Age-related Memory Loss (ARML) Program and Cognitive Aging and Memory (CAM-CTRP) Program

2017 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

Our newly-remodeled reception and waiting area.

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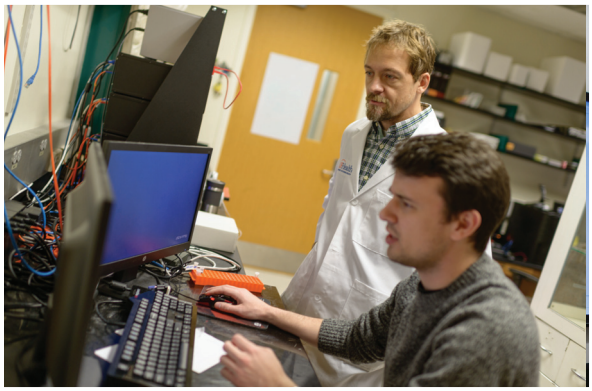

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January 16, 2018

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 (AMRL) program and Cognitive Aging and Memory - Clinical and Translational Research Program (CAM-CTRP).

The AMRL and CAM-CTRP programs are now thriving under one roof in the McKnight Brain Institute building. Recognized as an official UF Center, CAM-CTRP has dedicated clinical research space in the MBI building, which is almost completely occupied each day with study participants.

2017 proved to be a highly productive year for both programs. As can be seen in the attached report, extramural support for MBRF-sponsored programs has grown significantly, with several investigators in each program earning and/or renewing NIH funding. The numerous publications, presentations and honors are impressive, and pilot studies are generating informative data that advance our understanding of age-related cognitive decline and serve as the basis for extramural funding of further studies.

We look forward to the ongoing accomplishments from these programs and thank you again for your support.

Sincerely,

David S. Guzick, MD, PhD
Senior Vice President, Health Affairs
President, UF Health

Michael L. Good, MD
Dean, College of Medicine
Falke H. Peterson Dean's Distinguished Professor

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

UF Evelyn F. & William L. McKnight Brain Institute
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January 11, 2018

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

Dear Trustees,

It is our pleasure to submit the 2017 annual report for the ARML and CAM-CTRP programs supported by the MBRF. The leadership within the Health Science Center at the University of Florida is grateful for the long-lasting support of the MBRF and we are excited by the ongoing science in this area and the productivity of all the ARML and CAM-CTRP investigators.

We believe the annual report demonstrates that both programs are on great trajectories. One excellent indicator of maturing programs is their ability to attract junior investigators, who then become part of the program, or successfully launch independent careers at other institutions following their training. It is clear that both MBRF supported programs are now at that stage. Extramural support remains strong and continues to grow, and both groups are highly productive in terms of publication and visibility both within and outside the University.

We are delighted that CAM-CTRP is now reintegrated within the MBI, and that the newly renovated research space for the CAM-CTRP program is now located in close proximity to the AMRIS facility. The MBI itself contributed almost $400,000 to the renovation of the CAM-CTRP space. Located next to the new 3T Siemens Prisma MRI, this is an ideal location. Further, it heralds a new era for the MBI itself, where we hope to see more human subject research within the building itself.

As the MBI embraces programmatic science, we are confident that more collaborative grants between both the ARML and CAM-CTRP programs, as well as other groups on campus will be funded. Neuromedicine and neuroscience research at UF are arguably UF's strongest biomedical research programs, with programmatic brain aging research serving as a foundational component of the larger enterprise.

New initiatives conceived by the larger MBI executive committee to help support both educational and outreach activities are well underway in the MBI. These activities are designed to further enhance neuroscience education, achieve greater diversity in training opportunities, and promote our science both within and outside the University. All of these activities should further enhance and enrich the MBRF supported programs. Further, we now have both an outstanding dedicated science writer, Michelle Jaffe, as well as a Communications Director, Todd Taylor, to help support these activities and publicize our work.

Specifically, the newly formed Outreach and Education Committee launched several new programs to serve the UF neuroscience community. The MBI Visiting Scholars program will bring current and rising stars in the international neuroscientist community to UF. These visits will raise the profile of UF neuroscience, and create new opportunities for trainee and community engagement. This program will complement the Luttge Lectureship and enable additional prominent brain aging investigators to

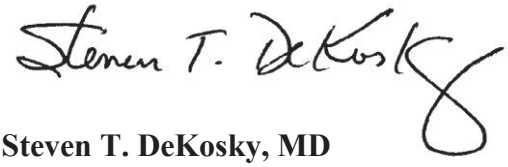
visit the UF campus. We have launched MBI Research Evenings that are thematically organized and include short presentations by UF neuroscientists. These events provide an opportunity to highlight research findings and promote collaboration among the UF neuroscience community. The new Trainee Enhancement Opportunities are similar to UF Faculty Enhancement Opportunities in that they will allow research fellows, clinical fellows and graduate students to diversify their skillsets by attending courses, learning new techniques or exploring new aspects of neuroscience not available in their home labs. We obtained donor funding (Toffler Awards) to fund neuroscience research, education and leadership pursuits by graduate and professional students enrolled in Ph.D., M.D. and M.D./Ph.D. combined programs. We continue to fund successful initiatives including the Summer Neuroscience Internship Program (SNIP), which has already trained two dozen undergraduates, including many under-represented minority students (~60%). We continue our Research Fellowship program to provide pilot funds to trainees and junior scientists with the goal of stimulating their growth. Finally, we continue to fund MBI travel awards to UF neuroscientists lacking sufficient resources to present their research at national and international conferences.

I think it especially important to applaud both Dr. Jennifer Bizon and Dr. Sarah Burke, members of the ARML program. In addition to conducting outstanding brain aging research, both have played a vital role in moving the MBI in new directions. Dr. Bizon is a new member of the MBI Executive Committee. She and Dr. Jada Lewis have played a vital role in conceptualizing and enacting many of the activities mentioned above with respect to MBI outreach and education. Dr. Sarah Burke has again collaborated with Dr. Lewis to lead the SNIP program that continues to expose talented and diverse undergraduates to neuroscience research.

We are currently in the midst of developing a 5-year strategic plan for the MBI, and we are beginning with programmatic based strategic plans. We will be working with members of the ARML and CAM-CTRP to develop a strategic plan for those programs. These plans will then be integrated into the larger MBI strategic plan. There is no doubt in our mind that these programs will be key foundational parts of that plan. Further, it is also clear from early discussions about that plan that cross-fertilizations between these MBRF supported programs and other MBI programs can further elevate our science. Indeed, preliminary discussions of developing a training program and programmatic research grants around brain aging and neurodegeneration are emerging.

We are proud of the CAM-CTRP and ARML programs and again thank you for longstanding support as well as passion for promoting this area of research.

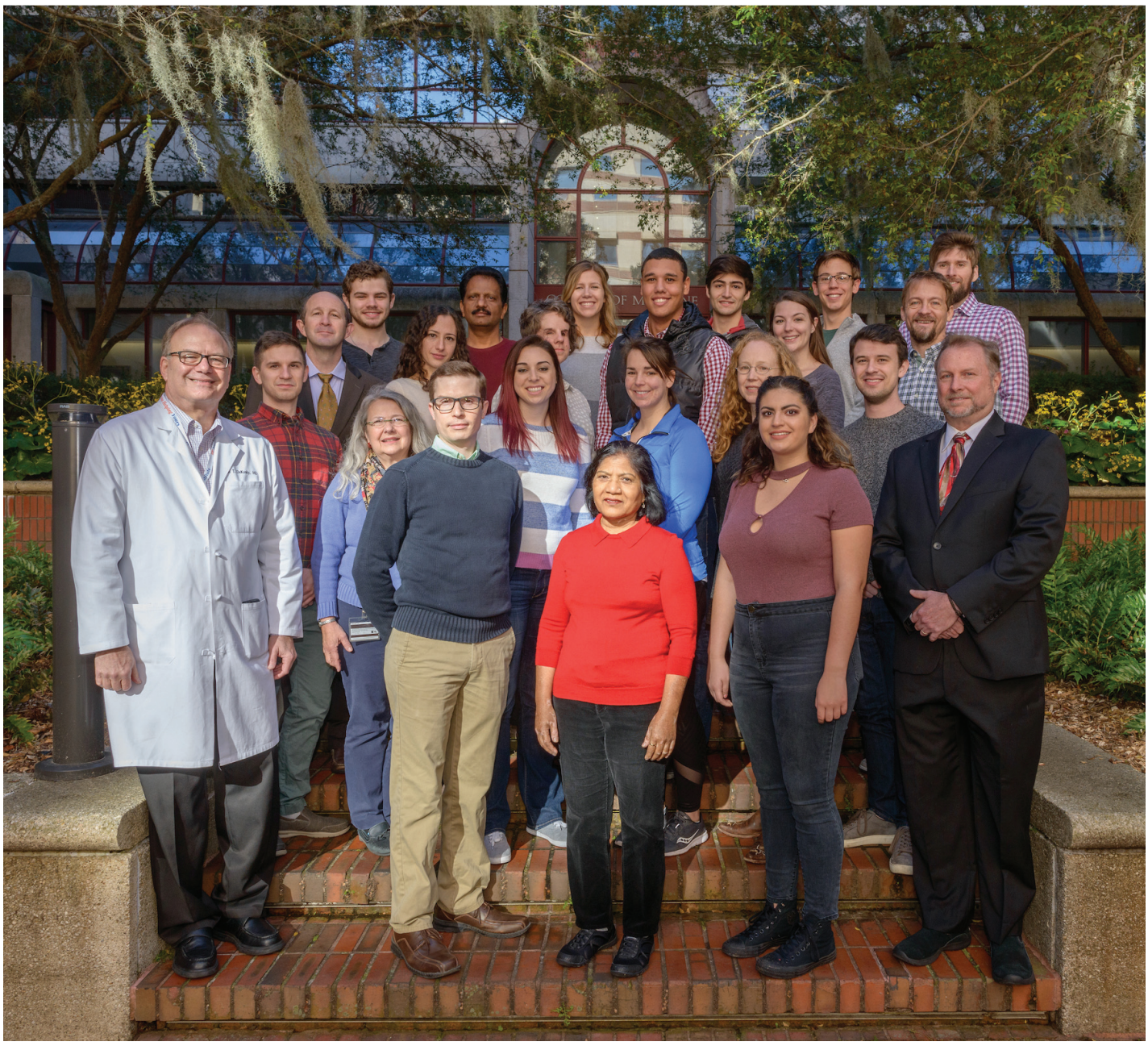
Todd E. Golde, M.D., Ph.D.
Director, Evelyn F. and William L. McKnight Brain Institute
Director, 1Florida Alzheimer's Disease Research Center
Professor, Department of Neuroscience
College of Medicine



Steven T. DeKosky, MD
Deputy Director, Evelyn F. and William L. McKnight Brain Institute
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

2017 Progress Report



December 12, 2017

Dear McKnight Brain Research Foundation Trustees:

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 committee 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 principle investigators: Drs. Thomas Foster, Jennifer Bizon, Sara Burke, and Andrew Maurer.

We are very proud of our ARML investigators that received recognition for achievements and contributions to science. Dr Sara Burke received the American Psychological Association Early Career Award for Distinguished Contribution in Cognitive and Behavioral Neuroscience. In addition, 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. Thomas Foster received the University of Florida Research Foundation Professorship award, which is 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. In addition, Dr Foster received the first Distinguished Alumnus Award in recognition of noteworthy service and achievement from Wake Forest University Graduate School of Arts & Sciences, Department of Physiology & Pharmacology.

Major goals of the ARML program include support for communication among researchers and nurturing scientists dedicated to the exploration and innovative research in the understanding and alleviation of age-related memory loss. This includes mentoring graduate students and postdoctoral scholars, who present their research at scientific meetings. During the past year associates of the ARML program presented posters at the McKnight Brain Research Foundation poster session at the Society for Neuroscience. Members of the Burke lab received first (Mr. S. Turner and Dr. L. Colon-Perez) and second place (Ms. A. Hernandez) and third place went to Caesar Hernandez from the Bizon lab. Moreover, graduate students and postdoctoral scholars from ARML labs have been recognized with funding for their research projects. Abbi Hernandez (Burke) received the Luttge Award and an NIH F31 award to examine metabolic mechanisms for treating cognitive aging. Dr. Caitlin Orsini (Bizon/Setlow) received a K99/R00 on neural circuits and mechanisms.

Lara Ianov (Foster) received the Kenneth & Laura Berns Award for Excellence in Genetics for her work on the epigenetics of age-related cognitive decline. Dr. Brittney Yegla (Foster) received pilot funding from the Claude D. Pepper Older Americans Independence Center to examine exosome mediate muscle/brain communication during aging.

The four principle investigators of the ARML continue to maintain a high level of productivity. Over the past year, the group had 23 unique publications (see Biosketches for details) and received funding for seven new projects.

Bizon/Burke Ed and Ethel Moore Alzheimer's Disease Grant
Bizon/Burke (PI Otto) Project 1.2 DARPA Cognitive augmentation through neuroplasticity
Bizon CAM-CTRP Pilot Award GABABR antagonists as a treatment for age-related cognitive decline
Maurer AG055544 Age-associated changes in hippocampal circuits and cognitive function
Foster R21NS091435 (PI Notterpek) Targeting the chaperone pathway for myelin repair in hereditary neuropathies
Esser/Foster Pepper Center pilot, Circadian clocks link sarcopenia and cognitive decline during aging.
Yegla/Foster/Esser Pepper Center pilot, Exosomal mediation of exercise-induced benefits in aging

ARML Program: Promoting Collaboration and Communication

The support of the MBRF has been fundamental in collaborative efforts and maintaining communication among researchers. The following represents a subset of collaborations related to funded projects, published papers, or grants submitted to NIH, and emphasizes collaborations between ARML members with the CAM-CTRP and the other MBRF sponsored institutes.

Ongoing collaborations across institutes have resulted in several manuscripts that highlight themes of functional connectivity and molecular mechanisms in age-related cognitive decline. Studies of functional connectivity emphasize circuits within and between specific brain regions. A collaboration between Drs Maurer (University of Florida) and Dr Barnes (University of Arizona) resulted in a paper examining changes in neuronal activity of cells in the perirhinal cortex of aged primates. This complements ongoing collaborations between Drs Maurer, Burke, and Bizon examining functional connectivity between the perirhinal cortex, entorhinal cortex, prefrontal cortex, and hippocampus during aging. Together, these researchers have published papers demonstrating that their newly developed tasks provide valid models of cognitive changes observed in humans, focused on specific brain regions that mediate the cognitive process of interest.

In addition, Dr Burke is the lead author on a submitted manuscript, which brings together researchers from the University of Florida (Burke, Bizon, Bauer), University of Arizona (Ryan, Barnes), and University of Alabama (Roberson). This work, examining the role of perirhinal and parahippocampal connectivity in cognitive aging forms the foundation for future grant proposals and inter-institute interactions examining functional connectivity of brain regions during aging.

A recent publication on molecular mechanisms of age-related cognitive decline brought together thirteen investigators from the University of Florida (Ianov, Rani, Kumar, Foster), University of Arizona (De Both, Chawla, Piras, Siniard, Barnes, Huentelman), and the University of Alabama (Kennedy, Day, Sweatt). This work characterized the transcriptional profile linked to aging and cognitive decline within different hippocampal subfield. Another paper from this group is currently in preparation.

A paper published in collaboration with CAM-CTRP (Rani et al., 2017), identified microRNA in plasma that predict cognitive function in individuals 60-89 years of age. This work forms the basis for future studies characterizing blood biomarkers of cognitive decline and examination of epigenetic mechanisms involving the brain and peripheral systems.

