols for next generation RNA sequencing (Ion Proton). Our work points to altered redox state as an early factor in regulation of synaptic plasticity and cognition during aging. Furthermore, the expression of genes involved in inflammation, synaptic function, and neural activity are altered with age and associated with cognitive decline. In addition, we have recently developed techniques for examining epigenetic mechanisms including DNA methylation microRNA. This work points to epigenetic factors in determining the resilience of synaptic function to the stressors of aging and provides biomarkers of cognitive decline in humans.

B. Positions and Honors

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

Academic Honors and Awards

National Advisory Council on Aging NIH Method to Extend Research in Time (MERIT) Award (2011-present)

McKnight Chair for Research on Aging and Memory, University of Florida 2003-present

Member of the planning Committee for the Cognitive Aging Summits I (2006), II (2010), III (2017)

Associate Editor Frontiers in Aging Neuroscience 2009-present

Distinguished Alumnus Award In recognition of noteworthy service and achievement Wake Forest University Graduate School of Arts & Sciences Department of Physiology & Pharmacology.

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. Published Manuscripts and Chapters

- a) Ivanov, 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 transcriptomic profiles: Subfield vulnerability to age and cognitive impairment. *Front Aging Neurosci* 2018, **PMCID: 4868850**
- b) 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* (2018a), 70, 184-193. **PMCID: 6119103**
- c) Kumar, A., Yegla, B., **Foster, T.C.** Redox signaling in neurotransmission and cognition during aging. *Antioxid Redox Signal* (2018b), 18, 1724-1745. **PMCID: 5962336**
- d) Barter, J.D. and **Foster, T.C.** Aging in the Brain: New Roles of Epigenetics in Cognitive Decline. *The Neuroscientist*, Published online 6/7/2018.
- e) Sartor, G.C., Malvezzi, A.M., Kumar, A., Andrade, N.S., Wiedner, H.J., Vilca, S.J., Janczura, K.J., Bagheri, A., Al-Ali, H., Powell, S.K., Brown, P.T., Volmar, C.H., **Foster, T.C.**, Zeier, Z., and Wahlestedt, C. Enhancement of BDNF expression and memory by HDAC3 inhibition requires BET reader proteins. *Journal of Neuroscience*, in press.
- f) Kumar, A. and **Foster, T.C.** Alteration in NMDA Receptor Mediated Glutamatergic Neurotransmission in the Hippocampus During Senescence. *Neurochemical Research* (2018c), in press.
- g) Barter, J.D. and **Foster, T.C.** *Cellular and Molecular Mechanisms for Age-Related Cognitive Decline*. In Heilman and Nadeau (Eds.) *Cognitive Changes and the Aging Brain*

Posters

J. BARTER, A. RANI, A. KUMAR, T. C. FOSTER. "Adulthood infections alters synaptic gene transcription and contributes to age-related memory loss" *Soc for Neurosci* 2018

A. KUMAR, T. C. FOSTER. "Both GluN2A and GluN2B contribute to the induction of the redox-mediated potentiation of NMDA receptor synaptic function at CA3-CA1 hippocampal synapses of aged animals" *Soc for Neurosci* 2018

G. SMITH, A. RANI, A. KUMAR, T.C. FOSTER. "Investigation of age-related impairment in pattern separation employing modified version of water maze beacon task" *Soc for Neurosci* 2018

B. YEGLA, T. FOSTER, A. KUMAR. "Frontal upregulation of serine racemase alters cognitive flexibility in middle age rats" *Soc for Neurosci* 2018

Talks

miRNA in circulating microvesicles as biomarkers for age-related cognitive decline, Winter Conference of Neural Plasticity Jan 27-Feb 3, 2018, Curacao.

Redox regulation of NMDA receptors contributed to age-related impairment of episodic memory, Winter Conference of Neural Plasticity Jan 27-Feb 3, 2018, Curacao.

Cellular and Molecular Mechanisms for Age-Related Cognitive Decline, for the Emerging Frontiers in Biomedical Research Seminar Series. Rutgers Robert Wood Johnson Medical School 9/25/2018.

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 AG037984 (PI: **Foster**)

9/15/2010 to 7/31/2016

Estrogen and cognition over the lifespan

The major goals of this project are to examine the hypothesis that estrogen protects memory and brain physiology from aging

through genomic and epigenetic mechanisms.

Role: PI

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

NIA R01 AG049711 (**PI Foster**)

09/01/2015 to 4/30/2020

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 P30AG028740 (PI Pahor)

7/1/2006 to 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

Completed Research Support

NINDS R37 NS040389 (PI Ranum)

8/1/2015 to 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 to 8/31/2017

This projects targets chaperone pathways for myelin repair in hereditary neuropathies

Role: advice on statistical analysis of behavior and transcription

Todd E. Golde, MD, PhD

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: Todd E Golde

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

POSITION TITLE: Professor of Neuroscience
Executive Director, McKnight Brain Institute University of Florida

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
Amherst College	BA	05/1985	Biology/Immunology
Case Western Reserve University	PhD	05/1991	Pathology
Case Western Reserve University	MD	05/1994	Medicine

A. Personal Statement

I am currently Director of the Evelyn F. and William L. McKnight Brain Institute at the University of Florida where I oversee, champion, and facilitate UF's neuroscience and neuromedicine research programs. I previously served as the founding director of the Center for Translational Research in Neurodegenerative Disease at UF, and, prior to that appointment, served as Chair of Mayo Clinic's Department of Neuroscience. In these administrative roles, I have been fortunate to have outstanding scientists and physicians as colleagues, and the record of accomplishment of scientific advances made by faculty in these groups has been, and continues to be, outstanding. I also direct the 1Florida ADRC (P50 AG047266), a consortium of Florida institutions that is one of the newer NIA funded Alzheimer's disease research centers.

B. Positions and Honors

Positions and Employment

1990-92 Postdoctoral Fellow, Institute of Pathology Case Western Reserve University
1994-96 Resident, Clinical Pathology and Laboratory Medicine, University of Pennsylvania
1996-97 Assistant Professor, Department of Pathology & Laboratory Medicine, University of Pennsylvania School of Medicine
1997-2001 Senior Associate Consultant and Assistant Professor Department of Pharmacology, Mayo Clinic
2001-2005 Consultant and Associate Professor, Department of Neuroscience, Mayo Clinic Jacksonville
2003-2009 Chair Department of Neuroscience, Mayo Clinic College of Medicine
2005-2009 Consultant and Professor, Department of Neuroscience, Mayo Clinic College of Medicine
2009- Professor, Department of Neuroscience;
2009-2016 Director, Center for Translational Research in Neurodegenerative Disease; University of Florida, Gainesville, FL
2016- Director, Evelyn F. and William L. McKnight Brain Institute, University of Florida, Gainesville, FL

Honors

1993 Experimental Pathologist-in-Training Award, American Society for Investigative Pathology
1996 Chief Resident Clinical Pathology, University of Pennsylvania
1997 Paul Beeson Physician Faculty Scholar, American Federation for Aging Research
1998 Ellison Medical Foundation New Scholar
1999- Ad hoc reviewer MDCN-2 (1999-2000), MSDB (2000), BDCN-3 (2002), AFAR NSAC (2003-current), Member CDIN Study Section (2004-2007), AHAF/Bright Focus Scientific Review Board (2005-current), ADDF grant reviewer 2014-current), Member CNDBT study section 2018-
2005 Zenith Award, Alzheimer's Association
2007 CART Award
2010 Met Life Foundation Award for Medical Research
2010 Ellison Medical Foundation Senior Scholar Award

2011-15	AAIC planning committee
2012	Member State of Florida Purple Ribbon Task force For a Statewide Alzheimer's Plan
2013-	National Alzheimer's Association Medical and Scientific Advisory Committee
2016-	Scientific Advisory Board for Alzheimer's Research UK Drug Discovery Institutes

C. Contributions to Science. (from over 260 publications, h index (Google Scholar) 87, >32000 Citations)

1. As an MD PhD student and postdoc with Dr. Steven Younkin, I played a pivotal role in studies showing that the amyloid β protein ($A\beta$) was a normal metabolite and that mutations that cause AD alter $A\beta$ production in a manner that promote $A\beta$ aggregation. These studies provided pivotal support for the $A\beta$ aggregate (amyloid) hypothesis of AD and enabled drug discovery programs aimed at altering $A\beta$ accumulation.
 - a. Suzuki N, Cheung TT, Cai XD, Odaka A, Otvos L, Jr., Eckman C, **Golde TE**, Younkin SG. An increased percentage of long amyloid beta protein secreted by familial amyloid beta protein precursor (beta APP717) mutants. *Science*. 1994;264(5163):1336-40.
 - b. Cai XD, **Golde TE**, Younkin SG. Release of excess amyloid beta protein from a mutant amyloid beta protein precursor. *Science*. 1993;259(5094):514-6.
 - c. Shoji M*, **Golde TE***, Ghiso J, Cheung TT, Estus S, Shaffer LM, Cai XD, McKay DM, Tintner R, Frangione B, et al. Production of the Alzheimer amyloid beta protein by normal proteolytic processing. *Science*. 1992;258(5079):126-9. (equal contribution)
 - d. **Golde TE**, Estus S, Younkin LH, Selkoe DJ, Younkin SG. Processing of the amyloid protein precursor to potentially amyloidogenic derivatives. *Science*. 1992;255(5045):728-30.
2. In studies conducted in collaboration with Dr. Edward Koo's laboratory (UCSD), we demonstrated that select non-steroidal anti-inflammatory agents (NSAIDs) could modulate $A\beta_{42}$ production and that this effect was attributable to direct alteration of β -secretase activity. Subsequently we identified compounds that lowered $A\beta_{42}$ but lacked cyclooxygenase activity. These data provided the rationale for many other pharmaceutical companies to develop and test what we now refer to as β -secretase modulators (GSMs) as potential therapeutics for AD. We have also identified compounds that increased $A\beta_{42}$; thus, mimicking the effect of AD causing mutations and raising the possibility that small molecules could modulate β -secretase cleavage in a way that might increase one's risk for AD. Finally, we demonstrated that the target of NSAID-like β -secretase modulators was not the enzyme alone but likely involve tripartite interactions with the substrate. These later studies not only have implications for AD therapeutics but also more generally broaden the notion of what is "druggable." Most recently we have identified cholesterol metabolites as a putative endogenous β -secretase modulator, and conducted studies showing that short $A\beta$ peptides are potentially protective form $A\beta_{42}$ toxicity.
 - a. Moore, B.D., Martin, J., de Mena, L., Sanchez, J., Cruz, P.E., Ceballos-Diaz, C., Ladd, T.B., Ran, Y., Levites, Y., Kukar, T.L., Kurian, J.J., McKenna, R., Koo, E.H., Borchelt, D.R., Janus, C., Rincon-Limas, D., Fernandez-Funez, P., and **Golde, T.E.** (2018). Short Abeta peptides attenuate Abeta42 toxicity in vivo. *J Exp Med* 215, 283-301.
 - b. Jung JI, Ladd TB, Kukar T, Price AR, Moore BD, Koo EH, **Golde TE***, Felsenstein KM*. Steroids as gamma-secretase modulators. *FASEB journal: official publication of the Federation of American Societies for Experimental Biology*. 2013;27(9):3775-85. PMID: 3752532. *Co-corresponding authors
 - c. Kukar T, Murphy MP, Eriksen JL, Sagi SA, Weggen S, Smith TE, Ladd T, Khan MA, Kache R, Beard J, Dodson M, Merit S, Ozols VV, Anastasiadis PZ, Das P, Fauq A, Koo EH, **Golde TE**. Diverse compounds mimic Alzheimer disease-causing mutations by augmenting Abeta42 production. *Nature medicine*. 2005;11(5):545-50.
 - d. Weggen S, Eriksen JL, Das P, Sagi SA, Wang R, Pietrzik CU, Findlay KA, Smith TE, Murphy MP, Bulter T, Kang DE, Marquez-Sterling N, **Golde TE**, Koo EH. A subset of NSAIDs lower amyloidogenic Abeta42 independently of cyclooxygenase activity. *Nature*. 2001;414(6860):212-6.
3. A parallel area of interest to GSMs has been the therapeutic utility of targeting intramembrane cleaving protease in a variety of indications. In 2002, in collaboration with Dr. Chris Ponting, we identified a family of intramembrane protease that was related to β -secretase. In work conducted in collaboration with Drs. Osborne (UMASS), Miele (LSU/Tulane), and Greenbaum (U Penn), we have evaluated targeting these proteases in cancer, immunologic disease, and malaria.
 - a. Ponting CP, Hutton M, Nyborg A, Baker M, Jansen K, **Golde TE**. Identification of a novel family of presenilin homologues. *Human molecular genetics*. 2002;11(9):1037-44.
 - b. Ran Y, Ladd GZ, Ceballos-Diaz C, Jung JI, Greenbaum D, Felsenstein KM, **Golde TE**. Differential Inhibition of Signal Peptide Peptidase Family Members by Established gamma-Secretase Inhibitors. *PLoS one*. 2015;10(6):e0128619. doi: 10.1371/

- c. Harbut MB, Patel BA, Yeung BK, McNamara CW, Bright AT, Ballard J, Supek F, **Golde TE**, Winzeler EA, Diagana TT, Greenbaum DC. Targeting the ERAD pathway via inhibition of signal peptide peptidase for antiparasitic therapeutic design. *Proceedings of the National Academy of Sciences of the United States of America*. 2012;109(52):21486-91. PMCID: 3535666.
- d. Ran, Y., Hossain, F., Pannuti, A., Lessard, C.B., Ladd, G.Z., Jung, J.I., Minter, L.M., Osborne, B.A., Miele, L., and **Golde, T.E.** (2017). β -Secretase inhibitors in cancer clinical trials are pharmacologically and functionally distinct. *EMBO Mol Med* 9, 950-966.
4. Another focus of my laboratory has been to try to understand how anti-A β immunotherapy works. These studies have led to a number of publications suggesting that the antibodies work centrally and that efficacy does not require effector functions. The knowledge and experience gained from these studies is integral to the current proposal.
 - a. Levites Y, Smithson LA, Price RW, Dakin RS, Yuan B, Sierks MR, Kim J, McGowan E, Reed DK, Rosenberry TL, Das P, **Golde TE**. Insights into the mechanisms of action of anti-A β antibodies in Alzheimer's disease mouse models. *FASEB journal: official publication of the Federation of American Societies for Experimental Biology*. 2006;20(14):2576-8.
 - b. Levites Y, Jansen K, Smithson LA, Dakin R, Holloway VM, Das P, **Golde TE**. Intracranial adeno-associated virus-mediated delivery of anti-pan amyloid beta, amyloid beta40, and amyloid beta42 single-chain variable fragments attenuates plaque pathology in amyloid precursor protein mice. *The Journal of neuroscience: the official journal of the Society for Neuroscience*. 2006;26(46):11923-8.
 - c. Levites Y, Das P, Price RW, Rochette MJ, Kostura LA, McGowan EM, Murphy MP, **Golde TE**. Anti-A β 42- and anti-A β 40-specific mAbs attenuate amyloid deposition in an Alzheimer disease mouse model. *The Journal of clinical investigation*. 2006;116(1):193-201. PMCID: 1307561.
 - d. Das P, Howard V, Loosbrock N, Dickson D, Murphy MP, **Golde TE**. Amyloid-beta immunization effectively reduces amyloid deposition in FcR γ -/- knock-out mice. *The Journal of Neuroscience: the official journal of the Society for Neuroscience*. 2003;23(24):8532-8.
5. Over the last 10 years, my research has expanded into the area of innate immunity's role in neurodegenerative disease. Recent work from my lab has challenged a long-standing hypothesis that inflammatory processes in AD accelerate A β deposition. Published studies also reveal a potential novel role of interferon- β in nigrostriatal degeneration. We have now expanded these studies to broadly explore immune modulators as mediators of neurodegenerative pathways. Notably, these studies have utilized a novel method for gene delivery to the brain that results in widespread transduction, and we are currently evaluating how we may harness innate immunity for therapeutic benefit in AD, PD, and ALS.
 - a. Chakrabarty P, Li A, Ceballos-Diaz C, Eddy JA, Funk CC, Moore B, DiNunno N, Rosario AM, Cruz PE, Verbeeck C, Sacino A, Nix S, Janus C, Price ND, Das P, **Golde TE**. IL-10 Alters Immunoproteostasis in APP Mice, Increasing Plaque Burden and Worsening Cognitive Behavior. *Neuron*. 2015;85(3):519-33. PMCID: 4320003.
 - b. Chakrabarty P, Rosario A, Cruz P, Siemienski Z, Ceballos-Diaz C, Crosby K, Jansen K, Borchelt DR, Kim JY, Jankowsky JL, **Golde TE**, Levites Y. Capsid serotype and timing of injection determines AAV transduction in the neonatal mice brain. *PLoS one*. 2013;8(6):e67680. PMCID: 3692458.
 - c. Chakrabarty P, Ceballos-Diaz C, Lin WL, Beccard A, Jansen-West K, McFarland NR, Janus C, Dickson D, Das P, **Golde TE**. Interferon-gamma induces progressive nigrostriatal degeneration and basal ganglia calcification. *Nature Neuroscience*. 2011;14(6):694-6. PMCID: 3780582.
 - d. Ayers, J.I., Fromholt, S., Sinyavskaya, O., Siemienski, Z., Rosario, A.M., Li, A., Crosby, K.W., Cruz, P.E., DiNunno, N.M., Janus, C., Ceballos-Diaz, C., Borchelt, D.R., **Golde, T.E.**, Chakrabarty, P., and Levites, Y. (2015). Widespread and efficient transduction of spinal cord and brain following neonatal AAV injection and potential disease modifying effect in ALS mice. *Mol Ther* 23, 53-62.

Complete List of Published Work in my Bibliography

<http://www.ncbi.nlm.nih.gov/myncbi/1PYpZnZ1P9V5n/cv/10576/>

D. Additional Information: Research Support

Ongoing Research Support

1P01CA166009-05 (Osborne, PI, **Golde PL**) 09/01/2009 – 08/31/2019 (on a NCE) 0.6 months while on NCE

NIH/NIA \$200,000 direct/yr

P01 Title: Targeting Multiple Diseases through Gamma Secretase

Project 2: Profiling β -Secretase activity and inhibition

Major Goals are to understand why different GSI have different biological activities.

Overlap: None

U01AG046139-05 (**Golde Contact MPI**) 9/020/2013 -8/30/2018 2.4 months

NIH/NIA \$995,000 direct/yr

A system approach to targeting innate immunity in AD

The major goal of this proposal is to use a systems biology approach to identify novel targets in the immune system for AD.

Overlap: None (About to be renewed NGA anyway)

R01 AG018454-15 (**Golde, PI**) 05/15/2014 – 02/28/2019 2.4 months

NIH/NIA \$290,763 direct/yr

Immune Mediated Mechanisms Underlying CNS Abeta Clearance

Major goals of this grant will explore (Aim 1) sTLRs as novel immunotherapies for AD and mechanism of action of these sTLRs, (Aim 2) how preconditioning by altering innate immune activation states alters efficacy of anti-A β immunotherapy, and (Aim 3) the pharmacokinetics of antibody exposure in the brain.