The ARML group has established protocols to be employed in cross institute collaborations involving the McKnight Brain Aging Registry and Neuroimaging Core and McKnight Brain Aging Cognitive Core. In addition, an informal “MBRF Blood Biomarkers” group has formed and includes researchers from Miami (Sun, Rundek, Blanton), Arizona (Huentelman) and Florida (Foster, Cohen, Leeuwenburgh).

There are no easy solutions to age-related cognitive decline. This complex and multifaceted problem requires the collaborative efforts supported by the MBRF. The MBRF support ensures the continued progress, as evidenced by continued research publications and newly funded research projects.

Sincerely,

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

Active Federal Funding

PI	Project Number	Project Title	NIH Inititute	FY	FY Total Cost
Foster, Thomas C	5 R37 AG036800 08	SIGNALING CASCADES AND MEMORY DEFICITS DURING AGING	NIA	2017	$ 295,992.00
Foster, Thomas C	5 R01 AG049711 03	SYSTEMIC INFLAMMATION IN REGULATING THE ONSET AND PROGRESSION OF BRAIN AGING	NIA	2017	$ 307,500.00
Foster, Thomas C	5 R01 AG052258 02	SYSTEMIC INFLAMMATION IN REGULATING THE ONSET AND PROGRESSION OF BRAIN AGING	NIA	2017	$ 375,000.00
Bizon, Jennifer L	5 R01 AG029421 10	Neural Mechanisms of Cognitive Decline in Aging	NIA	2017	$ 303,640.00
Burke, Sara N	5 R01 AG049722 03	THE CONTRIBUTION OF DECLINES IN FUNCTIONAL CONNECTIVITY TO COGNITIVE AGING	NIA	2018	$ 337,648.00
Burke, Sara N	5 R21 AG051004 02	SINGLE-CELL IMAGING OF FUNCTIONAL CONNECTIVITY AS A WINDOW INTO COGNITIVE AGING	NIA	2017	$ 190,462.00
Maurer, Andrew P	1 R01 AGT055544 01	AGE-ASSOCIATED CHANGES IN HIPPOCAMPAL CIRCUITS AND COGNITIVE FUNCTION	NIA	2017	$ 393,673.00
Maurer, Andrew P	5 R01 MN109548 02	TESTING AND FORECASTING HIPPOCAMPAL THETA WAVE PROPAGATION IN LEARNING AND MEMORY	NIHM	2017	$ 381,250.00
Setlow, Barry/Maurer, Andrew P	5 R21 DA039701 02	DEVELOPMENT OF A RAT MODEL OF CANNABIS SMOKE SELF-ADMINISTRATION	NIDA	2016	$ 185,625.00

SUMMARY OF SCIENTIFIC ACHIEVEMENTS SINCE LAST REPORT:

Jennifer Bizon, PhD

Published 10 peer-reviewed manuscripts. Highlights include:

- **A Journal of Neuroscience paper (Dec 2016) from Dr. Joe McQuail, a postdoctoral fellow in my laboratory.** This manuscript identifies a specific alteration in NMDA receptors that is particularly relevant for age-associated alterations in working memory decline and suggests a novel therapeutic strategy to improve working memory in older subjects.
- **A second Journal of Neuroscience paper currently in press from Dr. Caitlin Orsini, another postdoc in the lab, co-mentored by myself and Dr. Barry Setlow.** This manuscript uses temporally discrete optogenetic inhibition to identify unique roles for the basolateral amygdala in decision making. A second manuscript using the same approach in aged rats is currently in preparation. The aging work was presented at the recent Society for Neuroscience meeting in Washington DC where it was picked by the Society as a "hot topic" and where my graduate student, Caesar Hernandez, received 3rd place at the annual McKnight reception.
- **An invited submission to Neuroscience for a special issue on the neural mechanisms of cognitive flexibility (April 2017).** The first author of this study was my former graduate Sofia Beas and her study showed that GABAergic signaling dysfunction in prefrontal cortex contributes to impairments in cognitive flexibility. She further showed that an agonist at GABA(B) receptors can improve this aspect of cognitive function in aged rats.
- **A manuscript in Neurobiology of Aging showing that olfactory discrimination learning is sensitive to age-related mnemonic decline and that aged rats are disproportionately impaired as stimuli become more similar.** A parallel paper using visual cues (on which I was a co-author) was published this year by Dr. Sara Burke's group. These latter two papers are foundational for a funded DOH Pilot proposal ($100,000.00) and R21 that was recently scored in the 8th percentile on which Dr. Burke and I are MPIs.
- **Contributed over 15 presentations (invited and posters)** Highlights include being invited to serve as one of the faculty members at a Neuroscience School of Advanced Studies course on "Cognitive Decline and Aging" in Tuscany, Italy in September 2017, being invited to be the keynote speaker at a Society for Neuroscience Hudson-Berkshire Chapter Conference in Albany, and being invited to give a seminar as part of the Office of the Director Seminar Series at the National Institute on Aging.
- **Success in grant funding.** My lab funding has increased in this past year and now includes: serving as PI on one NIA R01, co-I on 3 R01s, MPI (contact) on 1 DOH Pilot Proposal (new), serving as Project leader on a DARPA grant (new), serving as PI on two private foundation grants (new), and Sponsor on a F32 (McQuail) and co-Sponsor on a K99/R00 (Orsini, new), a K01 (Porges, new), a F31 (Hernandez, new) and a K99/R00 that was scored in funding range (Johnson, new).
- **Service in neuroscience of aging field.**
- **Senior Editor at Neurobiology of Aging (Impact Factor 5.2),**
- **Chair of the NIH F03 (Neurodevelopment, Synaptic Plasticity and Neurodegeneration Fellowship) Study Section.**
- **I also regularly serve on the neuroscience study section for the National Institute on Aging (NIA-N).**

Sara N. Burke, PhD

The focus of my research continues to be on determining the neurobiology of age-related memory loss using a systems approach that emphasizes how different areas of the brain communicate and perhaps even compensate in advanced age. In the past year, however, my research has gone in two novel directions that compliment current ongoing projects in the lab. First, we have been examining the role of metabolic dysfunction in cognitive aging and determining whether a ketogenic diet can improve brain function in older animals. Second, in collaboration with Drs. Otto (BME), Bizon, Maurer and Setlow, we are determining the mechanisms by which vagus nerve stimulation enhances cognitive function. Should this 4-yr DARPA-funded project prove successful, we will have identified a new avenue for treating cognitive aging in older adults. In terms of my other funded projects, I am year 2 of my R01 and R21, and have completed progress reports (noncompetitive renewals) for both awards.

In terms of scientific advancements from my research program, the long-term objectives of determining the network-level interactions that support learning and memory in old age, necessitate an understanding of the neurobiological factors that distinguish normal aging from disease, as well as an enhancement of the predictive validity of animal models. To push this research

trajectory forward, the Burke and Bizon labs have collaboratively developed a novel rat model of mild cognitive impairment using adeno-associated viral (AAV) technology that targets neurons in the perirhinal and lateral entorhinal cortices, which show the earliest signs of vulnerability (Khan et al., 2014). We have shown that this approach leads to tau hyperphosphorylation in area beyond the AAV infusion – suggesting propagation. We are currently in the process of validating this model using both biochemistry and behavioral assays. Concurrently, my group has developed new behavioral paradigms in rodents that better reflect the cognitive processes in humans that become vulnerable in old age and the early stages of dementia. For example, we have recently established a rodent-variant of the mnemonic similarity task, which uses objects constructed from LEGOS to parametrically manipulate stimulus similarity between a target and a foil object. We have found that, similar to humans, old animals perform poorly on this task when the target and foil objects are similar, but not when they are distinct (Johnson et al., 2017). This behavioral deficit in old animals is recapitulated when hippocampal activity is blocked (Johnson et al., in preparation). Additionally, we have recently developed an object-place paired association task into a dual-task that requires simultaneous working memory and object recognition while gait is measured. As reported in humans (Theill et al., 2011), we are finding that the dual-task component exacerbates the effects of age on performance. This will enable future mechanistic studies aimed at determining the cellular and systems-level changes that account for multi-tasking deficits in aging.

Regarding the mentorship of my trainees, my graduate student (Abbi Hernandez) and postdoc (Dr. Sarah Johnson) have both had an immensely successful year. Ms. Hernandez submitted an F31 and was honored with the Advancement to Candidacy Award as well as the Luttge Award. Moreover, her F31 was awarded and began on 9-15-18. Dr. Johnson was given the MBI fellowship and submitted a K-award, which scored an impact of 20. Finally, in addition to mentoring my own trainees, I directed the second year of the UF Summer Neuroscience Internship Program (SNIP) and we begin accepting applications for our third cohort in January 2018. In year 2, we obtained additional funding from the IDP and Dept of Neurology so that, along with the support of the MBI, we were able to host 13 students from around the country to participate in this program for the summer of 2017. The average GPA of the 2017 cohort of SNIP students was 3.6, and 7 of the 13 students were under-represented minorities.

Other achievements include:

- **Published 8 peer-reviewed manuscripts, 2 under consideration. Highlights include:**
- **A Hippocampus publication from Dr. S.A. Johnson** documenting that when a human behavioral paradigm for assessing medial temporal lobe-dependent object discrimination is adapted to rodents, similar age-related deficits are observed.
- **A Journal of Gerontology, Series A publication from Ms. A. Hernandez** documenting the physiological and biochemical impact of a long-term ketogenic diet in aged rats. Notably, 12 weeks of an isocaloric ketogenic diet resulted in loss of body fat and restored levels of several ATP-dependent transporters in the hippocampus.
- **A Journal of Neuroscience publication by Drs. S.N. Burke and A.P. Maurer** documenting age-associated declines in perirhinal cortical interneuron activity and monosynaptic connectivity.
- **Contributed over 14 presentations and invited talks.** Highlights include: Speaking at the Cognitive Aging Summit in Washington D.C., giving invited seminars at the University of Iowa and Brown University, and mentees being awarded first (Mr. S. Turner and Dr. L. Colon-Perez) and second place (Ms. A. Hernandez) at the McKnight Brain Research Foundation Poster Reception.
- **Success in grant funding.** My lab funding has increased in this past year and now includes: serving as PI on one NIA R01 and a R21, co-I on 2 R01s (new), MPI (contact PI, Bizon) on 1 DOH Pilot Proposal (new), serving as Project leader on a DARPA grant (new), Sponsor on a F31 (Hernandez, new) and Sponsor on a K99/R00 that was scored in funding range (Johnson, new). Additionally, a MPI R21 with Dr. J. Bizon (contact) scored in funding range.
- **Service in neuroscience of aging field.**
- **Served on P50 grant review panel for NIA.**
- **Regular ad hoc reviewer for Neurobiology of Aging.**

Thomas C. Foster, PhD

Much of the published scientific work from the Foster lab, in collaboration with several other MBRF sponsored researchers, has focused on the idea that epigenetic mechanisms contribute to cognitive decline with aging and these mechanisms are engaged by environmental and lifestyle factors to influence brain resiliency and cognitive reserve. Work in collaboration with CAM-CTRP

examined exosomal miRNA in community dwelling individuals (Rani et al., 2017). Stringent criteria (age, health status, cognitive function) was used to obtain individuals that were likely free of Alzheimer's disease. Individuals were tested on a comprehensive neuropsychological battery and plasma collected for biological measures. Despite stringent criteria, results demonstrated an age-related decrease in cognitive function. Collection of plasma exosomes was established and sequencing confirmed miRNA expression patterns similar to previous reports. When cognitive variability due to age was taken into account, several miRNA continued to correlate with cognitive function. The pattern did not match that for Alzheimer's disease and suggested biomarkers of brain function (brain specific miRNA) and possible mechanisms by which miRNA could induce age-related functional changes. A separate study, involving thirteen collaborators from three MBRF sponsored institutes; identified distinct hippocampal subfield transcriptional profiles related to vulnerability to aging and cognitive decline (Ianov et al., 2017c). This work indicates that measures of episodic memory decline with age are robust and point to changes in Ca2+ regulation and synaptic transmission as contributing to cognitive decline.

Another series of studies employed a rodent model of age-related impairment in executive function to examine the relationship of DNA methylation in the prefrontal cortex to executive function and mRNA expression. Results indicate aging and cognition related changes in non-CpG DNA methylation and CpG methylation in DNA gene body regions. In particular, hypermethylation of synaptic genes was associated with decreased expression of synaptic genes and cognitive decline. The results indicate that epigenetic mechanisms (i.e. DNA methylation) contributes to synaptic modification observed in brain aging and age-related cognitive impairment (Ianov et al., 2017b). Another paper examined DNA methylation in regulation of estrogen receptors expression in the hippocampus during aging (Ianov et al., 2017a). Finally, studies in collaboration with Dr Ormerod examined the role of systemic inflammation in cognitive decline (McGuiness et al., 2017) and ongoing studies suggest a possible role for epigenetic influences on resiliency to systemic inflammation.

Comprehensive reviews were published illustrating the link between aging mechanisms (i.e. increased redox stress) and the emergence of cognitive deficits in middle-age (e.g. impaired episodic memory); through senescent physiology of synaptic plasticity mechanisms that underlie episodic memory (Kumar et al., 2017). In addition, a review was published which illustrated the link between redox stress of aging and age-related neurodegenerative diseases Foster et al., 2017).

Andrew Maurer, PhD

This marks the closure of the 1st year of the Maurer lab being "open for business." 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. In collaboration with Dr. Carol Barnes at the University of Arizona EMBI, we have published a paper demonstrating a change in neuronal communication with the perirhinal cortex of aged animals. Moreover, in collaboration with Dr. Sara Burke, we have demonstrated a change in functional connectivity between the lateral entorhinal cortex and hippocampus of aged-impaired rats. Finally, we have kicked off our high-density electrophysiology from the hippocampus of aged rats. With these early successes, we believe that we can keep this momentum towards some significant achievements in 2018.

PUBLICATIONS IN PEER REVIEWED JOURNALS:

Jennifer Bizon, PhD

1. Orsini CA, Hernandez CM, Kelly KB, Singhal S, Frazier CJ, **Bizon JL**, Setlow B. Optogenetic inhibition reveals distinct roles for basolateral amygdala activation during discrete timepoints in risky decision making. Epub ahead of print. *The Journal of Neuroscience*.

2. Hernandez, AR, Hernandez CM, Campos K, Truckenbrod LM, McQuail JA, Carter C, **Bizon JL**, Maurer AP, Burke SN. (2017) The Anti-Epileptic Ketogenic Diet Alters Hippocampal Transporter Levels and Reduces Adiposity in Aged Rats. Epub ahead of print. *Journal of Gerontology*.

3. Hernandez CM, Vetere LM; Orsini CA; McQuai JA; Maurer AP; Burke SN; Setlow B, **Bizon, JL**. Decline of prefrontal cortical-mediated executive functions but attenuated delay discounting in aged Fischer 344 x Brown Norway hybrid rats. *Neurobiology of Aging*, 2017 Dec;60:141-152

4. Johnson SA, Turner SM, Santacroce LA, Cartly K, Shafiq L, **Bizon JL**, Maurer AP, Burke SN, Age-related impairments in discriminating perceptually similar objects parallel those observed in humans. *Hippocampus*, 27(7):759-776.

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

6. Setlow, B. & **Bizon JL** (2017) Adolescent cannabinoid use and cognition; unexpected results from a rat model of cannabinoid self-administration. *Neuropsychopharmacology*. 42:983-984

7. Orsini CA, Mitchell MR, Heshmati SC, Shimp KG, Spurrell MS, **Bizon JL**, Setlow B (2017) "Effects of nucleus accumbens amphetamine administration on performance in a delay discounting task. *Behavioral Brain Research* 321:130-136. doi: 10.1016/j.bbr.2017.01.001.