Overlap: None

P50 AG047266-01A1/P50 AG047266 03S1 (**Golde, Director**) 08/01/2015 -05/31/2020 2.4 months

One Florida ADRC \$996,381 direct/yr administrative supplement \$99,741 for 2017-18

The UF-MSMC ADRC "1Florida ADRC" is focused on achieving a number of specific goals spanning a variety of research and educational activities. Clinical research activities include identification of i) markers for the earliest prodromal stages of cognitive impairment and ii) predictors of cognitive and functional decline in Hispanic and non-Hispanic individuals. Another important patient oriented aspect of the ADRC is to facilitate testing of novel therapies for AD and related dementias in our diverse population. Further the ADRC will provide unique community and professional training and educational opportunities relevant to AD and related dementias, and thus have a broad state-wide educational impact, including training junior investigator training and recruiting trainees and investigators at all levels to participate in dementia research. Finally, the ADRC will support translational research studies that are designed to provide additional insights into Alzheimer's disease that may one day lead to the development of novel therapeutic approaches and novel diagnostic paradigms.

1R56AG057933-01 (Borchelt, PI, **Golde Co-I**) 09/01/2017 – 08/31/2018 0.36 months

NIH/NIA \$456,066 direct/yr

APOE AS A MODIFIER OF PRION-LIKE SPREAD IN DEMENTIA

Major Goals: This grant looks at the role of APOE in spread of proteinopathies

Overlap: None

1R21NS102926-01 (Lakshmyya, PI, **Golde Co-I**) 08/01/2017 – 07/31/2019 0.12 months

NIH/NINDS \$456,066 direct/yr

PERIODONTAL BACTERIA AND ALZHEIMER'S DISEASE

Major Goals: Oral bacteria may be associated with AD, but the role of these bacteria in induction of AD are not known. This proposal will explore the complex interplay between the oral bacteria, overt infection, and the brain immune system that could play a role in AD pathology.

Overlap: None

T32 NS082168 (Bowers, Vaillancourt, MPI, **Golde Co-I**) 05/01/2015 – 04/30/2020 0.00 months

Interdisciplinary Training in Movement Disorders and Neurorestoration

NIH/NINDS \$191,419 direct

Major Goals: This T32 will expose predoctoral students to training in molecular and cellular biology, translational neuroscience and physiology, and human motor and cognitive neuroscience with a central focus on movement disorders. The goal is to train a new cadre of researchers in movement disorders.

Damon Geoffrey Lamb, PhD

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: Research Health Science Specialist (Malcom Randall VAMC), Assistant Professor (UF)

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 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
MBL, Woods Hole, MA	~	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 amnesic mild cognitive impairment (aMCI) to enhance cognition both in healthy individuals as well as amnesic 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, Germantown, MD

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, MD

2003 - 2005 Acoustic Modeling Software Developer, Acoustic Design Ahnert

2004 - 2007 Data Analyst, Brain-Body Center, University of Illinois, Chicago, IL

2007 - 2013 Graduate Student, Emory University, Atlanta, GA

2013 - 2017 Research Health Science Specialist, Malcom Randal VAMC, Gainesville, FL

2013 - Assistant Professor, University of Florida, Gainesville, FL

2017 - Research Health Scientist, Malcom Randal VAMC, Gainesville, FL

Other Experience and Professional Memberships

Member, Society for Neuroscience

Member, American Association for the Advancement of Science

Member, Institute of Electrical and Electronics Engineers

Member, American Physical Society

Honors

2005 Computer Science Faculty Commendation, University of Chicago

2007 - 2009 IGERT: Hybrid Neural Microsystems Fellow, NSF (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. Correlated ionic conductances and interactions underlie coordinated neuronal activity

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 correlational 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. The primary publication from this large, multi-year modeling work has already been cited 14 times its publication and extensions of the work to interactions with synaptic variability are ongoing.

- a. **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.**
- b. **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.**
- c. **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.**

2. 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 improve and enable 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 about aggregating 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.**

3. Putative mechanisms and treatments for symptoms of emotional dysregulation associated with posttraumatic stress disorder and mild traumatic brain injury

Posttraumatic stress disorder and mild traumatic brain injury have overlapping mechanistic profiles in some domains, particularly those tied to autonomic regulation and function. My work continues to elucidate the underlying mechanisms of this relationship, as well as development of putative treatment approaches.

- 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*, 4: 124, July 2017
- b. Williamson JB, Porges EC, **Lamb DG**, Porges SW. Maladaptive autonomic regulation in PTSD accelerates physiological aging. *Frontiers in Psychology* 5:1571, January 2014.
- c. 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. *Frontiers in Neuroengineering* 6:13, December 2013.

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*.

My NCBI bibliography is available at: <http://www.ncbi.nlm.nih.gov/sites/myncbi/1j9Hg8t4ygtkW/bibliography/47495904/public/?sort=date&direction=descending>

A citation report is available on google scholar:

<http://scholar.google.com/citations?user=X49GAQkAAAAJ&hl>

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

Ongoing Research Support

IK2RX002490, VA Rehabilitation Research and Development

Lamb, Damon G (PI)

06/01/18-05/31/23

Brain changes underlying emotional and executive alterations in TBI

Role: Principal Investigator

R21AG054876, NIH-NIA

Williamson, John (PI)

09/01/17-05/31/19

Treatment of mild cognitive impairment with transcutaneous vagal nerve stimulation

Role: Co-Investigator

12179085 (BAA-16-24 - Targeted Neuroplasticity Training), DARPA

Otto, Kevin (Team Lead)

01/01/17-12/31/18

Cognitive Augmentation through Neuroplasticity (TNT-CAN)

Role: Performer

R56HL127175, 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

Completed Research Support

1K2RX000707, Veterans Health Administration

Williamson, John (PI)

08/25/13-04/30/17

White Matter Changes Emotional and Autonomic Consequences

Role: Co-Investigator

5I01CX000744, VA Clinical Science Research & Development

Heilman, Kenneth (PI)

08/25/13-09/30/16

Vertical Neglect

Role: Co-Investigator

0214BRRC-17, VA Rehabilitation Research & Development

Lamb, Damon (PI)

02/21/14-12/31/14

External autonomic nervous system modulation for the treatment of PTSD

Role: Co-PI

Demetrius M. Maraganore, PhD

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: Maraganore, Demetrius M.

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

POSITION TITLE: BJ & Eve Wilder Professor, Department of Neurology, University of Florida, Gainesville, FL

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
Northwestern University, Evanston, IL	B.S.	1983	Medicine
Northwestern University Medical School, Chicago, IL	M.D.	1985	Medicine
Mayo Clinic, Rochester, MN	Residency	1989	Neurology
National Hospital for Neurol/Neurosurg, London, UK	Fellow	1990	Movement Disorders

A. Personal Statement

I am the Principal Investigator (PI) of the Florida Health Ed and Ethel Moore Alzheimer's Disease Research Program application entitled "Utilizing Data from the Electronic Medical Record to Predict Alzheimer's and Dementia Risk". This was awarded on December 13, 2018. That grant aims to develop an Alzheimer's prediction model using data routinely captured by the University of Florida (UF) electronic medical record (EMR), to replicate the model using EMR data shared by the OneFlorida Clinical Research Consortium, to implement the replicated model into the UF EMR using clinical decision support (CDS) tools, and to share the replicated model and CDS tools with OneFlorida Clinical Research Consortium sites. The long-term goal is to create a Florida statewide Alzheimer's prediction and prevention initiative. I am also the PI of the Agency for Healthcare Research and Quality grant R01HS024057 entitled "Quality Improvement and Practice Based Research in Neurology Using the EMR". I supervised the building of structured clinical documentation support (SCDS) and CDS toolkits within the EMR, for the evaluation and management of patients with 11 different neurological indications (including memory disorders and brain health). These toolkits support the clinical practices of neurologists and are also used to support clinical research (including in cognitive decline, mild cognitive impairment, dementia, and Alzheimer's disease). The EMR toolkits that my team built are being shared with 15+ academic departments across the nation, and in return the participating sites are sharing deidentified electronically captured data into a registry, with the aims of quality improvement and practice-based research in neurology using the EMR. One of the projects includes an EMR-based pragmatic trial comparing the effectiveness of three memory and cognitive enhancing drugs in mild cognitive impairment. Regarding brain health (primary prevention of aging related cognitive decline, dementias, including Alzheimer's disease), as the past Chair of Neurology at NorthShore University HealthSystem in Evanston, IL, I developed and led the NorthShore Center for Brain Health. My team and I targeted populations at risk for dementia through community outreach and continuing medical education of physicians. The Center provided outpatient consultations that included risk assessments (of genetic and modifiable factors), personalized interventions (lifestyle, behavioral, and medical), and annual surveillance (early disease detection). In two years, more than 550 patients were evaluated and managed. This was one of the first brain health clinics in the United States. In the Center, my team and I also conducted clinical research, including point of care electronic data capture via SCDS and CDS tools built into the EMR. We developed a preliminary Alzheimer's prediction model using data routinely captured by the EMR. At the University of Florida, I am building and directing a similar Brain Health Clinic (that will evaluate and manage persons at high risk for dementia identified by the prediction model to be refined, replicated, implemented into the EMR as clinical decision support, and disseminated to OneFlorida Clinical Research Consortium practices via the recently awarded Ed and Ethel Moore grant).

B. Positions and Honors

Positions

1985-1986 Medical Intern, Mayo Graduate School of Medicine, Rochester, MN

1986-1989 Neurology Resident, Mayo Graduate School of Medicine, Rochester, MN

1989-1990 Honorary Clinical Fellow to Professor C.D. Marsden in Movement Disorders, Institute of Neurology, National Hospital, Queen Square, London (United Kingdom)

1990-1993 Senior Associate Consultant, Mayo Clinic and Associated Hospitals, Rochester, MN

1993-2009 Consultant, Mayo Clinic and Associated Hospitals, Rochester, MN

1997-2002 Associate Professor of Neurology, Mayo Medical School, Rochester, MN

2002-2009 Professor of Neurology, Mayo Medical School, Rochester, MN

2009-2009 Chair, Movement Disorders Division, Mayo Clinic (Arizona, Florida, and Minnesota)

2009-2018 Ruth Cain Ruggles Chairman, Department of Neurology, NorthShore University HealthSystem

2010-2018 Medical Director, Neurological Institute, NorthShore University HealthSystem

2018- BJ and Eve Wilder Professor, Department of Neurology, University of Florida, Gainesville, FL

Honors

1989-1990 Mayo Foundation Scholarship

1997-2002 Member, Medical Advisory Board, Society for Progressive Supranuclear Palsy

2001-2004 Chair, Bylaws Committee, Movement Disorders Society

2002-2006 Editorial Board, Movement Disorders

2006-2010 Member, Neurological, Aging, Musculoskeletal Epidemiology (NAME) study section, NIH

2006-2010 International Executive Committee, Movement Disorders Society (elected member at large)

2007 Paul M. Silverstein Community Service Award, from the Methodist Hospital and Struthers Parkinson Center, Golden Valley, MN

2009-2010 Visiting Professor Faculty Appointment, University of Milano-Bicocca

2009 Ruth Cain Ruggles Endowed Chair, NorthShore University HealthSystem

2010 Clinical Professor of Neurology, University of Chicago

2012-2015 Editorial Board, Parkinsonism and Related Disorders

2014-2016 Member, Registry Committee, American Academy of Neurology

2015- Fellow, American Academy of Neurology, by Board of Directors election

C. Contribution to Science

Performed the first High-resolution whole-genome association study of any neurological disorder

Parkinson's disease (PD) is a common age-related progressive neurodegenerative disorder. Over the last 15 years, advances have been made in our understanding of the etiology of the disease with the greatest insights perhaps coming from genetic studies, including our genome-wide association approaches. These large-scale studies allow the identification of genomic regions harboring common variants associated to disease risk. The first genome-wide association study on sporadic PD (or of any neurological disorder) was performed by my group in 2005 (see citation below).

1. **Maraganore DM**, de Andrade M, Lesnick TG, Strain KJ, Farrer MJ, Rocca WA, Pant PV, Frazer KA, Cox DR, Ballinger DG. High-resolution whole-genome association study of Parkinson disease. *Am J Hum Genet.* 2005 Nov;77(5):685-93. Epub 2005 Sep 9. **PubMed PMID: 16252231; PubMed Central PMCID: PMC1271381.**
2. Evangelou E, **Maraganore DM**, Ioannidis JP. Meta-analysis in genome-wide association datasets: strategies and application in Parkinson disease. *PLoS One.* 2007 Feb 7;2(2):e196. **PubMed PMID: 17332845; PubMed Central PMCID: PMC1805816.**
3. Lesnick TG, Papapetropoulos S, Mash DC, Ffrench-Mullen J, Shehadeh L, de Andrade M, Henley JR, Rocca WA, Ahlskog JE, **Maraganore DM**. A genomic pathway approach to a complex disease: axon guidance and Parkinson disease. *PLoS Genet.* 2007 Jun;3(6):e98. **PubMed PMID: 17571925; PubMed Central PMCID: PMC1904362.**

Founder and multi-year principal investigator of the Genetic Epidemiology of Parkinson Disease (GEO-PD) Consortium.

The GEO-PD Consortium was launched in 2004 through the Edmond J. Safra Global Genetics Consortia initiative and with funding from the Michael J. Fox Foundation. The goal was to form a collaborative team of investigators to tackle critical questions in the Parkinson's disease genetics field. The Consortium members collaborate and share findings to advance the understanding of the genetics and epidemiology of PD. The GEO-PD includes 60 sites from 30 countries and six continents. We share DNA and data for 41,988 PD cases and 41,505 control subjects. Many sites also conduct family studies, leading to the discovery of genes that cause familial PD. The main goal of GEO-PD is to perform large-scale genetic association studies and serve as a replication engine to test the significance of discoveries in the PD genetics research field. 25+ papers have been published by the group (5 recent listed below). In September 2014, I launched the Longitudinal Clinical and Genetic Study of Parkinson's Disease (LONG-PD) study. This major new study aims to enroll and follow more than 4,000 PD patients worldwide over 15 years.

1. Wang L, Heckman MG, Aasly JO, Annesi G, Bozi M, Chung SJ, Clarke C, Crosiers D, Eckstein G, Garraux G, Hadjigeorgiou GM, Hattori N, Jeon B, Kim YJ, Kubo M, Lesage S, Lin JJ, Lynch T, Lichtner P, Mellick GD, Mok V, Morrison KE, Quattrone A, Satake W, Silburn PA, Stefanis L, Stockton JD, Tan EK, Toda T, Brice A, Van Broeckhoven C, Uitti RJ, Wirdefeldt K, Wszolek Z, Xiromerisiou G, **Maraganore DM**, Gasser T, Krüger R, Farrer MJ, Ross OA, Sharma M; GEOPD Consortium.. Evaluation of the interaction between LRRK2 and PARK16 loci in determining risk of Parkinson's disease: analysis of a large multicenter study. *Neurobiol Aging*. 2017 Jan;49:217.e1-217.e4. doi: 10.1016/j.neurobiolaging.2016.09.022. Epub 2016 Oct 6. **PubMed PMID: 27814993; PubMed Central PMCID: PMC5154911.**
2. Wang L, Aasly JO, Annesi G, Bardien S, Bozi M, Brice A, Carr J, Chung SJ, Clarke C, Crosiers D, Deuschländer A, Eckstein G, Farrer MJ, Goldwurm S, Garraux G, Hadjigeorgiou GM, Hicks AA, Hattori N, Klein C, Jeon B, Kim YJ, Lesage S, Lin JJ, Lynch T, Lichtner P, Lang AE, Mok V, Jasinska-Myga B, Mellick GD, Morrison KE, Opala G, Pihlstrøm L, Pramstaller PP, Park SS, Quattrone A, Rogaeva E, Ross OA, Stefanis L, Stockton JD, Silburn PA, Theuns J, Tan EK, Tomiyama H, Toft M, Van Broeckhoven C, Uitti RJ, Wirdefeldt K, Wszolek Z, Xiromerisiou G, Yueh KC, Zhao Y, Gasser T, **Maraganore DM**, Krüger R, Sharma M; GEO-PD Consortium. Large-scale assessment of polyglutamine repeat expansions in Parkinson disease. *Neurology*. 2015 Oct 13;85(15):1283-92. doi: 10.1212/WNL.0000000000002016. Epub 2015 Sep 9. **PubMed PMID: 26354989; PubMed Central PMCID: PMC4617164.**
3. Theuns J, Verstraeten A, Sleegers K, Wauters E, Gijssels I, Smolders S, Crosiers D, Corsmit E, Elinck E, Sharma M, Krüger R, Lesage S, Brice A, Chung SJ, Kim MJ, Kim YJ, Ross OA, Wszolek ZK, Rogaeva E, Xi Z, Lang AE, Klein C, Weissbach A, Mellick GD, Silburn PA, Hadjigeorgiou GM, Dardiotis E, Hattori N, Ogaki K, Tan EK, Zhao Y, Aasly J, Valente EM, Petrucci S, Annesi G, Quattrone A, Ferrarese C, Brighina L, Deuschländer A, Puschmann A, Nilsson C, Garraux G, LeDoux MS, Pfeiffer RF, Boczarska-Jedynak M, Opala G, **Maraganore DM**, Engelborghs S, De Deyn PP, Cras P, Cruts M, Van Broeckhoven C; GEO-PD Consortium.. Global investigation and meta-analysis of the C9orf72 (G4C2)_n repeat in Parkinson disease. *Neurology*. 2014 Nov 18;83(21):1906-13. doi: 10.1212/WNL.0000000000001012. Epub 2014 Oct 17. **PubMed PMID: 25326098; PubMed Central PMCID: PMC4248456.**
4. Chung SJ, Biernacka JM, Armasu SM, Anderson K, Frigerio R, Aasly JO, Annesi G, Bentivoglio AR, Brighina L, Chartier-Harlin MC, Goldwurm S, Hadjigeorgiou G, Jasinska-Myga B, Jeon BS, Kim YJ, Krüger R, Lesage S, Markopoulou K, Mellick G, Morrison KE, Puschmann A, Tan EK, Crosiers D, Theuns J, Van Broeckhoven C, Wirdefeldt K, Wszolek ZK, Elbaz A, **Maraganore DM**; Genetic Epidemiology of Parkinson's Disease Consortium.. Alpha-synuclein repeat variants and survival in Parkinson's disease. *Mov Disord*. 2014 Jul;29(8):1053-7. doi: 10.1002/mds.25841. Epub 2014 Feb 27. **PubMed PMID: 24578302; PubMed Central PMCID: PMC4172351.**
5. Heckman MG, Elbaz A, Soto-Ortolaza AI, Serie DJ, Aasly JO, Annesi G, Auburger G, Bacon JA, Boczarska-Jedynak M, Bozi M, Brighina L, Chartier-Harlin MC, Dardiotis E, Destée A, Ferrarese C, Ferraris A, Fiske B, Gispert S, Hadjigeorgiou GM, Hattori N, Ioannidis JP, Jasinska-Myga B, Jeon BS, Kim YJ, Klein C, Kruger R, Kyrtzi E, Lin CH, Lohmann K, Lioriot MA, Lynch T, Mellick GD, Mutez E, Opala G, Park SS, Petrucci S, Quattrone A, Sharma M, Silburn PA, Sohn YH, Stefanis L, Tadic V, Tomiyama H, Uitti RJ, Valente EM, Vassilatis DK, Vilariño-Güell C, White LR, Wirdefeldt K, Wszolek ZK, Wu RM, Xiromerisiou G, **Maraganore DM**, Farrer MJ, Ross OA; Genetic Epidemiology Of Parkinson's Disease (GEO-PD) Consortium. Protective effect of LRRK2 p.R1398H on risk of Parkinson's disease is independent of MAPT and SNCA variants. *Neurobiol Aging*. 2014 Jan;35(1):266.e5-14. doi:10.1016/j.neurobiolaging.2013.07.013. Epub 2013 Aug 17. **PubMed PMID: 23962496; PubMed Central PMCID: PMC3829604.**

First to identify α -synuclein gene (SNCA) promoter polymorphisms as risk factor for PD worldwide.