8. Beas BS, McQuail JA, Bañuelos C, Setlow B, **Bizon JL**. (2017) Prefrontal cortical GABAergic signaling and impaired behavioral flexibility. *Neuroscience*. 345:274-286 doi: 10.1016/j.neuroscience.2016.02.014.

9. Hernandez AR, Reasor JE, Truckenbrod LM, Lubke KN, Johnson SA, **Bizon JL**, Maurer AP, Burke SN. (2017) Medial prefrontal-perirhinal cortical communication is necessary for flexible response selection. *Neurobiology of Learning and Memory* 137:36-47. doi: 10.1016/j.nlm.2016.10.012.

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

Sara N. Burke, PhD

1. Gray DT, Smith AC, **Burke SN**, Gazzaley A, Barnes CA (2017). Attentional updating and monitoring and affective shifting are impacted independently by aging in macaque monkeys. *Behavioural Brain Research*, 322(Pt B):329-338.

2. Hernandez AR, Reasor JE, Truckenbrod LM, Lubke, K, Johnson SA, Bizon JL, Maurer AP, **Burke SN** (2017). Medial Prefrontal-Perirhinal Cortical Communication is Necessary for Flexible Response Selection. *Neurobiology of Learning and Memory*, 137:36-47.

3. Yoder WM, Lyman M, Muizza O, Ormerod BK, **Burke SN**, Setlow B, Smith DW, Bizon JL (2017). Interaction between age and perceptual difficulty in olfactory discrimination learning: relationship with hippocampal-dependent spatial learning. *Neurobiology of Aging*, 53:122-137.

4. Johnson SA, Turner SM, Santacroce LA, Bizon JL, Maurer AP, **Burke SN** (2017). Rodent age-related impairments in discriminating perceptually similar objects parallel those observed in humans. *Hippocampus*, 27(7):759-776.

5. Maurer AP, Johnson SA, Hernandez AR, Reasor J, Cossio DM, Fertal KE, Mizell JM, Lubke KN, Clark BJ, **Burke SN** (2017). Age-related changes in lateral entorhinal and CA3 neuron allocation predict poor performance on object discrimination. *Frontiers in Systems Neuroscience*, 30;11:49.

6. Maurer AP*, **Burke SN***, Diba K, Barnes CA (2017). Advanced Age is Associated with Attenuated Principal Cell and Interneuron Activity in the Perirhinal Cortex. *Journal of Neuroscience*, 37(37):8965-8974. *These authors contributed equally.

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

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

9. **Burke SN**, Gaynor LS, Barnes CA, Bauer RM, Bizon JL, Roberson RD, Ryan L (2017). Perirhinal and Parahippocampal Cross Talk: Implications for Cognitive Aging. Under revision, *Trends in Neurosciences*.

10. Hernandez AR, Reasor JE, Truckenbrod LM, Fertal KE, Maurer AP, **Burke SN** (2017). Differential effects of advanced age on neuronal ensemble activity in hippocampus, perirhinal cortex, and prefrontal cortex, Submitted to *Neurobiology of Aging*.

11. Gaynor LS, Mizell J, Johnson SA, Maurer AP, **Burke SN**. Aging disproportionately affects dual-functions of the perirhinal cortex: discrimination versus association. Submitted to *Behavioral Neuroscience*.

Thomas C. Foster, PhD

1. **Foster TC**, Kyritsopoulos C, Kumar A (2017) Central role for NMDA receptors in redox mediated impairment of synaptic function during aging and Alzheimer's disease. *Behav Brain Res* 322:223-232.

2. Ianov L, Kumar A, **Foster TC** (2017a) Epigenetic regulation of estrogen receptor alpha contributes to age-related differences in transcription across the hippocampal regions CA1 and CA3. *Neurobiol Aging* 49:79-85.

3. Ianov L, Riva A, Kumar A, **Foster TC** (2017b) DNA methylation of synaptic genes in the prefrontal cortex is associated with aging and age-related cognitive impairment. *Front Aging Neurosci* 9:249.

4. Kumar A, Yegla B, **Foster TC** (2017) Redox signaling in neurotransmission and cognition during aging. *Antioxid Redox Signal*.

5. McGuiness JA, Scheinert RB, Asokan A, Stadler VC, Lee CS, Rani A, Kumar A, **Foster TC**, Ormerod BK (2017) Indomethacin increases neurogenesis across age groups and improves delayed probe trial difference scores in middle-aged rats. *Front Aging Neurosci* 9:280.

6. Rani A, O'Shea A, Ianov L, Cohen RA, Woods AJ, **Foster TC** (2017) miRNA in circulating microvesicles as biomarkers for age-related cognitive decline. *Front Aging Neurosci* 9:323.

7. Ianov, L., De Both, M., Chawla, M.K., Rani, A., Kennedy, A.J., Piras, I., Day, J.J., Siniard, A., Kumar, A., Sweatt, J.D., Barnes, C.A. Huentelman, M.J. **Foster, T.C.** (2017c) Hippocampal transcriptiomic profiles: Subfield vulnerability to age and cognitive impairment. *Front Aging Neurosci* (in press).

Andrew Maurer, PhD

1. The Anti-Epileptic Ketogenic Diet Alters Hippocampal Transporter Levels and Reduces Adiposity in Aged Rats. Hernandez AR, Hernandez CM, Campos KT, Truckenbrod LM, Sakarya Y, McQuail Ph D JA, Carter CS, Bizon JL, **Maurer AP**, Burke SN. *J Gerontol A Biol Sci Med Sci*. 2017 Oct 12. doi: 10.1093/gerona/glx193. [Epub ahead of print] PMID: 29040389

2. Decline of prefrontal cortical-mediated executive functions but attenuated delay discounting in aged Fischer 344 × brown Norway hybrid rats. Hernandez CM, Vetere LM, Orsini CA, McQuail JA, **Maurer AP**, Burke SN, Setlow B, Bizon JL. *Neurobiol Aging*. 2017 Dec;60:141-152. doi: 10.1016/j.neurobiolaging.2017.08.025. Epub 2017 Sep 5. PMID: 28946018

3. Attenuated Activity across Multiple Cell Types and Reduced Monosynaptic Connectivity in the Aged Perirhinal Cortex. **Maurer AP**, Burke SN, Diba K, Barnes CA. *J Neurosci*. 2017 Sep 13;37(37):8965-8974. doi: 10.1523/JNEUROSCI.0531-17.2017. Epub 2017 Aug 11. PMID: 28821661

4. Age-related Changes in Lateral Entorhinal and CA3 Neuron Allocation Predict Poor Performance on Object Discrimination. **Maurer AP**, Johnson SA, Hernandez AR, Reasor J, Cossio DM, Fertal KE, Mizell JM, Lubke KN, Clark BJ, Burke SN. *Front Syst Neurosci*. 2017 Jun 30;11:49. doi: 10.3389/fnsys.2017.00049. eCollection 2017. PMID: 28713251

5. Rodent age-related impairments in discriminating perceptually similar objects parallel those observed in humans. Johnson SA, Turner SM, Santacroce LA, Carty KN, Shafiq L, Bizon JL, **Maurer AP**, Burke SN. *Hippocampus*. 2017 Jul;27(7):759-776. doi: 10.1002/hipo.22729. Epub 2017 Apr 18. PMID: 28342259

6. Entorhinal-CA3 Dual-Input Control of Spike Timing in the Hippocampus by Theta-Gamma Coupling. Fernández-Ruiz A, Oliva A, Nagy GA, **Maurer AP**, Berényi A, Buzsáki G. *Neuron*. 2017 Mar 8;93(5):1213-1226.e5. doi: 10.1016/j.neuron.2017.02.017. PMID:28279355

7. Network Patterns Associated with Navigation Behaviors Are Altered in Aged Nonhuman Primates. Engle JR, Machado CJ, Permenter MR, Vogt JA, **Maurer AP**, Bulleri AM, Barnes CA. *J Neurosci*. 2016 Nov 30;36(48):12217-12227. Epub 2016 Nov 30.

8. Medial prefrontal-perirhinal cortical communication is necessary for flexible response selection. Hernandez AR, Reasor JE, Truckenbrod LM, Lubke KN, Johnson SA, Bizon JL, **Maurer AP**, Burke SN. *Neurobiol Learn Mem*. 2017 Jan;137:36-47. doi: 10.1016/j.nlm.2016.10.012. Epub 2016 Nov 1. PMID: 27815215

PUBLICATIONS (OTHER):

Sara N. Burke, PhD

1. McQuail JA, Johnsn 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

2. **Burke SN** (in press). Award for Distinguished Scientific Early Career Contributions to Psychology: Sara N. Burke. *American Psychologist*.

PRESENTATIONS AT SCIENTIFIC MEETINGS:

Jennifer Bizon, PhD

Upcoming/Invited Talks

1. *"Neural mechanisms of executive function and decision making in aging"* Office of Scientific Director Seminar Series, National Institute on Aging, Baltimore, Maryland. November 2017.

2. *"Excitatory-Inhibitory Signaling Dynamics across the Lifespan: Implications for Cognitive Decline."* Cognitive Decline and Aging Course. Neuroscience School of Advanced Studies. Tuscany, Italy. September 2017.

3. *"Hippocampal and prefrontal cortical GABA(B) receptors and mnemonic decline in aging."* Spring Hippocampal Research Conference. Taormina, Italy. June 2017.

4. *"Using rodent models of prefrontal cortical-mediated cognitive decline in aging to identify drug targets in GABA and glutamate systems."* American Society of Pharmacology and Experimental Therapeutics. Chicago, Illinois. April 2017.

5. *"Using olfactory discrimination to understand mechanisms of age-related cognitive decline."* Neurobiology of Learning and Memory Conference. Park City, Utah, January 2017.

2016

6. *"Shifting Excitatory-inhibitory signaling and age-related decline of prefrontal-cortical dependent cognition"* Department of Physiology Seminar Series. University of Florida. Gainesville, Florida.

7. *"Glutamate signaling alterations contribute to age-associated decline in working memory."* Memory Mechanisms in Health and Disease conference. Tampa, Florida, December 2016.

2018

8. *"Neural mechanisms of age-associated alterations in cost-benefit decision making."* Winter Conference on Brain Research. Whistler, British Columbia. January 2018.

9. *"Effects of normal aging on spatial memory."* Irvine Learning and Memory Conference. Irvine, California. April 2018.

Poster Presentations

1. *Optogenetic inactivation of basolateral amygdala in young rats recapitulates aged rats' ability to delay gratification in an intertemporal choice task** C. M. Hernandez, iii[1,4], C. A. Orsini[2,4], C. Labiste[1], S. M. Singhal[3], S. N. Burke[1,4], C. J. Frazier[3], b. Setlow[2,4], **J. L. Bizon**[1,4]; Society for Neuroscience meeting, Washington DC *picked as hot topic by Society for Neuroscience and Third-place McKnight Brain Research Foundation Poster Award

2. *Brain aging is associated with regional and isoform-specific reductions to glutamic acid decarboxylase* J. M. Moats[1], J. A. Mcquail[2], M. M. Bruner[2], C. Banuelos[3], D. A. Scheuer[4], ***J. L. Bizon**[2]; 1Florida Intl. Univ., Miami, FL; Society for Neuroscience meeting, Washington DC

3. *Role of CA3 and dentate gyrus in the discrimination of perceptually similar objects depends on novelty of stimuli**S. A. Johnson, S. M. Turner, K. E. Fertal, l. A. Santacroce, **J. L. Bizon**, A. P. Maurer, S. N. Burke; Society for Neuroscience meeting, Washington DC

4. *Impact of age- and stress-related neuroendocrine dysfunction on working memory and gabaergic synaptic markers in prefrontal cortex**J. A. Mcquail[1], S. Ghay[1], M. M. Bruner[1], E. G. Krause[2], B. Setlow[3], D. A. Scheuer[4], **J. L. Bizon**[1]; Society for Neuroscience meeting, Washington DC

5. *Optogenetic inactivation reveals multiple distinct roles for BLA in regulating risky decision making**C. A. Orsini[1], C. M. Hernandez, iii[2], S. M. Singhal[3], K. B. Kelly[4], C. J. Frazier[5], **J. L. Bizon**[7], B. SETLOW[6]; Society for Neuroscience meeting, Washington DC

6. *Regulation of risky decision making by gonadal hormones**S. L. Blaes[1], C. A. Orsini[3], **J. L. Bizon**[4], B. Setlow[2] Society for Neuroscience meeting, Washington DC

7. *Untangling the cortical-hippocampal circuitry of spatial delay discounting**J.M. Mizell[1], D. K. Chetram[1], M. A. Kreher[1], H. Wasanwala[1], S. Garcia-sosa[1], S. A. Johnson[1], B. Setlow[2], **J. Bizon**[1], S. N. Burke[1], A. P. Maurer[1] Society for Neuroscience meeting, Washington DC

8. *Enhancing effects of cannabis smoke exposure on working memory performance* Barry Setlow, Shelby L. Blaes, Caitlin A. Orsini, Toneisha D. Stubbs, Shandera N. Ferguson, Sara C. Heshmati, Shannon C. Wall, Marcelo Febo, Adriaan W. Bruijnzeel, **Jennifer L. Bizon** American College of Neurospsychopharmacology Annual Meeting, 2017

9. *Impact of age- and stress-related neuroendocrine dysfunction on executive functions and GABAergic synaptic markers in the prefrontal cortex* Joseph A. McQuail, Sahil Ghay, Matthew M. Bruner, Eric G. Krause, Barry Setlow, Deborah A. Scheuer, **Jennifer L. Bizon** American College of Neurospsychopharmacology Annual Meeting, 2017

10. *Optogenetic manipulation of the basolateral amygdala during risky decision making in rats* C.A. Orsini, C.M. Hernandez, S. Singhal, K. B. Kelly, C.J. Frazier, **J.L. Bizon**, B. Setlow American College of Neurospsychopharmacology Annual Meeting, 2017

Sara N. Burke, PhD

Symposiums Organized

June 16, 2017 Spring Hippocampal Research Conference (International). The hippocampus and prospective processing. Speakers: Alison Preston (University of Texas at Austin, USA), Andrew Maurer (University of Florida, Gainesville, USA). Benjamin Dunn (Kavli Center for Neuroscience, Norway), Amy Griffin (University of Delaware, USA). **Role: Organizer and co-chair**

Jan 7, 2017 Park City Winter Conference on the Neurobiology of Learning and Memory (International). The Role of the Medial Temporal Lobe in Sensory Discrimination and the Relationship with Memory. Speakers: **Jennifer Bizon** (University of Florida), Andrew Maurer (University of Florida), Michael Yassa (UC Irvine), and Sarah Johnson (University of Florida). **Role: Organizer and chair.**

Invited Talks

Nov 28, 2017 Kavli Institute for Systems Neuroscience Symposium, Trondheim, Norway. "Working Towards a Systems-level Understanding of Cognitive Aging" **Invited - International**

Sept 1, 2017 Department of Psychological and Brain Sciences Colloquium, University of Iowa. "Working Towards a Systems-level Understanding of Cognitive Aging" **Invited**

April 6, 2017 Cognitive Aging Summit, Washington DC. "An animal model of cognitive aging: Do compensatory neural processes confer resilience?" **Invited**

Poster Presentations

1. Colon-Perez LM, Turner SM, **Burke SN**, Febo M (2017). Connectivity changes after cognitive training in young and aged rats. *Society for Neuroscience*, 47: Washington D.C.

2. Hernandez AR, Truckenbrod LM, Reasor JE, Fertal KE, Johnson SA, Clark BJ, Maurer AP, **Burke SN** (2017). Age-related changes in the perirhinal-hippocampal-prefrontal cortical circuit: evidence for neural compensation in aged rats. *Society for Neuroscience*, 47: Washington D.C.