In 1997, the PD field was transformed by the discovery that a point mutation in the SNCA gene is a cause of familial parkinsonism. While the mutation discovered was very rare, within weeks it was discovered that alpha-synuclein is a principle protein component of Lewy bodies, the pathological hallmark of PD. Our group subsequently demonstrated that while the SNCA point mutations or multiplication mutations that cause familial parkinsonism are very rare, that common variations in the SNCA gene are reproducibly associated with susceptibility to PD in populations worldwide (reference 1 below). Specifically, we demonstrated that short, intermediate, and long allele length variations in the dinucleotide repeat sequence REP1, within the core 5' promoter of the SNCA gene, occurred with different frequencies in PD cases versus controls. Genotypes defined by short alleles were associated with a reduced risk for PD, while genotypes defined by long alleles were associated with an increased risk for PD. Indeed, there was a two-fold difference in PD susceptibility between persons homozygous for short alleles versus persons homozygous for long alleles.

1. **Maraganore DM**, de Andrade M, Elbaz A, Farrer MJ, Ioannidis JP, Krüger R, Rocca WA, Schneider NK, Lesnick TG, Lincoln SJ, Hulihan MM, Aasly JO, Ashizawa T, Chartier-Harlin MC, Checkoway H, Ferrarese C, Hadjigeorgiou G, Hattori N, Kawakami H, Lambert JC, Lynch T, Mellick GD, Papapetropoulos S, Parsian A, Quattrone A, Riess O, Tan EK, Van Broeckhoven C; Genetic Epidemiology of Parkinson's Disease (GEO-PD) Consortium. Collaborative analysis of alpha-synuclein gene promoter variability and Parkinson disease. *JAMA*. 2006 Aug 9;296(6):661-70. **PubMed PMID: 16896109.**

Principal investigator of “The DodoNA Project: DNA Prediction to Improve Neurological Health”

“DodoNA” is a metaphor. Dodona was an oracle of ancient Greece, where priestesses interpreted the rustling leaves of a sacred oak tree to predict the future and to guide actions to improve fate. Just as at Dodona, we can interpret subtle variations in DNA, the “tree of life,” to improve neurological health. Specifically, with intramural funding support, at the Department of Neurology at NorthShore University HealthSystem (where I was the Chair) we developed medical informatics tools to capture standardized data via routine office visits that measure the progression and outcomes of patients with the following neurological disorders: brain tumors, epilepsy, memory disorders, migraine, mild traumatic brain injury, multiple sclerosis, neuropathy, Parkinson’s disease, restless legs syndrome and stroke. We also studied persons who are neurologically healthy but at increased risk for Alzheimer’s disease and related brain disorders (brain health). Although DodoNA was a clinical practice initiative (note-writing and workflow efficiencies) and a quality initiative (best practices), it was also a research initiative. We enrolled up to 1,000 subjects for each of the 11 projects (11,000 subjects total) to provide, via informed consent, a blood sample for DNA extraction and storage. We then associated information in their blood with information in their medical record (to develop molecular prognostics and therapeutics).

The specific goals of the DodoNA project were to:

- Identify DNA fingerprints that predict outcomes in patients with neurological disorders
- Identify DNA fingerprints that predict therapeutic responses in patients with neurological disorders
- Identify DNA targets for the development of new disease modifying therapies.

Founder and principal investigator of the Neurology Practice Based Research Network (NPBRN).

The NPBRN was launched in 2013 with the goal to advance quality improvement and practice-based research in neurology using the EMR. There are few EMR tools available to standardize neurology office visits according to Best Practices, to provide alerts when neurological care is deviating from American Academy of Neurology (AAN) guidelines, to capture data regarding adherence to AAN or other quality parameters, to measure the effects of compliance with guidelines on outcomes, or to share longitudinal data and to compare effectiveness of care across neurological practices. The Department of Neurology at NorthShore University HealthSystem (NorthShore) built into its commercial EMR “Epic” structured clinical documentation support (SCDS) and clinical decision support (CDS) tools that standardize care, write progress notes, and capture up to 1,000 discrete and cascading fields of neurological data per office visit. With funding from the Agency for Healthcare Research and Quality (AHRQ) in 2015, we are sharing SCDS and CDS tools for 10 common neurological disorders (brain tumors, epilepsy, migraine, mild cognitive impairment, mild traumatic brain injury, multiple sclerosis, neuropathy, Parkinson’s disease, restless legs syndrome, and stroke) and for brain health (primary prevention of Alzheimer’s disease) with 15 Departments of Neurology that also use the Epic EMR platform. We are also conducting at the NorthShore site pragmatic trials to demonstrate the feasibility of subgroup based adaptive assignment of treatments, electronic consenting, and outcomes data capture at the point of care using the EMR. We will identify the most effective treatments for common neurological disorders and seek replication by the NPBRN.

1. Simon K, Tideman S, Hillman L, Lai R, Jathar R, Ji Y, Bergman-Bock S, Castle J, Franada T, Freedom T, Marcus R, Mark A, Meyers S, Rubin S, Semenov I, Yucus C, Pham A, Garduno L, Szela M, Frigerio R, and **Maraganore DM**. Design and implementation of pragmatic clinical trials using the electronic medical record and an adaptive design. *JAMIA Open*, 0(0), 2018, 1–8 doi: 10.1093/jamiaopen/ooy017
2. Rasmussen E, Fosnacht Morgan A-M, Munson R, Ong A, Patel S, Yucus C, Pham A, Patel V, Frigerio R, Lai R, Hillman L, Tideman S, Wang C, Simon K, Martínez-González MS, **Maraganore DM**. Use of an Electronic Medical Record to Track Adherence to the Mediterranean Diet in a US Neurology Clinical Practice. *Mayo Clin Proc Inn Qual Out* n XXX 2018;nn(n):1-11 doi. org/10.1016/j.mayocpiqo.2017.12.003
3. Meyers S, Simon K, Bergman-Bock S, Campanella F, Marcus R, Mark A, Freedom T, Rubin S, Semenov I, Lai R, Hillman L, Tideman S, Pham A, Frigerio R, **Maraganore DM**. Structured Clinical Documentation to Improve Quality and Support Practice-Based Research in Headache. *Headache*. 2018 Aug 1. doi: 10.1111/head.13348. [Epub ahead of print] **PMID: 30066412**
4. Narayanan J, Dobrin S, Choi J, Rubin S, Pham A, Patel V, Frigerio R, Maurer D, Gupta P, Link L, Walters S, Wang C, Ji Y, **Maraganore DM**. Structured clinical documentation in the electronic medical record to improve quality and to support practice-based research in epilepsy. *Epilepsia*. 2017 Jan;58(1):68-76. doi: 10.1111/epi.13607. Epub 2016 Nov 19. **PubMed PMID: 27864833; PubMed Central PMCID: PMC5245120**.
5. **Maraganore DM**, Frigerio R, Kazmi N, Meyers SL, Sefa M, Walters SA, Silverstein JC. Quality improvement and practice-based research in neurology using the electronic medical record. *Neurol Clin Pract*. 2015 Oct;5(5):419-429. **PubMed PMID: 26576324; PubMed Central PMCID: PMC4634157**.

6. Fosnacht AM, Patel S, Yucus C, Pham A, Rasmussen E, Frigerio R, Walters S, **Maraganore D**. From Brain Disease to Brain Health: Primary Prevention of Alzheimer's Disease and Related Disorders in a Health System Using an Electronic Medical Record-Based Approach. *J Prev Alz Dis*. 2017. <http://dx.doi.org/10.14283/jpad.2017.3>

D. RESEARCH SUPPORT

Ongoing Research Support

Agency for Healthcare Research and Quality (AHRQ); **Maraganore (PI)**; 05/01/15-04/30/20

Quality Improvement and Practice Based Research in Neurology Using the EMR

Aim 1: We will create a national network for quality improvement and practice based patient-centered outcomes research in Neurology using the electronic medical record (EMR) to make health care safer and to improve healthcare efficiency, in keeping with the mission and priority areas of the Agency for Healthcare Research and Quality. Aim 2: We will conduct pragmatic trials using the EMR and subgroup-based adaptive design tools that determine which treatments are most effective for specific patients, individualizing medicine at the point of care.

Florida Health Ed and Ethel Moore Grant; Maraganore (PI); 12/14/18-12/14/20

Utilizing Data from the Electronic Medical Record to Predict Alzheimer's and Dementia Risk

Aim 1: We will utilize data captured by the EMR at UF, to develop a cognitive impairment/dementia/AD prediction model (UF AD prediction model). Aim 2: We will replicate the model using historical data captured by the EMRs at OneFlorida Clinical Research Consortium sites (<http://onefloridaconsortium.org>). Aim 3: If the model is replicated, we will integrate it into the UF EMR and build CDS tools that identify patients at highest risk for cognitive disorders and guide referral by PCPs to brain health specialists. Aim 4: We will share the model and CDS tools with other OneFlorida sites.

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.)