3. Hernandez CM, Orsini CA, Labiste C, DInghal SM, **Burke SN**, Frazier CJ, Setlow B, Bizon JL (2017). Optogenetic inactivation of basolateral amygdala in young rats recapitulates aged rats' ability to delay gratification in an intertemporal choice task. *Society for Neuroscience*, 47: Washington D.C.

4. Kennedy J, Qin Y, Mizell JM, Elvira Martin C, Guenther DT, Herdegen C, **Burke SN**, Sheremet A, Maurer AP (2017). Spectral evolution of the medial entorhinal local-field potential across behavior. *Society for Neuroscience*, 47: Washington D.C.

5. Mizell JM, Chetram DK, Kreher MA, Wasanwala H, Garcia-Sosa S, Johnson SA, Setlow B, Bizon JL, **Burke SN**, Maurer AP (2017). Untangling the cortical-hippocampal circuitry of spatial delay discounting. *Society for Neuroscience*, 47: Washington D.C.

6. Johnson SA, Turner SM, Fertal KE, Santacroce LA, Bizon JL, Maurer AP, **Burke SN** (2017). Role of CA3 and dentate gyrus in the discrimination of perceptually similar objects depends on novelty of stimuli. *Society for Neuroscience*, 47: Washington D.C.

7. Kyle C, Smith AC, Gray DT, **Burke SN**, Barnes CA (2017). Temporal contiguity predicts reward association learning in bonnet macaques. *Society for Neuroscience*, 47: Washington D.C.

8. Malem-Shinitski N, Zhang Y, Gray DT, **Burke SN**, Smith A, Barnes CA (2017). A separable state-space model of learning across trials and days in an aging study in macaque monkeys. *Society for Neuroscience*, 47: Washington D.C.

9. Gray DT, Smith AC, **Burke SN**, Barnes CA (2017). The alpha-2 noradrenergic receptor agonist guanfacine impairs flexible attention in young and aged macaques. *Society for Neuroscience*, 47: Washington D.C.

Thomas C. Foster, PhD

Invited Talks

1. Cognitive Aging Summit III, Washington DC. On biomarkers, animal models, and senescence (5/5-7/17)

2. In search of the senescent synapse: Memories of an aging researcher. Bowman Gray School of Medicine, Winston-Salem, NC. (4/30/2017)

3. Oxidative stress, aging and neurodegeneration, 38th World Congress of the International Union of Physiological Sciences, Rio de Janeiro, Brazil

Poster Presentations

1. Elevated systemic expression of interleukin-6 modulates resting state functional connectivity in hippocampal and cortical areas. (2017) Febo, M., Colon-Perez, L.M., Barter, J.D., Yegula, B., Chakrabarty, P., Kumar, A., **Foster, T.C.** *Soc for Neurosci* 82.02

2. Influence of systemic inflammation on the transcriptional profile in the hippocampus. (2017) Barter, J.D., Rani., A., Kumar, A., **Foster, T.C.** *Soc for Neurosci* 82.03

3. Peripheral inflammation induces age-dependent attentional impairments in rats. (2017) Yegula, B., Eikenberrry, S., **Foster, T.C.** *Soc for Neurosci* 82.04

4. Patch-clamp study of the mechanism for NMDA receptor hypofunction in CA1 hippocampal pyramidal neurons during aging. (2017) Kumar, A., Thinschmidt, J.S., **Foster, T.C.** *Soc for Neurosci* 82.05

5. Circulating exosomal miRNA as a biomarker for age-related cognitive decline and decreased hippocampal volume. (2017) Rani, A., O'Shea, A., Ianov, L., Cohen, R., Woods, A.J., **Foster, T.C.** 128.06.

Andrew Maurer, PhD

1. Multiple posters at SfN. 2016.

2. Co-chair and presenter at the Spring Hippocampal Research Conference 12-16 June, 2017 in Taormina, Sicily. "Hippocampal-orbitofrontal contributions to dynamic inter-temporal choice"

PRESENTATIONS AT NON-SCIENTIFIC MEETINGS OR EVENTS:

Sara N. Burke, PhD

1. Oct 20, 2017 Cade Museum Public Talk, Gainesville, FL. "Is there a blueprint for successful aging? Lessons from centenarians."

AWARDS (OTHER):

Jennifer Bizon, PhD

1. University of Florida Term Professor (2017-2020)

2. College of Medicine Excellence in teaching award, 2016

Sara N. Burke, PhD

1. 2017 Exemplary Teaching Award, University of Florida College of Medicine
2. 2017 American Psychological Association Early Career Award for Distinguished Contribution in Cognitive and Behavioral Neuroscience

Thomas C. Foster, PhD

1. Distinguished Alumnus Award (Foster): In recognition of noteworthy service and achievement Wake Forest University Graduate School of Arts & Sciences Department of Physiology & Pharmacology.
2. University of Florida Research Foundation Professorship award (Foster). This award is awarded to tenured faculty members in at the University of Florida who have a distinguished current record of research.
3. Kenneth & Laura Berns Award for Excellence in Genetics (Ianov).
4. Recognition for excellence in teaching (Yegla). University of Florida Center for Precollegiate Education and Training.
5. Pilot and Exploratory Study (Yegla/Foster) from the University of Florida, Claude D. Pepper Older Americans Independence Center.
6. Frontiers' Research Topic "Neuroimaging approaches to the study of cognitive aging," (Febo/Foster) qualified for consideration for the First Annual Spotlight Award.

FACULTY BIOGRAPHICAL SKETCHES: See page 77

TRAINEES:

Jennifer Bizon, PhD

a. Post-doctoral
Dr. Joe McQuail
Dr. Caitlin Orsini (co-mentored with Dr. Barry Setlow)
Dr. Amanda Crider (co-mentored with Dr. Sara Burke)

b. Pre-doctoral
Caesar Hernandez
Shelby Blaes (co-mentored with Dr. Barry Setlow)

c. Other
IDS Neuroscience Undergraduate majors and University Scholars Program
Lauren Vetere (2017 graduate, now PhD student at Mt. Sinai School of Medicine)
Miranda Schwabe (2017 graduate, now PhD student at University of Wisconsin)
Oyku Barut (2018 graduate)
Ovgu Baut (2018 graduate)
Sahil Ghay (2018 graduate)

Sara N. Burke, PhD

a. Post-doctoral
Sarah A. Johnson, PhD
Amanda Crider (co-chair with Bizon)

b. **Pre-doctoral:**
Abbi R. Hernandez
Nicholas DiCola (co-chair with Maurer)

c. **Other:**
Keila Campus (University Scholar Recipient)
Brianna Moon (University Scholar Recipient)
Leah Truckenbrod (University Scholar Recipient)
Sean Turner (University Scholar Recipient, Honor's graduate)

Thomas C. Foster, PhD

a. **Post-doctoral**
Brittney Yelga, PhD

b. **Pre-doctoral**
(i) **Lara Ianov, PhD** (graduated 2017)

(ii) **Jolie Barter** (PhD student)

(iii) **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**
Currently talks are ongoing with those from MBRF sponsored institutions concerning possible blood/plasma biomarkers of cognitive function.

Currently talks are ongoing with a group at the University of Florida interested in sepsis and cognitive decline during aging.

A initial proposal to examine an NMDA receptor agonist (d-cycloserine) on age-related memory decline was submitted to the MBRF Cognitive Aging and Memory Intervention Core. After consulting with MBRF members across institutions this proposal was withdrawn.

b. **Update on existing clinical studies**
We completed and published a study examining exosomal miRNA in relation to cognitive aging in elderly (ages 60-89 years).

TECHNOLOGY TRANSFER: NA

BUDGET UPDATE: See page 61

Jennifer Bizon, PhD

Current and pending grant support

2R01 AG029421 5/1/14- 5/1/19 $1,500,000 total
"Neural mechanisms of age-related cognitive decline"
Role: Bizon, PI
National Institute on Aging

Ed and Ethel Moore AD Grant 2/1/17-2/1/19 $100,000 total
"Impact of perirhinal cortical tau pathology on pre-clinical cognitive decline"
Role: Bizon MPI (Burke MPI)
Florida Department of Health

R01 DA036534 3/15/15-3/31/20 $1,800,000 total ($325,000 to Bizon)
"Risk taking and cocaine use: interactions, mechanisms, and therapeutic targets"
Role: Bizon co-I (Setlow, PI)
National Institute on Drug Abuse

R01 AG049722 1/1/16-12/31/20 $1,800,000 total ($50,000 to Bizon)
Title: *"The contribution of declines in functional connectivity to cognitive aging"*
Role: Bizon co-I (Burke PI)
Agency: National Institute on Aging

R01MH109548 11/1/16-10/1/21 $1,800,000 total ($250,000 to Bizon)
Title *"Testing and forecasting hippocampal theta wave propagation in learning and memory"*
Role: Bizon co-I (Maurer PI)
Agency: National Institute on Metal Health

DARPA-TNT Award 1/1/17-1/1/19 $2,500,106 total ($397,096 to Bizon)
Title *"Cognitive Augmentation through Neuroplasticity"*
Role: Bizon Project 1.2 Lead (Otto PI)
Agency: DARPA

CAM-CTRP Pilot Award 1/1/17-1/1/19 $40,000.00 (direct)
Title *"GABABR antagonists as a treatment for age-related cognitive decline"*
Role: PI
Agency: Cognitive Aging and Memory Program, University of Florida

Private Foundation Grant $30,000.00 (direct)
Title *"Xtraordinary Joy, Inc. Fund for Rare Chromosomal Disorders Research"*
Role: PI
Agency: Xtraordinary Joy, Inc.

1 R21 AG058240-01 Pending, Scored in 8th percentile $400,000.00 (requested)
Title: *Interactions of Perirhinal Tau Pathology and Aging in Cognitive Dysfunction*
Role: Bizon PI (Burke MPI)
Agency: NIA

Current mentored support

F32AG051371 (Joseph A McQuail) $171,018.00 (direct)
"Molecular and physiological determinants of age-related working memory decline"
6/1/15-5/31/18
National Institute on Aging
Sponsor: Bizon

K99AD041493 (Caitlin A Orsini) $950,000.00 (direct)
"Neural circuits and mechanisms underlying maladaptive risk-taking following cocaine self-administration"
National Institute on Drug Abuse
Co-Sponsor: Bizon

K01AA025306 (Eric Porges)
"Cognitive and functional deficits associated with reduced cortical GABA in HIV-infected heavy drinkers"
National Institute on Alcohol Abuse
Co-Sponsor: Bizon

F31AG058455 (Abigail Hernandez) $71, 758.00
Metabolic mechanisms for treating cognitive aging
National Institute on Aging
Co-Sponsor: Bizon

K99 AG058786-01 Pending (Score = 20)
Hippocampal and dopaminergic mechanisms of novelty detection underlying cognitive resilience in aging
National Institute on Aging
Co-Sponsor: Bizon

Other trainee awards
Caesar Hernandez
- Research Scholars travel fellowship from the central chapter of SfN ($1000).
- Bryan Robinson Research Award ($1500) for his dissertation research using optogenetics to determine the role of BLA circuits in decision making.
- Mcknight Brain Research Poster Award, society for neuroscience meeting Washington DC

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

Andrew Maurer, PhD

R01 AG055544 01
AGE-ASSOCIATED CHANGES IN HIPPOCAMPAL CIRCUITS AND COGNITIVE FUNCTION
UNIVERSITY OF FLORIDA 2017 NIA NIA $393,673

5 R01 MH109548 02
TESTING AND FORECASTING HIPPOCAMPAL THETA WAVE PROPAGATION IN LEARNING AND MEMORY
UNIVERSITY OF FLORIDA 2017 NIMH NIMH $381,250

5 R21 DA039701 02
DEVELOPMENT OF A RAT MODEL OF CANNABIS SMOKE SELF ADMINISTRATION
SETLOW, BARRY et al.
UNIVERSITY OF FLORIDA 2016 NIDA NIDA $185,625

EDUCATIONAL PROGRAMS FOCUSING ON AGE RELATED MEMORY LOSS:

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

- Member of the planning committee for the Cognitive Aging Summit III. Cognitive Aging Summit III, Washington DC (5/5-7/17)
- Organizer for a session on Oxidative stress, aging and neurodegeneration, 38th World Congress of the International Union of Physiological Sciences, Rio de Janeiro, Brazil
- Organizer and chair for a symposium Redox Signaling and Pathophysiology, Winter Conference on Neural Plasticity, Curacao.
- Organizer for a symposium on Exosomes in therapeutic application and biomarkers of brain function, Winter Conference on Neural Plasticity, Curacao.

b. Public

- University of Florida Center for Precollegiate Education and Training (Dr Brittney Yegla).

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

Sara N. Burke, PhD

Revising 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

A paper was published examining mRNA in relation to an age-related decline in spatial episodic memory. This was part of the Epigenetic Core and involved the Universities of Florida, Arizona, and Alabama.

A paper was published examining miRNA from plasma of humans as a biomarker of cognitive function. This was part of a collaboration with CAM-CTRP.

Andrew Maurer, PhD

We have recently completed a study with Dr. Carol Barnes at the University of Arizona, which has been published in the *Journal of Neuroscience*.

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).

Thomas C. Foster, PhD

An ongoing collaboration with Karyn Esser, Christiaan Leeuwenburgh, and others from the Aging Institute at the University of Florida is examining a possible muscle-brain link, which contributes to age-related memory decline. The underlying hypothesis is that signals from muscle are transported through the blood to influence brain aging.

Andrew Maurer, PhD

As part of our recent NIA R01, we are collaborating with Dr. Kamran Diba at the University of Michigan, attempting to understanding 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 submission on the mechanisms of the ketogenic to improve metabolism and cognition in age animals. Target Date: February 5th 2018.
- Numerous manuscript submissions, most notably, several using novel measurements of functional connectivity in the context of cognitive aging.

Thomas C. Foster, PhD

- We will continue to examine the role of peripheral systemic inflammation in contributing to brain aging and cognitive decline.
- We will continue to examine possible blood biomarkers (cytokines, exosomes) and determine if these factors contribute to cognitive decline.

Andrew Maurer, PhD

- This is the start of my 2nd 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 initative.

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

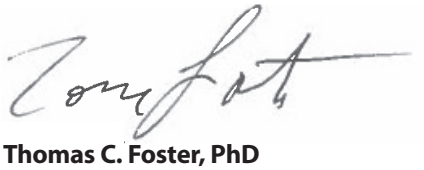
DO YOU RECOMMEND ANY MODIFICATION TO THE PURPOSE OR MANDATES IN THE GIFT AGREEMENT? No

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

2017 Progress Report

UF Evelyn F. & William L. McKnight Brain Institute
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December 04, 2017

Dear Trustees of the McKnight Brain Research Foundation:

We are pleased to provide a progress report for the Center for Cognitive Aging and Memory Clinical Translational Research Program (CAM-CTRP) for the year ending December 31, 2017. The current report summarizes progress that was reported at mid-year for trustee's site visit to University of Florida with a more detailed update for the remainder of the year. Overall, 2017 was an excellent year for us. We continued to make significant progress meeting our research objectives, and also had several new initiatives. These efforts were greatly facilitated by major changes that occurred in administrative structure, academic affiliation, and research operations. These changes are summarized first, followed by some highlights of research accomplishments and programmatic developments.

The faculty and staff of the CAM-CTRP are now fully settled in the Clinical and Health Psychology (CHP) department. We worked closely with Dr. Smith, the chair of CHP, to integrate our group in the department, including in the development of Cognitive and Emotion Neuroscience area. We completed the move of study staff to four offices across from faculty offices in CHP. We hired additional research staff to meet the needs of our projects, so that there is now a total of 14 study coordinators supporting our research. We also have seven undergraduate volunteers at UF who are helping with on projects and gaining research experience. The move to our research space in the McKnight Brain Institute (MBI) is complete and fully functional. The space is almost completely occupied each day with study participants from the various ongoing projects. The neuromodulation lab in this space is also fully functional and utilized for participants in the ACT and other projects. The phlebotomy laboratory is now operative as well, and a half time phlebotomist is now drawing and processing blood for our studies, with these samples stored locally in our new freezer space. This position is supported by external grant support (80%) We have also expanded recruitment efforts with implementation of sites in Orlando and Jacksonville from which larger samples can be recruited for our projects. Dr. Woods is leading this effort. Other core infrastructure is now in place as well, including the HiPerGator neuroimaging processing pipeline, which enables batch analysis of a large number of MRI images from multiple modalities.

Our faculty and students have been extremely successful over the past year. Both Drs. Woods and Porges were awarded K01 career development awards for projects that are now fully operational. The project being conducted by Dr. Woods dovetails with our ACT grant. Dr. Porges is conducting fMRI research examining cognitive set shifting in relationship to brain GABA levels measured by MRS. Dr. Porges has been able to transition to a tenure tract position in CHP. The plan is for Dr. Woods to go up for tenure this coming year. We also recruited two new post-doctoral fellows who joined our center in September; one working with Dr. Woods, another with me. Dr. Gullett who is mentored by me, has interests and expertise in diffusion tensor imaging, and is conducting neuroimaging analyses that will increase our manuscript output. Dr. Indahlastari, who is mentored by Dr. Woods, has expertise in transcranial direct current stimulation (tDCS) and biomedical engineering and is working alongside Dr. Woods in his Phase 2 and 3 cognitive training and tDCS trials in older adults. I have had two graduate students complete their doctoral dissertations on topics related to cognitive aging that employ neuroimaging (Garcia-semantic functions; Seider-visual functions). I have another graduate student completing his dissertation this spring. Dr. Woods has a neuroscience doctoral student.

Our affiliate faculty have been successful as well. Dr. Lamb was awarded a career development award from the Veterans Administration to conduct a study examining age associated changes in the brain's white matter connectivity. I am one of his mentors for this career development project. Two other post-doctoral fellows were also successful in obtaining K award support with mentoring support by me. Dr. Lisa Domenico, a post-doctoral fellow in nursing is conducting a fMRI study examining alcohol effects on cognitive attributional processing, and has now transitioned to faculty status in the College of Nursing. Dr. Ellen Terry received an award to study age associated differences in catastrophizing among African-American adults experiencing pain.

In addition to the career development awards described above, the CAM-CTRP faculty has been extremely productive and successful in obtaining extramural funding over the past year. Dr. Cohen received funding as

Co-I for a study of the cognitive effects of chronic marijuana use in the context of aging among adults with HIV (Cook, PI). We also received another U01 award to examine the effects of G-I dysfunction in HIV on functional and cognitive outcome in HIV. Dr. Woods is co-investigator on one R01 study and 2 R21 studies that were funded this year; one with Dr. Thomas Mareci (R01), another with Dr. Mingzhou Ding (R21) and with Dr. David Clark(R21). All three advance the field of neuromodulation, examining current flow in the brain and related topics that have bearing on the application of tDCS to clinical trials, investigating combined tDCS and complex walking training to enhance executive function and mobility in older adults, and using a novel form of alternative current neurostimulation to enhance working memory function. Dr. Williamson, an affiliate faculty member was successful in obtaining R21 funding to study transcranial vagal nerve stimulation to enhance cognitive function in older adults. He also received VA support for a study of this type of stimulation for treating sleep disturbances. He has a merit award to the VA under review focusing on tDCS in cognitive aging. There are several pending grants as well.

The ACT grant is actively collecting data and over the next year, we will have results from Phase 1. 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." and follow-up post-surgery assessments are underway. We are beginning to complete manuscripts based on analysis of the baseline data. The ARCH-2 grant from NIAAA to study HIV and alcohol consumption effects on the brains in the context of aging is funded and underway. We expanded recruitment for this 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. We have overcome many obstacles, and the study logistics are now flushed out. We are excited to examine results as they accumulate.

The McKnight Brain Research Foundation (MBRF) inter-institute initiatives continue to be on track with considerable progress made on all fronts. The MBAR study of successful cognitive aging in people over the age of 85 is also now fully active at the four McKnight Brain Institute sites, with approximately 35 participants assessed so far. We are planning on submitting an R01 grant proposal to NIA in the spring of 2018 with Dr. Alexander as PI, and the other site leaders as co-PIs. The McKnight Brain Research Foundation Cognitive Aging and Memory Intervention Core (MBRF-CAMIC) has also been very active with considerable effort by faculty from the four McKnight Brain Institutes directed at developing the core. A plan for the pilot project program was created and approval to move forward obtained from the MBRF trustees. Initially we obtained letters of intent to submit proposals from 12 investigators. These pre-proposals were reviewed by the core faculty of the MBRF-CAMIC. Full applications were then requested for seven of the proposals. We reached agreement across the four sites on external reviewers. Pilot proposals are in the process of undergoing external review. Based on these reviews, the core faculty will make recommendations to the MBRF trustees in January, 2018 regarding projects considered to be of high merit and worthy of consideration for funding.

In the context of all of this NIH- and MBRF-funded research, our faculty continues to publish a large number of manuscripts, as evident from the publications listed in the individual biosketches. 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 Program (CAM-CTRP)
Evelyn McKnight Chair for Clinical Translation in Cognitive Aging

Active Federal Funding

PI	Project Number	Project Title	NIH Inititute/Federal Department	FY	FY Total Cost
Cohen,Ronald A	R01DK099334	OBESITY AND TYPE-2 DIABETES: BARIATRIC SURGERY EFFECTS ON BRAIN FUNCTION	NIDDK	2017	$ 521,543
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	2017	$ 850,538
Woods,Adam J/ Cohen, Ronald A	1R01AG054077	AUGMENTING COGNITIVE TRAINING IN OLDER ADULTS - THE ACT GRANT	NIH	2017	$ 1,154,713
Woods,Adam J	1K01AG050707	NEUROMODULATION OF COGNITION IN OLDER ADULTS	NIA	2017	$ 122,704
Porges,Eric S Carter	K01AA025306	COGNITIVE AND FUNCTIONAL DEFICITS ASSOCIATED WITH REDUCED CORTICAL GABA IN HIV-INFECTED HEAVY DRINKERS	NIAAA	2017	$ 161,990
Lamb,Damon	HR0011-17-2-0019	BRAIN CHANGES UNDERLYING EMOTIONAL AND EXECUTIVE ALTERATIONS IN TBI	DOD	2017	$ 10,149
Cruz-Almieda, Yenisel	5K01AG048259	NEUROIMAGING AGE-RELATED CHANGES I PAIN MODULATION	NIA	2017	$ 118,742
Williamson, John B	R21AG054876	TREATMENT OF MILD COGNITIVE IMPAIRMENT WITH TRANSCUTANEOUS VAGAL NERVE STIMULATION	NIA	2017	$ 228,750
Williamson, John B	R56HL121175	BRAIN AND COGNITION EFFECTS OF CARDIO RESYNCHRONIZATION THERAPY IN HEART FAILURE	NHLBI	2015	$ 544,587

SUMMARY OF SCIENTIFIC ACHIEVEMENTS SINCE LAST REPORT:

Ronald A. Cohen, PhD

1. The ACT R01 grant from NIA of a multi-site MBI study to examine the augmenting effects of tDCS brain stimulation on cognitive training in the elderly (Cohen, Woods, Marskike, MPIs). This study was funded in 2016, but all IRB and DSMB approvals were finalized this year. The study is now underway with respect to recruitment and data collection.
2. The McKnight Brain Research Foundation Inter-Institutional neuroimaging and cognitive initiatives to creates a brain aging registry (MBAR) and establish normative databases for successful cognitive aging in people over 85 years is now fully operative. We have collected approximately 30 of the planned participants thus far. We are beginning preliminary analyses of the neuroimaging data.
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 (e.g., WISE study that examines bariatric surgery induced weight loss effects on the brain and cognition;
5. Publications and initiation of a pilot project to study chemotherapy effects for breast cancer in older women (CAM-CTRP-Nursing-Cancer Institute initiative)
6. K01 award to Dr. Woods from NIA (Cohen, Primary mentor)
7. K01 award to Dr. Porges NIAAA (Cohen, Primary mentor)
8. VA career development award to Dr. Damon Lamb to study white matter connectivity in aging.
9. K23 award to Dr. Lisa Demonico from the College of Nursing for FMRI study of alcohol effects on cognitive processing (Cohen, secondary mentor).
10. Multiple manuscripts related to current CAM-CTRP lines of research.
11. Now fully integrated into academic department in Clinical and Health Psychology.
12. Renovation of CAM laboratory in MBI completed. Studies are underway. Occupancy is near 100%.
13. Phlebotomy laboratory in MBI for CAM-CTRP clinical studies (and other MBI investigators) now staffed and functional with equipment for processing and storing blood.
14. CAM-CTRP has been recognized as an official Center of the University of Florida.

Yenisel Cruz-Almeida, PhD

We have successfully completed data collection on multiple projects and we have started data analysis as well as manuscript and grant preparations. We have a pending NIH R01 project submission (PI) and State of Florida project submission.

Damon Geoffrey Lamb, PhD

Continued to advance research program through successfully competing for NIH and VA funding (appx $1.7m in funding awarded during this reporting period for the execution of research over the next several years). This included several proposals to investigate safe, non-invasive forms of this stimulation in an aging human population have been funded by NIH and are under way.

Eric Porges, PhD

1. Receipt of K01 award from NIAAA/NIH to investigate the impact of heavy drinking, HIV and accelerated aging on cortical GABA and cognitive flexibility.

2. Publication of the age related changes in GABA concentrations measured in humans, GABA's role in cognitive function during aging and the impact of age related atrophy upon these findings. Published in Neuroimage and Biological Psychiatry: CNNI. These effects suggest that proton MRS may provide a clinically useful method for the assessment of normal and abnormal age-related cognitive changes and the associated physiological contributors.

John B. Williamson, PhD

Since the last report, I have been active in completing data collection on my VA funded CDA-2 (VA K award equivalent) designed to assess the impact of neurological contributions of mild traumatic brain injury to the development of emotional dysregulation in the continuum of Post Traumatic Stress Disorder. We have completed protocol. We have multi-modal, cognitive, neuroimaging and autonomic data in these patients. Both mild traumatic brain injury and post traumatic stress disorder are significant risk factors for accelerated aging and early cognitive decline in older adults. We have identified white matter damage in pathways that project from prefrontal cortex to the amygdala such that lower white matter integrity in these systems that is associated with the presentation of symptoms of post traumatic stress disorder. These results are currently being written up for publication. We have submitted two manuscripts from the dataset, one published, and another under review.

Following up on this mechanistic study, we have completed a pilot study examining the impact of vagal nerve stimulation on symptoms of post traumatic stress disorder in combat exposed Veterans with and without history of post traumatic stress disorder and mild traumatic brain injury. We published these data recently, the first published data showing modification of hyperarousal symptoms in PTSD with transcutaneous vagal nere stimulation.

We have submitted a Merit Review grant to the VA to conduct a larger scale clinical trial in this population using this tool. The first score on this proposal was good, but not below the funding line (impact score 217). The resubmission is currently in preparation, going out next month.

Relatedly, due to overlapping functional neuroanatomy and based on other pilot data from our lab, we have received NIH funding (R21) to evaluate the effects of tVNS on learning in patients with amnestic mild cognitive impairment. This is a center for Cognitive and Aging and Memory (CAM-CTRP) affiliated initiative and includes Drs. Cohen, DeKosky, Lamb, and Porges, among others. This study recently received IRB approval (9/01/2017 start date). We have piloted our protocol and are starting to recruit participants.

In a heart failure population, capitalizing on my interest in peripheral and central nervous system interactions in the support of cognitive and emotional behaviors, I started an NIH funded project (discontinuation date, August, 2018). This is an R56 supported feasibility study to demonstrate cognitive and brain health improvement mechanisms via cardiac resynchronization therapy (CRT). This project is designed to longitudinally assess brain, cognitive and cardiovascular changes associated with CRT using MRI and MRS. MRI safe devices have just recently come to market and thus, this is a timely and cutting edge study. We have enrolled 6 people and are currently actively recruiting at UF and at the VA. We have also added Mayo Jacksonville as a collaborator to increase recruiting effectiveness. This study involves CAM-CTRP members (Cohen, Porges, Lamb, Woods) and collaborators from Cardiology. We will submit a follow-up R01 in 2018.

I have three technological innovation disclosures that the University of Florida has exercised their rights on for further development. The first one of these has been submitted for full patent consideration and is currently pending. The other two are in preparation for provisional patent application. As these are pending, I cannot discuss their content.

I received funding through a competitive VA BRRC pilot mechanism on an intervention to modify sleep architecture in patients with PTSD with or without history of TBI. We have enrolled 4 Veterans in this study in the past month with a target enrollment of 20.

Refereed Articles/Book chapters

1. **Williamson, J. B.**, Lamb, D. G., Burtis, D. B., Haque, S., Zilli, E. M., Kesayan, T., . . . Heilman, K. M. (2017). Right hemispatial ipsilesional neglect with chronic right hemisphere strokes. *J Clin Exp Neuropsychol*, 1-10. doi:10.1080/13803395.2017.1347606

2. Lamb, D. G., Porges, E. C., Lewis, G. F., & **Williamson, J. B.** (2017). Non-invasive Vagal Nerve Stimulation Effects on Hyperarousal and Autonomic State in Patients with Posttraumatic Stress Disorder and History of Mild Traumatic Brain Injury: Preliminary Evidence. *Front Med* (Lausanne), 4, 124. doi:10.3389/fmed.2017.00124

3. Harris, A. D., Porges, E. C., Woods, A. J., Lamb, D. G., **Williamson, J. B.**, Cohen, R. A., & Edden, R. A. (2017). Impact of tissue correction strategy on GABA-edited MRS findings. *Neuroimage*, in press.

4. Woods, M., **Williamson, J. B.**, White, K. D., Maitland, C. G., & Heilman, K. M. (2017). Shifting Spatial Neglect With Repeated Line Bisections: Possible Role of Lateralized Attentional Fatigue. *Cogn Behav Neurol*, 30(1), 30-36. doi:10.1097/wnn.0000000000000118

5. Wang, C., Burtis, D. B., Ding, M., Mo, J., **Williamson, J. B.**, & Heilman, K. M. (2017). The effects of left and right monocular viewing on hemispheric activation. *J Clin Exp Neuropsychol*, 1-7. doi:10.1080/13803395.2017.1332169

6. Porges, E. C., Woods, A. J., Edden, R. A., Puts, N. A., Harris, A. D., Chen, H., **Williamson, J. B.**, Cohen, R. A. (2017). Frontal Gamma-Aminobutyric Acid Concentrations Are Associated With Cognitive Performance in Older Adults. *Biol Psychiatry Cogn Neurosci Neuroimaging*, 2(1), 38-44. doi:10.1016/j.bpsc.2016.06.004

7. **Williamson, J. B.** (2017). Post trauma vision syndrome *Encyclopedia of clinical neuropsychology*.

8. **Williamson, J. B.**, & Cohen, R. A. (2017). Arousal *Encyclopedia of clinical neuropsychology*.

9. Heilman, K. M., **Williamson, J. B.** Lamb, D. G. (2017). Vertical Neglect *Encyclopedia of clinical neuropsychology*.