Table with 4 columns: INSTITUTION AND LOCATION, DEGREE (if applicable), Completion Date MM/YYYY, FIELD OF STUDY. Rows include University of Pittsburgh, University of Arizona, Tucson, AZ, and University of Arizona, Tucson, AZ with degrees BS, PHD, and Postdoctoral Fellow.

A. Personal Statement

Throughout my scientific career, I have been focused on trying to understand the mechanisms that govern information propagation in the brain. 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.

After relocating to the University of Florida, where there is a strong research focus on the neurobiology of cognitive decline, I have become interested in extending my research approach to incorporate technological advancements. The fifty-five million Americans that are projected to be over the age of sixty five by 2020 presents a significant financial and public health crisis.

I am excited to be joined by Dr. Sara Burke, whom I have collaborated with for over a decade. Since arriving at the University of Florida, this continuing collaboration has already produced a novel research manuscript (ref 3; another article in press).

Part way through my post-doctoral training, in 2009, I fell chronically ill with an eventual diagnosis of lymphocyte predominant Hodgkin lymphoma. This diagnosis coincided with the birth of our first child, Miles.

- 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. Hernandez AR*, Maurer AP*, Reasor JE, Turner SM, Barthle SE, Johnson SA, Burke SN. Age-related impairments in object-place associations signify a decline in systems-level neural communication. Behav Neuro, 2015 Oct: 129(5):599-610. PubMed PMID: 26413723; PubMed Central PMCID: in process.

3. Shilnikov A, **Maurer AP** (2016) The Art of grid fields: Geometry of neuronal time. *Frontiers in Neural Circuits* 10:12. PubMed PMID: 27013981; PubMed Central PMCID: PMC4782041.
4. Sheremet A, Burke SN, **Maurer AP** (2016) Movement Enhances the Nonlinearity of Hippocampal Theta. *J Neurosci* 36:4218-4230. PubMed PMID: 27076421; PubMed Central 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, University 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. The examination of hippocampal activity patterns across the long axis of the hippocampus is a central component of the current proposal.
 - 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 is 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 characteristics. 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 exhibited 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

1R01AG049722-01A1, 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.

15% effort

1R21DA039701, NIH - National Institute on Drug Abuse

MAURER, ANDREW (M-PI), Setlow, Barry (M-PI)

Development of a rat model of cannabis smoke self-administration

In conjunction with Dr. Barry Setlow (a leading expert in drug addiction), we designed an apparatus that will allow precisely-calibrated, response-contingent delivery of cannabis smoke using experimental designs similar to those employed with other drugs of abuse. We will use this apparatus to determine whether rats will reliably show operant responding for cannabis smoke delivery. Successful development of a rodent cannabis smoke self-administration model will lay the groundwork for a larger research program on neurobehavioral mechanisms of cannabis smoking as well as allow us to bridge animal and human research.

15% effort

2015/08/15-2017/05/31

1R03AG049411, NIH - National Institute on Aging

MAURER, ANDREW (M-PI), Burke, Sara (M-PI), Ormerod, Brandi (M-PI)

Neurogenesis and Memory Network Dynamics during Normal Aging.

This collaborative R03 is designed to develop preliminary data aimed at understanding of the role of neurogenesis in memory and

learning. Simply, there has yet to be a high-density electrophysiological investigation of dentate gyrus neural dynamics in aged, freely-behaving animals. As this region appears to be highly vulnerable to the aging process, we are in the process of relating functional change to alteration in neurogenesis.

5% 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)	START DATE MM/YYYY	END DATE MM/YYYY	FIELD OF STUDY
Hampshire College, Amherst, MA	BA	09/1999	01/2004	Cognitive Science
University of Chicago, Chicago, IL	MA	09/2008	09/2012	Neuroscience
University of Chicago, Chicago, Illinois	PHD	09/2008	08/2013	Neuroscience
University of Florida, Gainesville, FL	Postdoctoral Fellow	09/2013	12/2015	Neuroscience of Alcohol & HIV

A. Personal Statement

Dr. Porges is currently an Assistant Professor in the department of Clinical and Health Psychology at the University of Florida and a member of the Center for Cognitive Aging and Memory Clinical Translational Research (CAM). He is PI of an NIH K01 grant focused on the application of GABA MRS in HIV-positive and heavy alcohol use populations with a focus on the role these play in accelerating age related cognitive consequences. He has extensive experience in the design, collection, analysis and interpretation of Magnetic Resonance Imaging data, specifically fMRI, MRI, 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). Dr. Porges has longstanding collaborations with Drs. Edden and Lamb, and has published with both using GABA MRS. He has collaborated with Drs. Campbell-Thompson and Lamb as CO-I on a pending NSF grant for autonomic neural-engineering. He has served as development partner with Dr. Edden while implementing and testing GABA MRS sequences and software prior to their public dissemination.

In addition to expertise in multimodal human Magnetic Resonance Imaging, Dr. Porges 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 autonomic nervous system (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, the first publication from this line of work has recently been accepted and as well as an NIH/NIA R21 awarded for the development of the application of this methodology in a mild cognitive impairment cohort.

1. **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 Sep 5;162:249-256. **PubMed PMID: 28882635**.
2. 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.
3. **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**.
4. 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**.

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, Department of Aging and Geriatric Research, Institute on Aging, Center for Cognitive Aging and Memory, University of Florida, Gainesville, FL
- 2016 - Assistant Professor, Center for Cognitive Aging and Memory, Institute on Aging, Department of Aging and Geriatric Research, University of Florida, Gainesville, FL

Other Experience and Professional Memberships

- 2010 - Member, Society for Neuroscience
- 2011 - Member, Society for Social Neuroscience
- 2011 - Ad Hoc Reviewer, *International Journal Psychophysiology*
- 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. 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.**
 - c. Seider TR, Fieo RA, O'Shea A, **Porges EC**, Woods AJ, Cohen RA. Cognitively Engaging Activity Is Associated with Greater Cortical and Subcortical Volumes. *Front Aging Neurosci*. 2016;8:94. **PubMed PMID: 27199740; PubMed Central PMCID: PMC4852201.**
 - d. Clark DJ, Rose DK, Ring SA, **Porges EC**. Utilization of central nervous system resources for preparation and performance of complex walking tasks in older adults. *Front Aging Neurosci*. 2014;6:217. **PubMed PMID: 25202270; PubMed Central PMCID: PMC4142860.**

2. **GABA MRS and advanced multimodal neuroimaging:** Dr. Porges has played an integral role in the development and application of advanced neuroimaging methods to target populations. These inquiries have generated novel findings, including specific and unique functional connectivity from amygdala sub-nuclei to cortical targets that are predicted by psychopathic traits, the first exploration of the relationship between GABA MRS and higher-order cognitive function in older adults and the impact of advanced tissue correction methods on GABA-MRS findings.
 - 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 Sep 5;162:249-256. **PubMed PMID: 28882635.**
 - b. **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.**
 - c. **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.**
 - 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. **Autonomic Nervous System (ANS) research, design, implementation, analysis and interpretation:** Dr. Porges has extensive research expertise and experience utilizing ANS measures to characterize and predict individual differences in ANS response to cognitive and social challenges as well as in the context of genetics, pathology, and pharmacological intervention. Study a) explored alterations in ANS function in the context of PTSD. Study b) (a co-first author manuscript) reports the influence of Oxytocin receptor gene variation on ANS response to social stimuli. Study c) utilized ANS activity to predict endocrine response to observed violence. Study d) describes the impact of a tVNS on the ANS in a PTSD/TBI cohort.
 - a. **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.
 - b. **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.**
 - c. **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.**
 - d. **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.**

4. **Traumatic brain injury (TBI):** 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 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.
 - b. **Falchhook 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.**

- c. 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.**
 - 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. **Neuroendocrine function:** Neuroendocrine functions related to individual variability in response to 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 a strengthening of social bonds. I have had a long-term interest in exploring central and peripheral physiological predictors (e.g., parasympathetic activity) of individual differences in response to high-intensity social stimuli (e.g., violence and parental interaction). 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. 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.**
 - b. Zamzow RM, Ferguson BJ, Stichter JP, **Porges EC**, Ragsdale AS, Lewis ML, Beversdorf DQ. Effects of propranolol on conversational reciprocity in autism spectrum disorder: a pilot, double-blind, single-dose psychopharmacological challenge study. *Psychopharmacology (Berl).* 2016 Apr;233(7):1171-8. **PubMed PMID: 26762378.**
 - c. 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.**
 - d. Carter CS, **Porges EC**. Parenthood, stress, and the brain. *Biol Psychiatry.* 2011 Nov 1;70(9):804-5. **PubMed PMID: 21986092.**

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

Ongoing Research Support

K01 AA025306-01A1, NIH/NIAAA

Porges, Eric (PI)

08/01/17-01/31/22

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. To ensure an independent career post award, two critical areas of training will be addressed: 1) Behavioral and biological consequences of alcohol use in the context of HIV and 2) the development of expertise in the measurement of GABA, the principal inhibitory neurotransmitter, using Magnetic Resonance Spectroscopy (MRS). The PI is a cognitive neuroscientist with a strong research background in aging, cognition, experimental design, autonomic measurement, and magnetic resonance imaging (fMRI & MRI).

Role: PI

R21AG054876, NIH/NIA

Williamson, John (PI)

06/01/17-5/31/18

The goal of this study was to collect pilot data investigating the ability of transcutaneous vagal nerve stimulation (tVNS) to impact MCI symptoms.

Role: Co-I

R56HL127175, NIH/NHLBI

Williamson, John (PI)

09/08/15-08/31/16

Brain and cognition effects of cardio resynchronization therapy in heart failure

The goal of this study is to evaluate cognitive and brain consequences of cardiac resynchronization therapy in heart failure patients using functional neuroimaging, magnetic resonance spectroscopy, & arterial spin labeling.