Adam Joshua Woods, PhD

Since last report, I have acquired additional funding for my research on the use of transcranial direct current stimulation to combat 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) and a K01 performing a dose response companion study to my R01 (Stimulated Brain, n=80, $612K), I received funding through two R21s (1 PI, 1 Co-I) and an RF1 (Co-I). Each of these studies use non-invasive brain stimulation to better understand and combat cognitive aging in the human brain. Collectively, this body of work represents the CAM-CTRP's efforts to pioneer novel non-invasive interventions for combating cognitive aging in older adults. One of the new R21s uses tDCS combined with complex walking and executive function training to combat mobility loss and cognitive decline in older adults. The other R21 uses a form of alternating current electrical brain stimulation to facilitate working memory function by recording a person's unique theta EEG frequency and using stimulation to better synchronize working memory-related theta frequencies in the brain. The RF1 was awarded through the Brain Initiative led by the NIMH to pioneer a novel method for objectively measuring current flow in the brain from tDCS and use this tool to titrate dose for cognitive aging interventions.

PUBLICATIONS IN PEER REVIEWED JOURNALS:

Ronald A. Cohen, PhD

1. **Cohen RA**, Alexander GE. Using the Telephone Interview for Cognitive Status and Telephone Montreal Cognitive Assessment for Evaluating Vascular Cognitive Impairment: Promising Call or Put on Hold? *Stroke*. 2017 Nov;48(11):2919-2921. doi: 10.1161/STROKEAHA.117.018828.

2. Espeland MA, Lipska K, Miller ME, Rushing J, **Cohen RA**, Verghese J, McDermott MM, King AC, Strotmeyer ES, Blair SN, Pahor M, Reid K, Demons J, Kritchevsky SB; LIFE Study Investigators.. Effects of Physical Activity Intervention on Physical and Cognitive Function in Sedentary Adults With and Without Diabetes. *J Gerontol A Biol Sci Med Sci*. 2017 Jun 1;72(6):861-866. doi: 10.1093/gerona/glw179. **PubMed PMID: 27590629.**

3. Monnig MA, Kahler CW, Cioe PA, Monti PM, Mayer KH, Pantalone DW, **Cohen RA**, Ramratnam B. Markers of Microbial Translocation and Immune Activation Predict Cognitive Processing Speed in Heavy-Drinking Men Living with HIV. *Microorganisms*. 2017 Sep 21;5(4). pii: E64. doi: 10.3390/microorganisms5040064. **PubMed PMID: 28934108.**

4. Rochette AD, Spitznagel MB, Sweet LH, **Cohen RA**, Josephson R, Hughes J, Gunstad J. Gender Differences in Cognitive Test Performance in Adults With Heart Failure. *J Cardiovasc Nurs*. 2017 May/Jun;32(3):212-217. doi: 10.1097/JCN.0000000000000330. **PubMed PMID:**

5. Okafor CN, Kelso NE, Bryant V, Burrell LE 2nd, Míguez MJ, Gongvatana A, Tashima KT, de la Monte S, Cook RL, **Cohen RA**. Body mass index, inflammatory biomarkers and neurocognitive impairment in HIV-infected persons. *Psychol Health Med*. 2017 Mar;22(3):289-302. doi: 10.1080/13548506.2016.1199887. Epub 2016 Jun 20. **PubMed PMID: 27319430; PubMed Central PMCID: PMC5173436.**

6. Rosano C, Guralnik J, Pahor M, Glynn NW, Newman AB, Ibrahim TS, Erickson K, **Cohen R**, Shaaban CE, MacCloud RL, Aizenstein HJ. Hippocampal Response to a 24-Month Physical Activity Intervention in Sedentary Older Adults. *Am J Geriatr Psychiatry*. 2017 Mar;25(3):209-217. doi: 10.1016/j.jagp.2016.11.007. Epub 2016 Nov 15. **PubMed PMID: 27986412; PubMed Central PMCID: PMC5568026.**

7. 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. doi: 10.1016/j.bpsc.2016.06.004. **PubMed PMID: 28217759; PubMed Central PMCID: PMC5312683**.

8. Clark US, Sweet LH, Morgello S, Philip NS, **Cohen RA**. High early life stress and aberrant amygdala activity: risk factors for elevated neuropsychiatric symptoms in HIV+ adults. *Brain Imaging Behav*. 2017 Jun;11(3):649-665. doi: 10.1007/s11682-016-9542-5. **PubMed PMID: 27011015; PubMed Central PMCID: PMC5035553.**

9. Thompson PM, Andreassen OA, Arias-Vasquez A, Bearden CE, Boedhoe PS, Brouwer RM, Buckner RL, Buitelaar JK, Bulayeva KB, Cannon DM, **Cohen RA**, Conrod PJ, Dale AM, Deary IJ, Dennis EL, de Reus MA, Desrivieres S, Dima D, Donohoe G, Fisher SE, Fouche JP, Francks C, Frangou S, Franke B, Ganjgahi H, Garavan H, Glahn DC, Grabe HJ, Guadalupe T, Gutman BA, Hashimoto R, Hibar DP, Holland D, Hoogman M, Pol HE, Hosten N, Jahanshad N, Kelly S, Kochunov P, Kremen WS, Lee PH, Mackey S, Martin NG, Mazoyer B, McDonald C, Medland SE, Morey RA, Nichols TE, Paus T, Pausova Z, Schmaal L, Schumann G, Shen L, Sisodiya SM, Smit DJ, Smoller JW, Stein DJ, Stein JL, Toro R, Turner JA, van den Heuvel MP, van den Heuvel OL, van Erp TG, van Rooij D, Veltman DJ, Walter H, Wang Y, Wardlaw JM, Whelan CD, Wright MJ, Ye J; ENIGMA Consortium.. ENIGMA and the individual: Predicting factors that affect the brain in 35 countries worldwide. *Neuroimage*. 2017 Jan 15;145(Pt B):389-408. doi: 10.1016/j.neuroimage.2015.11.057. Epub 2015 Dec 4. **PubMed PMID: 26658930; PubMed Central PMCID: PMC4893347.**

10. Szymkowicz SM, Dotson VM, McLaren ME, De Wit L, O'Shea DM, Talty FT, O'Shea A, Porges EC, **Cohen RA**, Woods AJ. Precuneus abnormalities in middle-aged to older adults with depressive symptoms: An analysis of BDI-II symptom dimensions. *Psychiatry Res*. 2017 Oct 30;268:9-14. doi: 10.1016/j.pscychresns.2017.08.002. Epub 2017 Aug 15. **PubMed PMID: 28837829; PubMed Central PMCID: PMC5593781.**

11. Porges EC, Woods AJ, Lamb DG, Williamson JB, **Cohen RA**, Edden RAE, Harris AD. Impact of tissue correction strategy on GABA-edited MRS findings. *Neuroimage*. 2017 Nov 15;162:249-256. doi: 10.1016/j.neuroimage.2017.08.073. Epub 2017 Sep 5. **PubMed PMID: 28882635.**

12. 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 Oct 4;9:323. doi: 10.3389/fnagi.2017.00323. eCollection 2017. **PubMed PMID: 29046635; PubMed**

13. Cook RL, Zhou Z, Kelso-Chichetto NE, Janelle J, Morano JP, Somboonwit C, Carter W, Ibanez GE, Ennis N, Cook CL, **Cohen RA**, Brumback B, Bryant K. Alcohol consumption patterns and HIV viral suppression among persons receiving HIV care in Florida: an observational study. *Addict Sci Clin Pract*. 2017 Sep 27;12(1):22. doi: 10.1186/s13722-017-0090-0. **PubMed PMID: 28950912; PubMed Central PMCID: PMC5615807.**

14. Nissim N, O'Shea A, Bryant V, Porges E, **Cohen R**, Woods AJ. (2017). Frontal structural neural correlates of working memory performance in older adults. *Frontiers in Aging Neuroscience*, 8: 328.

15. Woods, AJ, **Cohen, RA**, Marsiske, M, Alexander, GE, Czaja, S, Wu, S. Augmenting cognitive training in older adults (The ACT Study): Design and Methods of a Phase III tDCS and cognitive training trial. *Contemporary Clinical Trials* (in press).

Yenisel Cruz-Almeida, PhD

1. **Cruz-Almeida Y**, Aguirre M, Sorenson H, Tighe P, Wallet SM, Riley JL 3rd. Age differences in salivary markers of inflammation in response to experimental pain: does venipuncture matter? *J Pain Res*. 2017 Oct 3;10:2365-2372. doi: 10.2147/JPR.S138460. eCollection 2017.

2. **Cruz-Almeida Y**, Rosso A, Marcum Z, Harris T, Newman AB, Nevitt M, Satterfield S, Yaffe K, Rosano C; Health ABC Study. Associations of Musculoskeletal Pain With Mobility in Older Adults: Potential Cerebral Mechanisms. *J Gerontol A Biol Sci Med Sci*. 2017 Sep 1;72(9):1270-1276. doi: 10.1093/gerona/glx084.

3. **Cruz-Almeida Y**, Cardoso J, Riley JL 3rd, Goodin B, King CD, Petrov M, Bartley EJ, Sibille KT, Glover TL, Herbert MS, Bulls HW, Addison A, Staud R, Redden D, Bradley LA, Fillingim RB. Physical performance and movement-evoked pain profiles in community-dwelling individuals at risk for knee osteoarthritis. *Exp Gerontol*. 2017 Nov;98:186-191. doi: 10.1016/j.exger.2017.08.026. Epub 2017 Aug 24.

4. Naugle KM, **Cruz-Almeida Y**, Fillingim RB, Riley JL 3rd. Loss of Temporal Inhibition of Nociceptive Information Is Associated With Aging and Bodily Pain. *J Pain*. 2017 Aug 26. pii: S1526-5900(17)30683-1. doi: 10.1016/j.jpain.2017.08.003. [Epub ahead of print]

5. Naugle KM, **Cruz-Almeida Y**, Fillingim RB, Staud R, Riley JL 3rd. Increased spatial dimensions of repetitive heat and cold stimuli in older women. *Pain*. 2017 May;158(5):973-979. doi: 10.1097/j.pain.0000000000000709.

6. Riley JL 3rd, **Cruz-Almeida Y**, Dasilva Ribeiro MC, Simon CB, Eckert NR, Aguirre M, Sorenson HL, Tighe PJ, Edwards RR, Wallet SM. Age Differences in the Time Course and Magnitude of Changes in Circulating Neuropeptides After Pain Evocation in Humans. *J Pain*. 2017 Sep;18(9):1078-1086. doi: 10.1016/j.jpain.2017.04.006. Epub 2017 Apr 29.

7. Eckert NR, Vierck CJ, Simon CB, **Cruz-Almeida Y**, Fillingim RB, Riley JL 3rd. Testing Assumptions in Human Pain Models: Psychophysical Differences Between First and Second Pain. *J Pain*. 2017 Mar;18(3):266-273. doi: 10.1016/j.jpain.2016.10.019. Epub 2016 Nov 22.

8. Eckert NR, Vierck CJ, Simon CB, Calderon S, **Cruz-Almeida Y**, Staud R, Fillingim RB, Riley JL 3rd. Methodological Considerations for the Temporal Summation of Second Pain. *J Pain*. 2017 Dec;18(12):1488-1495. doi: 10.1016/j.jpain.2017.07.009. Epub 2017 Aug 9.

9. Ho KWD, Wallace MR, Sibille KT, Bartley EJ, **Cruz-Almeida Y**, Glover TL, King CD, Goodin BR, Addison A, Edberg JC, Staud R, Bradley LA, Fillingim RB. Single Nucleotide Polymorphism in the COL11A2 Gene Associated with Heat Pain Sensitivity in Knee Osteoarthritis. *Mol Pain*. 2017 Jan-Dec;13:1744806917724259. doi: 10.1177/1744806917724259.

10. Sibille KT, King C, Garrett TJ, Glover TL, Zhang H, Chen H, Reddy D, Goodin BR, Sotolongo A, Petrov ME, **Cruz-Almeida Y**, Herbert M, Bartley EJ, Edberg JC, Staud R, Redden DT, Bradley LA, Fillingim RB. Omega-6: Omega-3 PUFA Ratio, Pain, Functioning, and Distress in Adults with Knee Pain. *Clin J Pain*. 2017 May 24. doi: 10.1097/AJP.0000000000000517. [Epub ahead of print]

11. Branco-de-Almeida LS, **Cruz-Almeida Y**, Gonzalez-Marrero Y, Huang H, Aukhil I, Harrison P, Wallet SM, Shaddox LM. Local and Plasma Biomarker Profiles in Localized Aggressive Periodontitis. *JDR Clin Trans Res*. 2017 Jul;2(3):258-268. doi: 10.1177/2380084417701898. Epub 2017 Apr 14.

12. Velsko IM, **Cruz-Almeida Y**, Huang H, Wallet SM, Shaddox LM. Cytokine response patterns to complex biofilms by mononuclear cells discriminate patient disease status and biofilm dysbiosis. *J Oral Microbiol*. 2017 Jun 12;9(1):1330645. doi: 10.1080/20002297.2017.1330645. eCollection 2017.

Damon Geoffrey Lamb, PhD

1. John B Williamson, **Damon G Lamb**, D Brandon Burtis, Salsabil Haque, Eduardo M Zilli, Tigran Kesayan, Michal Harciarek, Kenneth M Heilman. Right hemispatial ipsilesional neglect with chronic right hemisphere strokes. *Journal of Clinical and Experimental Neuropsychology*, 1-10, September 2017

2. **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 Historyof Mild Traumatic Brain Injury: Preliminary Evidence. *Frontiers in Medicine*, 4: 124, July 2017

3. Eric C Porges, Adam J Woods, Richard AE Edden, Nicolaas AJ Puts, Ashley D Harris, Huaihou Chen, Amanda M Garcia, Talia R Seider, **Damon G Lamb**, John B Williamson, Ronald A Cohen. Frontal gamma-aminobutyric acid concentrations are associated with cognitive performance in older adults. *Biological psychiatry: cognitive neuroscience and neuroimaging*, 2:1 38-44, January 2017

Eric Porges, PhD

1. Szymkowicz, S. M., Dotson, V. M., McLaren, M. E., De Wit, L., O'Shea, D. M., Talty, F. T., O'Shea, A., **Porges, E.C.**, Cohen, R.A. & Woods, A. J. (2017). Precuneus abnormalities in middle-aged to older adults with depressive symptoms: An analysis of BDI-II symptom dimensions. *Psychiatry Research: Neuroimaging*, 268, 9-14.

2. **Porges, E. C.**, Woods, A. J., Lamb, D. G., Williamson, J. B., Cohen, R. A., Edden, R. A., & Harris, A. D. (2017). Impact of tissue correction strategy on GABA-edited MRS findings. *NeuroImage*, 162, 249-256.

3. Nissim, N. R., O'Shea, A. M., Bryant, V., **Porges, E. C.**, Cohen, R., & Woods, A. J. (2017). Frontal structural neural correlates of working memory performance in older adults. *Frontiers in aging neuroscience*, 8, 328.

4. Lamb, D. G., **Porges, E. C.**, Lewis, G. F., & Williamson, J. B. (2017). 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.

5. **Porges, E. C.**, Woods, A. J., Edden, R. A., Puts, N. A., Harris, A. D., Chen, H., ... & Cohen, R. A. (2017). Frontal gamma-aminobutyric acid concentrations are associated with cognitive performance in older adults. *Biological psychiatry: cognitive neuroscience and neuroimaging*, 2(1), 38-44.

Adam Joshua Woods, PhD

1. Bikson M, Adair D, Paneri B, Datta A, Mourdoukoutas A, Fang XH, Wingeier B, Chao D, Alonso-Alonso M, Lee K, Knotkova H, **Woods AJ**, Hagedorn D, Jeffery D, Giordano J, Tyler WJ. Limited output transcranial electrical stimulation (LOTES-2017): Engineering principles, regulatory statutes, and industry standards for wellness, over-the-counter, or prescription devices with low risk. *Brain Stimulation*. Accepted October 2017. Impact Factor: 6.078

2. McLaren M, Nissim N, **Woods AJ**. The Effects of Medication Use in Transcranial Direct Current Stimulation. *Brain Stimulation*. Accepted October 2017. Impact Factor: 6.078

3. Rani A, O'Shea A, Ianov L, Cohen R, **Woods AJ**, Foster TC. miRNA in circulating microvesicles as biomarkers for age-related cognitive decline. *Frontiers in Aging Neuroscience*. Accepted September 2017. Impact Factor: 4.504

4. Harris A, Porges EC, **Woods AJ**, Lamb DG, Williamson JB, Cohen R, Edden RA. Impact of tissue correction strategy on GABA-Edited MRS findings. *Neuroimage*. Accepted August 2017. Impact Factor: 5.835

5. Szymkowicz SM, Dotson VM, McLaren M, De Witt L, O'Shea D, Talty FT, O'Shea A, Porges EC, Cohen RA, **Woods AJ**. Precuneus abnormalities in middle-aged to older adults with depressive symptoms: An analysis of BDI-II symptom dimensions. Psychiatry Research: *Neuroimaging*. Accepted August 2017. Impact Factor: 1.878

6. Mankowski R, Leeuwenbergh C, Manini T, **Woods AJ**, Anton SD. Effects of fermented papaya preparation (FPP) on safety outcomes in older adults – A short report of a placebo-controlled clinical trial. *Journal of Frailty & Aging*. Accepted August 2017. Impact Factor: pending

7. Bikson M, Grossman P, Zannou AL, Kronberg G, Truong D, Boggio P, Brunoni AR, Charvet L, Fregni F, Fritsch B, Gillick B, Hamilton RH, Hampstead BM, Kirton A, Knotkova H, Liebetanz D, Liu A, Loo C, Nitsche MA, Reis J, Richardson JD, Rotenberg A, Turkeltaub PE, **Woods AJ**. Response to Letter to the Editor: Safety of transcranial direct current stimulation: Evidence based update 2016, *Brain Stimulation*. Accepted July 2017. Impact Factor: 6.078

8. Fazeli P, **Woods AJ**, Pope CN, Vance D, Ball KK. The effect of transcranial direct current stimulation combined with cognitive training on cognitive functioning in older adults with HIV: a pilot study. *Applied Neuropsychology Adult*. Accepted July 2017. Impact Factor: 0.694

9. Ahn HC, **Woods AJ**, Kunik ME, Bhattacharjee A, Chen Z, Choi E, Fillingim R. Efficacy of Transcranial Direct Current Stimulation over Primary Motor Cortex (anode) and Contralateral Supraorbital area (cathode) on Clinical Pain Severity and Mobility Performance in Persons with Knee Osteoarthritis: An experimenter- and participant-blinded, Randomized, Sham-controlled Pilot Clinical Study. *Brain Stimulation*. Accepted May 2017. Impact Factor: 6.078

10. Porges, E.C., **Woods, AJ**, 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. Impact Factor: pending

11. Nissim N, O'Shea A, Bryant V, Porges E, Cohen R, **Woods AJ**. (2017). Frontal structural neural correlates of working memory performance in older adults. *Frontiers in Aging Neuroscience*, 8: 328. Impact Factor: 4.504

12. McLaren ME, Szymkowicz SM, O'Shea A., **Woods AJ**, Anton S, Dotson VM. (2017). Vertex-wise Examination of Symptom Dimensions of Subthreshold Depression and Brain Volumes. *Psychiatry Research*, 260: 70-75. Impact Factor: 2.528

13. Szynkowicz, S.M., McLaren, M.E., O'Shea, A., **Woods, AJ**, Anton, S., Dotson, V. (2017). Depressive Symptoms Modify Age Effects on Hippocampal Subfields. *Geriatrics and Gerontology International*, Accepted July 2016. Impact Factor: 2.351

PUBLICATIONS (OTHER):

Ronald A. Cohen, PhD

1. 20 Chapters in Encyclopedia of Clinical Neuropsychology (2017)

Eric Porges, PhD

1. Carter, C. S., Bartal, I. B. A., & **Porges, E. C.** (2017). 14 The Roots of Compassion: An Evolutionary and Neurobiological Perspective. *The Oxford Handbook of Compassion Science*, 173.
2. **Porges E.C.** Pre-Pulse Inhibition. *Encyclopedia of Clinical Neuropsychology*. 2017. In Press. New York, NY: Springer Science
3. **Porges E.C.** Attentional Blink. *Encyclopedia of Clinical Neuropsychology*. 2017. In Press. New York, NY: Springer Science
4. **Porges E.C.** Backwards Masking. *Encyclopedia of Clinical Neuropsychology*. 2017. In Press. New York, NY: Springer Science
5. **Porges E.C.** Priming. *Encyclopedia of Clinical Neuropsychology*. 2017. In Press. New York, NY: Springer Science
6. Lamb D.G.; **Porges E.C.** Flanker Task. *Encyclopedia of Clinical Neuropsychology*. 2017. In Press. New York, NY: Springer Science

PRESENTATIONS AT SCIENTIFIC MEETINGS:

Ronald A. Cohen, PhD

1. ARCH annual summer meeting: Brown University, Research Component 1 update
2. SHARC annual meeting: Miami, Florida
3. NIMH NeuroHIV meeting: Bethesda, Maryland

Damon Geoffrey Lamb, PhD

1. **D. G. Lamb**, J. B. Williamson, A. R. Walker, S. Datta, K. M. Heilman. *Attentional biases in vertical space with age.* Society for Neuroscience Annual Meeting, Washington DC, 2017
2. E. C. Porges, A. J. Woods, **D. G. Lamb**, J. B. Williamson, R. A. Cohen, R. A. E. Edden, A. D. Harris. *Tissue correction strategies impact GABA-edited MRS findings.* Society for Neuroscience Annual Meeting, Washington DC, 2017
3. Gunay C, Doloc-Mihu A, **Lamb DG**, Calabrese RL. *Synaptic strengths dominate phasing of motor neurons by a central pattern generator*, Computational Neuroscience Annual Meeting, Antwerp, Belgium, 2017
4. Williamson JB, **Lamb D**, Harciarek M, Heilman KM. *Lateralized limbic white matter integrity is associated with PTSD symptoms.* International Neuropsychological Society Annual Meeting, New Orleans, LA, 2017

Eric Porges, PhD

Talks:

1. *Cognitive and functional deficits associated with reduced cortical GABA in HIV-infected heavy drinkers.* Presented at "Southern HIV and Alcohol Research Consortium: Research Seminar." Gainesville, FL. 2017
2. *Cognitive and functional deficits associated with reduced cortical GABA in HIV-infected heavy drinkers.* Presented at "Brown University, Alcohol Research Center on HIV retreat." Providence, RI. 2017

3. *GABAergic contributions to cognitive aging.* Presented at the "McKnight Brain Research Foundation University of Florida Site Visit." Gainesville, FL. 2017

4. *Vagal nerve stimulation in PTSD.* Presented at "VA Brain-Heart Multisite Consortium Meeting." Columbia, SC. 2017

5. *GABA+ in frontal but not sensorimotor regions is associated with chronic pain intensity and disability in older adults.* Presented at "4th International Symposium on MRS of GABA." Leuven, Belgium. 2017

6. *Frontal GABA concentrations are associated with Cognitive Performance in Older Adults.* Presented at "University of Florida Department of Clinical and Health Psychology Faculty Research Series." Gainesville, FL. 2017

Abstracts:

1. Gulliford D.; Chen H.; **Porges E.C.**; Lin T.; Hayes R.; Fisher H.; Feifel D.; Cohen C.; Ebner N. *Sex-differential effects of intranasal oxytocin on resting-state anterior cingulate activity.* 2017. Organization for Human Brain Mapping, Vancover, CA.

2. Clark D.J.; Chatterjee S.; **Porges E.C.**; Fox E.J.; Balasubramanian C. *Sympathetic nervous system activity as an assessment of perceived challenge of walking after stroke.* 2017 Annual Conference of the American Congress of Rehabilitation Medicine. Atlanta, GA, October 26, 2017.

3. Wratchford C.; Chatterjee S.; **Porges E.C.**; Fox E.; Balasubramanian C.; Clark D. *Sympathetic nervous system activity as a physiological assessment of the perceived challenge of walking after stroke.* University of Florida College of Medicine Celebration of Research, February 27, 2017.

4. Chatterjee S.; Rose D.; **Porges E.C.**; Fox E.; Daly J.; Christou E.; Otzel D.; Butera K.; Clark D.J. *Quantifying the perceived challenge of walking after stroke by measuring sympathetic activation: a pilot study.* APTA Combined Sections Meeting, San Antonio, TX. 2017

5. Seider T.R.; **Porges E.C.**; Woods A.J.; Cohen R.A. *Age-Related Changes in Visual Discrimination.* Poster to be presented at the International Neuropsychological Society, New Orleans, LA. 2017.

6. Garcia A.M.; Seider T.R.; **Porges E.C.**; Cohen R.A. *The Relationship between DMN Activation and Intelligence in Older Adults. Poster presented to be presented at the International Neuropsychological Society*, New Orleans, LA. 2017.

7. McLaren M.E.; Dotson V.M.; Szymkowicz S.M.; O'Shea D.; O'Shea A.; **Porges E.C.**; Cohen R.A., Woods A.J. *Association of Subthreshold Depressive Symptoms with Cortical Thickness and Surface Area of the Insula.* Poster presented to be presented at the International Neuropsychological Society, New Orleans, LA. 2017.

John B. Williamson, PhD

1. Invited speaker, VA workshop – 2017
   Maladaptive features of chronic stress associated with PTSD and accelerated aging
   VAMC Brain-Heart Consortium
   South Carolina

2. Invited speaker, Myotonic Dystrophy Foundation – 2017
   Social cognition: Evolving ideas in myotonic dystrophy

3. Guest Lecturer, Neurodegenerative Research: From Bench-Bedside – 2017
   Graduate medical class, University of Florida

4. Lecturer and faculty – 2017
   Chronic PTSD after TBI, autonomic factors
   Florida Society of Neurology Annual Conference, CE course

5. Invited speaker, neuropsychology series – 2017
   TBI and potential contributions to PTSD
   Association of Neuropsychology Students, University of Florida

Adam Joshua Woods, PhD

1. **Woods AJ**. *Lecture.* Augmenting Cognitive Training in Older Adults: a Phase III tDCS trial. New Mexico Clinical Neurostimulation Meeting 2017. Albuquerque, NM, USA, October 5, 2017.
2. **Woods AJ**. *Symposium.* Pain and tDCS: Clinical trials. American Pain Society, Pittsburgh, PA, USA, May 19, 2017.
3. **Woods AJ**. *Lecture.* Successful cognitive aging. Penney Farms Annual Geriatric Medicine Symposium. Lunch Keynote Lecture. Penney Farms, FL, USA, April 21, 2017.
4. **Woods AJ**. *Lecture.* Clinical and research applications of transcranial direct current stimulation. Department of Clinical and Health Psychology ANST Brown Bag. University of Florida, Gainesville, FL, USA, March 24, 2017.
5. **Woods AJ**. *Lecture.* Research uses of tDCS. International Brain Stimulation, Barcelona, Spain, March 9, 2017.
6. **Woods AJ**. *Symposium.* Combating cognitive aging and dementia with transcranial direct current stimulation (tDCS). International Neuropsychological Society. New Orleans, LA, USA, February 2, 2017.
7. **Woods AJ**. *Symposium.* Is Neuromodulation Better Than Drugs? Prospects for tDCS in Age-related Cognitive Decline. NYC Neuromodulation 2017. New York, NY, USA, January 14, 2017.
8. **Woods AJ**. *Lecture.* Practical Demo: Modern tDCS/tACS Methodology. NYC Neuromodulation 2017. New York, NY. January 13, 2017.

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

AWARDS (OTHER):

Ronald A. Cohen, PhD

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 underling 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 vasculardysfunction, 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
ENIGMA Center for Worldwide Medicine, Imaging & Genomics $180,000
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
Augmenting Cognitive Training in Older Adults – The ACT Grant $21,538
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
Neuromodulation of Cognition in Older Adults $0
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

Overlap
None

Yenisel Cruz-Almeida, PhD

1. Faculty Enhancement Opportunity Fund ($15,000)

2. Mayday METER Initiative (co-PI) ($35,000)

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 imagining (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 resychronization 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. VA I01 Merit Review $1,100,000 2018-2022
   Efficacy of tVNS in reducing symptoms of PTSD with or without history of mild TBI
   Status: Follow-up to CDA-2 and BRRC Pilot
   Impact score = 217 (28th percentile, 1st submission)
   PI: Williamson
   Resubmission: December, 2017

2. NIH R01 ~$3,000,000 2019-2023
   Brain and cognition effects of cardiac resynchronization therapy in heart failure
   Status: Planned multi-site follow-up to currently funded R56HL127175
   PI: Williamson
   Submission: Early to mid-2018

3. 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)
   PI: Williamson
   Submission: Late 2018

Adam Joshua Woods, PhD

1. NIMH R21MH112206 (Woods/Ding, MPIs)
   National Institutes of Health
   $395,034
   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: PI

2. NIMH RF1MH114290-01 (Sadlier; PI) 07/19/17-07/18/21
   National Institutes of Health
   $2,046,092
   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

3. NIA R21AG053736-01A1 (Clark; PI) 07/01/17-06/31/19
   National Institutes of Health
   $189,233
   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

FACULTY BIOGRAPHICAL SKETCHES: See page 77

TRAINEES

Ronald A. Cohen, PhD

a. Post-doctoral

1. Mollie Monnig, PhD (Brown Univ.)
2. Joseph Gullett, PhD
3. Ellen Terry, PhD

b. Pre-doctoral

1. Amanda Garcia, PhD
2. Talia Seider, MS
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

Eric Porges, PhD

a. Post-doctoral
1. Joseph M. Gullett, PhD

b. Pre-doctoral
1. Vaughn Bryant, MA

c. Other
1. Sara Sosa-Garcia (undergraduate)

John B. Williamson, PhD

a. Post-doctoral
1. Joe Gullet, PhD – 2017-present. Neuropsychology.

b. Pre-doctoral
1. Vaughn Bryant, MS – Dissertation committee 2017-present. Clinical neuropsychology.
2. Amy Tran – undergraduate. 2017-present. Neuroscience, med student trajectory.
3. Ryan Pinosky – undergraduate. 2017-present. Biology, med student trajectory.
4. Zared Schwartz – undergraduate. 2013-present. Biology, grad student trajectory.

c. Other
1. Aaron Colverson, BA – Thesis committee 2015-present. Ethnomusicology.

Adam Joshua Woods, PhD

a. Post-doctoral
1. Aprinda Indahlastari, PhD

b. Pre-doctoral
1. Molly McLaren, MS
2. Nicole Nissim, MS

c. Other
1. Kathleen Frost (undergrad)
2. Cindy Hernandez (undergrad)
3. Klea Agollari (undergrad)
4. Sarah Lazzaro (SNIPs Summer 2017 Intern)

CLINICAL/TRANSLATIONAL PROGRAMS

Ronald A. Cohen, PhD

a. New programs:

1. MUSE: Marijuana effects in HIV and aging

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 underway
6. HIV-alcohol-aging studies continuing to recruit. Miami added as a site for SHARC and ARCH. Manuscripts have been published and new ones in preparation.
7. Study of bariatric surgery effects on brain function making excellent progress. We have over 110 participants. Manuscripts based on baseline data being prepared.
8. Heart failure project to examine effects of increasing cardiac output on cerebral perfusion and brain function in older adults underway.
9. Studies linked to all career development awards initiated.