Role: Co-I

Neuroimaging Consortium Grant , McKnight Brain Research Foundation
Clinton Wright (PI)

UF Neuroimaging Consortium Cohort

The goal of this project is to develop a cohort of 200 adults 85 years and older across four sites using multimodal neuroimaging and cognitive assessment.

Role: Co-I

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

Porges, Eric (PI)

CAM Pilot Study Pilot Study: Attentive Brain Study

Aging, HIV and Alcohol associated changes in set-shifting. Participants will perform a set-shifting task undergoing fMRI and MRS.

This study is intended to identify unique elements of set-shifting performance that decline in with heavy drinking in the context of Aging and HIV, and the brain systems that govern these elements.

Role: PI

BIOGRAPHICAL SKETCH

NAME: Williamson, John B

eRA COMMONS USER NAME: wjohnb

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
The Florida State University, Tallahassee Florida	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

In the proposed investigation, we seek to determine if transcutaneous vagal nerve stimulation can improve sleep quality in Veterans with PTSD with or without history of mild TBI. In my current role at the VA, I am the leader of the Emotion Function initiative at the Brain Rehabilitation Research Center. I have recently completed a VA funded CDA-2 study designed to examine factors influencing emotional cognitive and physiological differences in patients with PTSD subsequent to mild TBI in the context of white matter changes. We have several papers from this project either published, in review for publication, or under preparation. I have over 60 peer-reviewed research articles in topics related to this project. I have been the PI or Co-I on multiple funded grants from the federal government (NIH and VA) that employ neuroimaging, neuropsychological, and psychophysiological methods.

I have worked with vagally mediated systems research for many years. My postdoctoral fellowship in autonomic neuroscience was mentored by Stephen Porges (Polyvagal Theory). 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 amnesic mild cognitive impairment. 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. Damon Lamb (coinvestigator), Eric Porges (co-investigator), and I collaborated with Dr. Kevin Otto in the proposal of a targeted neuroplasticity training project through DARPA using VNS. The animal component of that proposal was funded and is currently underway. Further, our team has been developing closed-loop neurophysiological control models for tVNS. We have the necessary tVNS equipment to execute the proposed study and experience using it. Those data from the pilots in conjunction with my CDA-2 funded work encompass the proposed methodologies and demonstrate theoretical support for the aims presented for this proposal.

1. 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.
2. **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**.
3. **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**.
4. Arico D, Drago V, Foster PS, Heilman KM, **Williamson JB**, Ferri R. Effects of NREM sleep instability on cognitive processing. *Sleep Medicine*. 2010, 11, 791-798. **pubmed PMID: 20674488**.

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- Research Psychologist, Dept of Veteran Affairs, Gainesville FL

2012-2018 Assistant Professor Department of Neurology, University of Florida
 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, 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

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.
 - 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 research aimed at achieving a greater understanding of the bases of vascular dementia, and the contributions of vascular factors to the development of cognitive and emotional dysfunction in the elderly. This led to numerous studies of vascular cognitive impairment (dementia precursor) resulting in evidence showing the contribution of white matter hyperintensities in VCI to cognition and also 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 on cognitive and mood indicators. Further, Dr. Williamson was funded by an F32 to study the relationship of white matter disease on 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 reverts and nonreverts. *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* 2017, 1-10.
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 accelerated aging.* 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 (Williamson's CDA-2) and we are developing several lines of inquiry from the project including a CDA-2 submission this cycle (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.
 - b) **Williamson JB**, Porges EC, Lamb DG, Porges SW. Maladaptive autonomic regulation in PTSD accelerates physiological aging. *Frontiers in psychology* 2015.
 - 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.

My bibliography is available at: <http://www.ncbi.nlm.nih.gov/sites/myncbi/john.williamson.2/bibliography/48036192/public/?sort=date&direction=ascending>

D. Research Support

Ongoing Research Support

VAMC BRRC Pilot Award

2017-2018

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

NIH R21AG054876

9/01/2017-08/31/2019 2017 – 2019

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 amnesic mild cognitive impairment and whether structural changes in brain regions relevant for memory encoding (e.g., hippocampus) predict response.

PI: Williamson

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

NIH 1R56HL127175 (no cost extension)

09/01/2015-08/31/2019

Brain and cognition effects of cardio resynchronization therapy in heart failure.

The goal of this funding is to characterize brain changes as a result of improved cardiac output in heart failure including hemodynamic, task dependent regional brain activation and brain metabolic changes associated with improved cognitive performance and brain health.

Role: PI

Completed Research Support

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 is to extend knowledge of white matter damage contributions after TBI to the development of emotional dysregulation in veterans with PTSD. Preliminary analyses demonstrate independent (of PTSD symptom severity) contributions of TBI to emotional cognition. White matter and fMRI post-processing is ongoing.

Role: PI

VAMC Merit Review

2008-2012

Approach-Avoidance Spatial Neglect

The goal of this funding was to examine the contribution of unilateral stroke to neglect.

Role: Co-I (PI = Kenneth M. Heilman)

1 F32 AG027648-01A1

2006-2008

NIA funded individual training grant

White matter integrity and autonomic stress response

The goal of this study was to provide data on the effect of white matter disease on mobilization of autonomic resources to perform cognitive tasks.

Role: PI

VAMC BRRRC Pilot Award

2014

External Non-invasive vagal nerve stimulation for the treatment of post-traumatic stress disorder.

The goal of this funding was to provide pilot data for the effect of transcutaneous vagal nerve stimulation on emotional cognition and physiology in patients with TBI and PTSD. Preliminary data analyses demonstrate alleviation of anxiety (state) in patients with TBI/PTSD.

Role: PI

Adam Joshua Woods, PhD

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 Joshua

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

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
University of Alabama at Birmingham	B.S.	05/03	Psychology
George Washington University	Ph.D.	05/10	Cognitive Neuroscience
University of Pennsylvania	Post-Doctoral	06/13	Cognitive Neuroscience

A. Personal Statement

Dr. Woods is Assistant Director of the Center for Cognitive Aging and Memory Clinical Translational Research (CAM) in the McKnight Brain Institute at UF. He is the Director of the Neurophysiology and Neuromodulation Research Core in the CAM. Dr. Woods is also an Assistant Professor in the Department of Clinical and Health Psychology at UF, with a joint appointment to Neuroscience. He is an interventional cognitive neuroscientist with expertise in non-invasive brain stimulation, neuroimaging, and clinical trials. He is a national leader in the field of transcranial electrical stimulation (tES), and runs an international training workshop for this technology, held in the past in NYC, Singapore, Barcelona, Gainesville, and other locations each year. He has trained over 950 researchers and clinicians around the world to safely and appropriately use tES. He also works with numerous groups around the country for ongoing tES collaborations at the University of Pennsylvania, University of Arkansas for Medical Sciences, University of California San Diego, University of Arizona, Arizona State University, University of New Mexico and University of Miami. Dr. Woods' research focuses on discovery and application of novel non-invasive brain stimulation interventions for enhancing cognitive function in adults with and without neurodegenerative disease. This includes work in a variety of comorbid conditions that may accelerate the brain aging process, including HIV, stroke, obesity, and surgery. Dr. Woods has expertise in multi-disciplinary cognitive neuroscience methodologies (MRI/fMRI, electrophysiology, non-invasive brain stimulation), extensive experience with aging-related disorders, and past research with neurological diseases. His background, experience, and training in tES and human neuroimaging will be important for his role as a consultant on the current project. Dr. Woods has established one of the largest and most well-funded non-invasive electrical brain stimulation laboratory in the United States. He is PI of the largest phase III RCT for tES using transcranial direct current stimulation (tDCS), the ACT study (R01AG054077, n=360), 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). This infrastructure will serve as an important part of the overall success of the project. Dr. Woods will not only use his expertise in non-invasive electrical brain stimulation, but also neuroimaging to facilitate the interpretation and understanding of tDCS application in the current proposal. In addition, Dr. Woods has led multiple published field standards papers on tES methods, application and safety, including transcranial Alternating Current Stimulation (tACS), and directs the only CME certified tES training course. This will provide a strong foundation for rigorous and replicable application of tES in the current proposal.

- a. Bikson, M., Grossman, P., Thomas, C., Jiang, J., Adnan, T., Mourdoukoutas, P., Kronberg, G., Troung, D., Boggio, P., Brunoni, A., Charvet, L., Fregni, F., Fritsch, B., Gillick, B., Hamilton, R., Hampstead, B., Jankford, R., Kirton, A., Knotkova, H., Liebetanz, D., Liu, A., Loo, C., Nitsche, M., Richardson, J., Rotenberg, A., Turkeltaub, P., & **Woods, A.J.** Safety of transcranial Direct Current Stimulation (tDCS): evidence based update 2016. *Brain Stimulation*. 9(5): 641-661. **PMCID: PMC5007190**
- b. **Woods, A.J.**, Antal, A., Bikson, M., Boggio, P.S., Brunoni, A.R., Celnik, P. Cohen, L.G., Fregni, F., Herrmann, C.S., Kappenman, E., Knotkova, H., Liebetanz, D., Miniussi, C., Miranda, P.C., Paulus, W., Priori, A., Reato, D., Stagg, C., Wenderoth, N., Nitsche, M.A.

(2016). A technical guide to tDCS, and related non-invasive brain stimulation tools. *Clinical Neurophysiology*. 127(2): 1031-1048. **PMCID: PMC4747791**

- c. Porges, E.C., **Woods, A.J.**, Edden, R., Harris, A., Chen, H., Garcia, A., Lamb, D., Williamson, J.W., Cohen, RA. (2017). Frontal GABA concentrations are associated with cognitive performance in older adults. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*. 2(1): 38-44. **PMCID: PMC5312683**
- d. **Woods, A.J.**, Hamilton, R.H., Kranjec, A., Bikson, M., Minhaus, P., Yu, J., Chatterjee, A. (2014). Space, time, and causality in the human brain. *NeuroImage*, 92, 285-297. **PMCID: PMC4008651**

B. Positions and Honors

Positions and Employment

2010-2013 Post-Doctoral Fellow, Department of Neurology, University of Pennsylvania, Philadelphia, PA
2013-2016 Assistant Professor, Department of Aging and Geriatric Research, University of Florida, Gainesville, FL
2013-2014 Cognitive Aging and Memory Clinical Translational Research Program Scholar, University of Florida, Gainesville, FL
2013-2014 Pepper Scholar, Institute on Aging, University of Florida, Gainesville, FL
2014- Assistant Director, Center for Cognitive Aging and Memory, Institute on Aging, University of Florida, Gainesville, FL
2016- Assistant Professor, Department of Clinical and Health Psychology, University of Florida, Gainesville, FL

Academic and Professional Honors

2006-2009 National Science Foundation (NSF) Graduate Research Fellowship
2008 Research Enhancement Fund grant award for advanced dissertation research, GWU
2009-2010 Graduate Research Fellowship, GWU
2009-2010 Thelma Hunt Research Fellowship in Psychology, GWU
2010-2013 Post-Doctoral Fellowship, Intellectual and Developmental Disabilities Research Center, Children's Hospital of Philadelphia
2013-2015 Pepper Center/CAM-CTRP Scholar, Cognitive Aging and Memory Clinical Translational Research Program, University of Florida, Gainesville, FL
2014 Appointed Assistant Director of the Center for Cognitive Aging and Memory
2014 KL2 Scholar, Clinical Translational Science Institute
2014 Junior Fellow of the World Academy of Arts and Sciences
2015 Young Investigator Award in Neuromodulation, NYC Neuromodulation 2015, New York, NY, USA

C. Contributions to Science

1. **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-founded a CME certified practical training course in tES that has trained over 700 researchers and students to safely and consistently apply this method of non-invasive brain stimulation. I have published numerous papers aimed at enhancing replicability and safety for the method, in addition to exploring its impact on a variety of cognitive functions in the brain. In addition, I was awarded the 2015 NYC Neuromodulation Young Investigator Award for my technical and educational contributions to the field. Furthermore, I recently led a 20-author field consensus paper on technical and methodological standards in the field of tES, in addition to senior authorship on a 27 author field standards safety paper. Collectively, this work provides me with a strong foundation in the technical elements and application standards of tES.
 - a. Minhas, P., Bikson, M., **Woods, A.J.**, Rosen, A., Kessler, S. (2012). Transcranial direct current stimulation in the pediatric versus adult brain: A computational modeling study. *IEEE Xplore: EMBC*, 63: 859-862. **PMCID: PMC3641645**
 - b. Kessler, S., Minhas, P., **Woods, A.J.**, Rosen, A., Bikson, M. (2013). Dose considerations for transcranial direct current stimulation in children: a computational modeling study. *PLoS ONE*, 8(9): e76112. **PMCID: PMC3785412**
 - c. **Woods, A.J.**, Bryant, V., Sacchetti, D., Gervits, F., Hamilton, R. (2015). Effects of electrode drift on transcranial direct current stimulation. *Brain Stimulation*. 8(3): 515-519. **PMCID: PMC4461479**
 - d. Szyrkowicz, S.M., McLaren, M.E., Suryadevara, U., **Woods, A.J.** (2016). Transcranial direct current stimulation use in the treatment of neuropsychiatric disorders: A brief review. *Psychiatric Annals*, 46(11): 642-646. **PMCID: PMC5117191**
2. **Neuroimaging.** My work in neuroimaging has focused on understanding what brain networks 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. Dotson, V.M., Szymkowicz, S.M., Sozda, C.N., Kirton, J.W., Green, M.L., O'Shea, A., McLaren, M.E., Anton, S.D., Manini, T.M. & **Woods, A.J.** (2015). Age differences in prefrontal thickness and volumes in middle aged to older adults. *Frontiers in Aging Neuroscience*. 7: 250. **PMCID: PMC4717301**
 - b. Seider, T., Gongvatana, A., **Woods, A.J.**, Porges, E., Chen, H., Cummings, T., Kahler, C.W., Monti, P.M., Cohen, R.A. (2016). Age exacerbates HIV associated white matter abnormalities. *Journal of Neurovirology*. 22(2): 201-212. **PMCID: PMC4783252**
 - c. Szymkowicz, S.M., McLaren, M.E., Kirton, J.W., O'Shea, A., **Woods, A.J.**, et al. (2016). Depressive Symptom Severity Is Associated with Increased Cortical Thickness in Older Adults. *International Journal of Geriatric Psychiatry*. 31(4): 325-333. **PMCID: PMC4724336**
 - d. O'Shea, A., Cohen, R.A., Porges, E.C., Nissim, N., **Woods, A.J.** (2016). Cognitive aging and the hippocampus in older adults. *Frontiers in Aging Neuroscience*, 8: 298. **PMCID: PMC5143675**
3. **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. My background in age-related working memory/executive decline will be germane to the current project.
- a. Mark, V.W., **Woods, A.J.**, Ball, K.K., Roth, D.L., Mennemeier, M. (2004). Disorganized search is not a consequence of neglect. *Neurology*, 63(1), 78-84.
 - b. **Woods, A.J.**, Mark, V.W. (2007). Convergent validity of executive organization measures on cancellation. *Journal of Clinical and Experimental Neuropsychology*, 29(7), 719-723. **PMCID: PMC3275913**
 - c. **Woods, A.J.**, Goksun, T., Chatterjee, A., Zelonis, S., Mehet, A., Smith, S. (2013). The development of organized visual search. *Acta Psychologica*. 143(2), 191-199. doi: 10.1016/j.actpsy.2013.03.008 **PMCID: PMC3651801**
 - d. Nissim, N., O'Shea, A., Bryant, V., Porges, E., Cohen, R., **Woods, A.J.** (2017). Frontal structural neural correlates of working memory performance in older adults. *Frontiers in Aging Neuroscience*, 8: 328. **PMCID: PMC5210770**
4. **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 healthy cognitive populations to understand the relative contributions of frontal and parietal systems in attention. The double dissociation approaches developed in this line of work are germane to the current grant.
- a. Mennemeier, M., Pierce, C., Dowler, R., Chatterjee, A., Anderson, B., Jewell, G., **Woods, A.J.**, Mark, V.W. (2005). Biases in attentional orientation and magnitude estimation explain crossover: neglect is a disorder of both. *Journal of Cognitive Neuroscience*, 17, 1194-1211.
 - b. **Woods, A.J.**, Mennemeier, M., Garcia-Rill, E., Meythaler, J., Mark, V.W., Jewell, G.R., Murphy, H. (2006). Bias in magnitude estimation following left hemisphere injury. *Neuropsychologia*, 44, 1406-12.
 - c. **Woods, A.J.**, Lehet, M., Chatterjee, A. (2012). Context modulates the contribution of time and space in causal inference. *Frontiers in Psychology*, 3, 371. doi: 10.3389/fpsyg.2012.00371 **PMCID: PMC3498891**
 - d. **Woods, A. J.**, Mennemeier, M., Garcia-Rill, E., Huitt, T., Chelette, K. C., McCullough, G., Munn, T., Brown, G., Kiser, T. S. (2012). Improvement in arousal, visual neglect, and perception of stimulus intensity following cold pressor stimulation. *Neurocase*, 18, 115-122. **PMCID: PMC3266979**
5. **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. In this area of my research, I lead the largest Phase III tDCS and cognitive training trial funded to date, as well as one of the largest Phase II cognitive training and non-invasive brain stimulation clinical trials. Each of these trials focuses specifically on remediating age-related cognitive decline and slowing dementia onset.

- a. Mark, V.W., **Woods, A.J.**, Mennemeier, M., Abbas, S., Taub, E. (2006). Cognitive assessment for CI therapy in the outpatient clinic. *Neurorehabilitation*, 21, 139-46.
- b. **Woods, A.J.**, Mark, V.W., Pitts, A., & Mennemeier, M. (2011). Pervasive cognitive impairment in acute rehabilitation patients "without" brain injury. *PM&R*, 3(5), 426-432. **PMCID: PMC3275913**
- c. **Woods, A.J.**, Cohen, R.A., Pahor, M. (2013). Cognitive frailty: frontiers and challenges. *Journal of Nutrition, Health, and Aging*. 17, 741-743. **PMCID: PMC4471842**
- d. Anton, S., **Woods, A.J.**, Ashizawa, T., Barb, D., Buford, T., et al., Successful aging: Advancing the science of physical independence in older adults. *Aging Research Reviews*. 24, 304-27. **PMCID: PMC4661112**

Complete List of Published Work in MyBibliography: <http://www.ncbi.nlm.nih.gov/sites/myncbi/adam.woods.1/bibliography/45511051/public/?sort=date&direction=descending>

D. Research Support

Ongoing Research Support

NIA R01AG054077 (Woods/Cohen/Marsiske; 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: PI

NIA U01AG062368 Edwards (PI) 09/30/18-05/31/20 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 conversion 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

NIMH R21MH112206 **Woods, Adam**; Ding, Mingzhou (MPIs) 01/15/18-12/31/19 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 (overlap covered by K01)

NIA R21AG053736-01A1 Clark, David (PI) 07/01/17-06/31/19 National Institutes of Health
Combining tDCS and neurorehabilitation to treat age-related deficits of mobility and cognition

The goal of this study is to obtain pilot data for a full-scale clinical trial combining transcranial direct current stimulation (tDCS) and complex walking intervention to enhance mobility in older adults.

Role: Co-I (overlap covered by K01)

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