Eric Porges, PhD

a. New programs:

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 imagining (fMRI & MRI).
   Role: PI
   - **IRB approval received & recruitment initiated, first subject anticipated Jan.2017**
2. 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**
3. Brain Rehabilitation Research Center Pilot, VA Williamson, John (PI) 06/01/17-5/31/18
   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
   - **IRB approval received & recruitment initiated, first subject anticipated Dec.2017**

4. 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
   - **IRB approval received & recruitment initiated, first subject anticipated Dec.2017**

b. Update on existing clinical studies:

1. R56HL127175, NIH/NHLBI Williamson, John (PI) 09/08/15-08/31/16 (currently in no cost extension)
   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
   - **Data collection ongoing, recent FDA approval of 3tesla safe cardiac resynchronization device has facilitated the movement of the protocol from 1.5 tesla to 3 tesla scanner.**

John B. Williamson, PhD

a. New programs:

At the BRRC, VA Center of Excellence, we have started a TBI registry program. It is IRB approved and recruits patients with history of mild, moderate and severe TBI and also screens for common comorbidities including post traumatic stress disorder.

We have submitted an Engineering Research Center application through the NSF, Center for Autonomic Neural Engineering. I am co-lead on a testbed we designed to gain control of specific hypothalamic nuclei to modify eating behavior. This is a fully translational research program design, going from rats, to mini-pigs using methodologies that are adaptable to human populations.

b. Update on existing clinical studies

On my VA funded CDA-2 award, we have enrolled 82 participants across four groups including mild TBI and PTSD, mild TBI, PTSD, and health combat exposed controls. We have submitted one manuscript from this dataset that is currently pending and we have another in preparation. Further, we have used pilot data from this and a BRRC funded pilot on 22 veterans using electroceutical methods to modify emotional experience in PTSD to apply for additional VA funding through the Merit Review mechanism (pending).

Our heart failure program is now IRB approved (NIH R56 funding) and we are actively recruiting and enrolling participants in the protocol.

Adam Joshua Woods, PhD

a. New programs

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 the first 3 months of startup and will begin enrolling participants in December.

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.

Stimulating Theta Oscillations to Enhance Working Memory

This project is an 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

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.

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-CTRP 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. 15 participants have been recruited and randomized in the study over the past 6 months.

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

Williamson J.B.; Lamb D.G.; **Porges E.C.** *System and method for monitoring and controlling nervous system behavior using autonomic features.* U.S. Patent Application PCT/US15/535,965, filed June 2017. Patent Pending.

3 other patents disclosed to University of FL that they have exercised their right to support for submission to Patent Office (in progress)

John B. Williamson, PhD

b. Revenue generated from technology

My colleagues and I have disclosed three technological advancements to the University of Florida technology transfer office. We (Drs. Porges, Lamb and I) have one that has been submitted for a full patent that is pending. We have another one that has been optioned by UF and is in the process of preparation by patent attorneys for a provisional patent application. We (Drs. Porges, Lamb, Woods and I) have a third one that has been optioned by UF and is in the process of preparation by patent attorneys for a provisional patent application.

BUDGET UPDATE: See page 61

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 are 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.

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)

John B. Williamson, PhD

tVNS and cognitive training modification of cognitive performance in healthy older people (pending McKnight application, collaboration pending).

Adam Joshua Woods, PhD

MBRF Cognitive Aging and Memory Intervention Core – The CAMI Core solicited LOIs for applications to the CAMI Core Pilot Project RFA. 3 submissions were received from 8 invited applications. These applications are currently undergoing external review for informed review by the 5 CAMI Core committee members for further consideration.

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

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)

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.

Eric Porges, PhD

1. Multisite study with Dept. of Radiology at Johns Hopkins University to establish site to site variation in GABA MRS. The results of this collaboration will facilitate use of this measure as a possible clinical tool/biomarker.

We have entered into a collaborative relationship with Nexeon to deploy their prototype tVNS device in our research. This portable device may allow for at home stimulation facilitating clinical trials and applications.

John B. Williamson, PhD

1. Alzheimer's Disease Research center.
2. Brain Rehabilitation Research Center, TBI and PTSD programs, cognitive and emotion initiatives.
3. Nexeon Medsystems Inc. Transcutaneous vagal nerve stimulation device and application development

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, and Brown University

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. With respect to the above goal, establishing an inter-MBI clinical translational investigation
4. Longitudinal studies of the MBAR cohort
5. Obtain R01 funding for current heart failure research
6. Apply for funding to conduct neuroimaging studies of chemotherapy and cancer effects on brain function in women with breast cancer
7. Facilitate current work on pain effects in cognitive and brain aging in collaboration with Dr. Cruz and her collaborators
8. Collaborate with other CAM investigators on their lines of research, including tDCS and vagal nerve stimulation methods

Yenisel Cruz-Almeida, PhD

Currently preparing multiple manuscripts for peer review journal submissions and preparing 2 NIH R01 submissions as PI, 1 U01 submission as Co-I and 1 NSF submission as Co-PI.

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.'

Eric Porges, PhD

My near term plans will include 3 primary 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.
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) to be resubmitted this fall (initial score 15). 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.

John B. Williamson, PhD

Follow up grants to my VA funded work on application of our mechanistic results in mild TBI and PTSD are pending.

I have pending initiatives using nerve stimulation to enhance cognitive performance. A DARPA submission that my team collaborated on earned partial funding (for the animal component) from which we will get critical data on mechanism of cognitive enhancement with this technology. We have preliminary data in humans that we have used for a pending R01 submission to enhance cognitive performance in people at risk for Alzheimer's disease.

A follow up to our R56 funded heart failure initiative will be submitted as soon as pilot data are sufficient from the current recruitment efforts.

Adam Joshua Woods, PhD

Dr. Woods recently submitting an MPI 4 year clinical trial to the DOD investigating combined cognitive training and tDCS as an intervention for traumatic brain injury in younger and older adults. In addition, Dr. Woods is also currently preparing a multisite Phase III tDCS trial investigating efficacy of tDCS for treatment of chronic pain from knee osteoarthritis in adults 65-89. Our pilot data demonstrates a Cohen's d effect size improvement in clinical pain severity after 5 days of active tDCS treatment vs. sham tDCS. This grant will be in an R01 format submitted to NIA. In addition, Dr. Woods has a planned February submission of a two-site R01 Phase II trial leveraging the ACT intervention in patients with mild cognitive impairment and mild Alzheimer's disease to perform at home cognitive training and tDCS interventions.

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

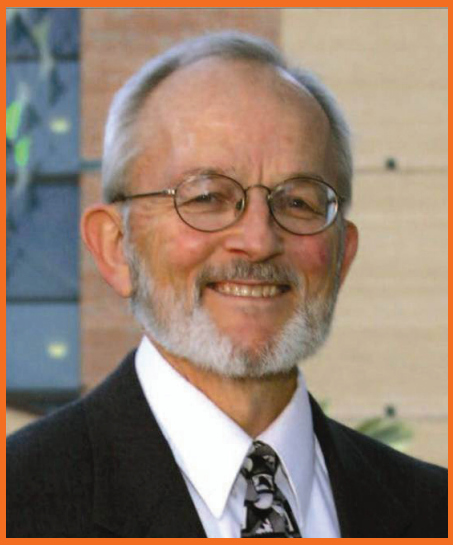
DID ALL ACTIVITIES DURING THE REPORT PERIOD FURTHER THE PURPOSE? Yes

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

UF UNIVERSITY of FLORIDA

College of Medicine
Department of Neuroscience
McKnight Brain Institute

1149 Newell Drive
Room L1-100
PO Box 100244
Gainesville, FL 32611-0244
352-627-9200 Tel
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November 9, 2017

Dear McKnight Brain Research Foundation Trustees,

On March 13, 2017 the 5th Annual William G. Luttge Lectureship in Neuroscience was held with Dr. James L. McGaugh as the lectureship speaker. Dr. McGaugh's lecture titled "Making Lasting Memories" was delivered to a full audience in the DeWeese Auditorium at the McKnight Brain Institute. Dr. McGaugh is an American neurobiologist working in the field of learning and memory, and is currently a Research Professor in the Department of Neurobiology and Behavior at the University of California, Irvine.

Dr. McGaugh received his PhD in Physiological Psychology from the University of California, Berkeley. He is founder of the University of California Irvine's Center for the Neurobiology of Learning and Memory and is recognized internationally for his pioneering studies of drug and stress-hormone influences on memory. Dr. McGaugh is the former President of the Association for Psychological Science and he has been recognized with an impressive number of awards and distinctions. Some of these honors include the Distinguished Scientific Contribution award of the American Psychological Association, the Association for Psychological Sciences' William James Fellow Award, the American Philosophical Society's Karl Lashley Prize in Neuroscience, and the Grawemeyer Award for Psychology, an award given for an "outstanding idea" that influenced the field of psychology. Dr. McGaugh has published more than 550 articles and book chapters on the link between emotion, stress hormones and memory.

Members of the Luttge Lectureship Committee are:

- Todd E. Golde, MD, PhD, Executive Director of the Evelyn F. and William L. McKnight Brain Institute at UF, and Professor of the Department of Neuroscience
- 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

The committee is now organizing the 6th Annual William G. Luttge Lectureship which will be held on Friday, March 16, 2018 with Dr. Michela Gallagher as speaker. The lectureship will be held at the conclusion of National Brain Awareness Week. Dr. Gallagher is the Krieger-Eisenhower Professor of Psychological and Brain Sciences & Neuroscience at Johns Hopkins University. Her laboratory is interested in neural systems that serve a role in memory and attention.

Sincerely,

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

Program Financials

Our new 3T MRI being delivered!

Age-related Memory Loss Program

Financial Summary
January 1 to December 31, 2017

Foundation Spendable Account		Amount	
Endowment income transferred in:			
Mar 31, 2017	$ 260,322		
Jun 30,2017	260,322		
Sept 30, 2017	260,322		
Dec 31, 2017	260,322		
Total endowment income transferred in		1,041,290	
Additional funds from MBRF:	-		
Transferred to UF Peoplesoft spendable accounts		1,041,290	(a)
Net change in foundation spendable account		-	
Beginning balance, Jan. 1, 2017		260,322	
Ending balance, Dec. 31, 2017		**$ 260,322**	

UF PeopleSoft Accounts		Amount	
Received from foundation spendable account		1,041,290	(a)
Residual funds from project support		25,424	
Total funds available		1,066,714	
Transferred out:			
Dr. Maurer startup and project support	141,000		
Dr. Bizon project support	36,411		
Dr. Burke project support	53,361		
CAM-CTRP transfer	781,762		
Total transferred out		1,012,534	
Expenditures:			
ARML faculty salaries	180,830		
Travel and other	1,505		
Epigenomics Core	(3,089)		
Total expenditures		179,245	
Total transfers out and expenditures		1,191,779	
Net change in UF Peoplesoft accounts		(125,065)	
Beginning balance, Jan. 1, 2017		770,978	
Ending balance, Dec. 31, 2017		**$ 645,913**	
Due to CAM-CTRP		130,161	(b)
Total funds available to ARML, Dec. 31, 2017		**$ 776,074**	

(a) Transfers from foundation spendable account to Peoplesoft account in 2017.

(b) Accumulation of the CAM-CTRP portion of the endowment interest income (50%), per the 2009 Gift Agreement Amendment. Scheduled to be transferred in Jan. 2018.

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

Financial Summary
January 1 to December 31, 2017

Foundation Spendable Account			Amount	
Endowment income transferred in:				
March 31, 2017	$	34,953		
June 30,2017		34,953		
Sept 30, 2017		34,953		
Dec 31, 2017		34,953		
Total endowment income transferred in			139,814	
Transferred to UF Peoplesoft spendable accounts			139,814	(a)
Net change in foundation spendable account			-	
Beginning balance, January 1, 2017			34,953	
Ending balance, Dec. 31, 2017			**$ 34,953**	

UF PeopleSoft Accounts			Amount	
Received from foundation spendable account			$ 139,814	(a)
Transfers and Expenditures:				
Transfers		20,000	(b)	
Faculty and research staff salaries		46,746		
Research equipment, supplies, and services		65,659		
Travel and other		15,228		
Total transfers and expenditures			147,632	
Net change in UF Peoplesoft accounts			(7,818)	
Beginning balance, January 1, 2017			550,012	
Ending balance, Dec. 31, 2017			**$ 542,194**	
Total funds avail. to McKnight ARML Chair, Dec. 31, 2017			**$ 577,147**	

(a) Transfers from foundation spendable account to Peoplesoft account in 2017.

b) Support for imaging services

Cognitive Aging & Memory
Clinical Translational Research Program

Financial Summary
January 1 to December 31, 2017

UF PeopleSoft Accounts			Amount	
Received from McKnight Brain Research Grant		$	781,762	
Program expenditures and commitments:				
Faculty, Research Staff & Staff Earnings	298,021			
Graduate Assistant & Student Assistant Earnings	46,743			
Project Support	32,648			
Research equipment, supplies, and services	68,037			
Tuition Waivers	14,135			
Publications	4,233			
Travel and other	1,530			
Total program expenditures and commitments			465,347	
Net change in UF Peoplesoft accounts			316,415	
Beginning balance, Jan. 1, 2016			619,513	
Ending balance, Dec. 31, 2017		**$**	**935,928**	
Due from McKnight Brain Research Grant			130,161	[a]
Total funds available to CAM-CTRP, Dec. 31, 2017		**$**	**1,066,090**	

[a] Accumulation of the CAM-CTRP portion of the endowment interest income (50%), per the 2009 Gift Agreement Amendment. Scheduled to be transferred in Jan. 2018.

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

Financial Summary
July 1 to December 31, 2017

Foundation Spendable Account		**Amount**	
Endowment income transferred in:			
March 31, 2017	$ 34,938		
June 30,2017	34,938		
Sept 30, 2017	34,938		
Dec 31, 2017	34,938		
Total endowment income transferred in		139,754	
Transferred to UF Peoplesoft spendable accounts		139,754	[a]
Net change in foundation spendable account		0	
Beginning balance, January 1, 2017		34,938	
Ending balance, Dec. 31, 2017		**$ 34,938**	

UF PeopleSoft Accounts		**Amount**	
Received from foundation spendable account		$ 139,754	[a]
Expenditures:			
Faculty and research staff salaries	162,813		
Research equipment, supplies, and services	-		
Travel and other	-		
Total expenditures		162,813	
Net change in UF Peoplesoft accounts		(23,059)	
Beginning balance, January 1, 2017		84,261	
Ending balance, Dec. 31, 2017		**$ 61,202**	
Total funds avail. to McKnight CAM Chair, Dec. 31, 2017		**$ 96,141**	

[a] Transfers from foundation spendable account to Peoplesoft account in 2017.

Dr. William G. Luttge
Lectureship in Neuroscience

Financial Summary
January 1 to December 31, 2017

Endowment account balance, Dec. 31, 2017	**$**	**272,084**

Spendable account activity		**Amount**
Endowment income transfers, 4 quarters ending Dec. 31, 2017	$	9,628
Less UF Foundation gift overhead fees		2
Total funds available		9,626
Expenses for March 2017 lectureship		6,099
Net change in spendable funds		3,527
Beginning balance, January 1, 2017		63,955
Ending balance, December 31, 2017	**$**	**67,482**

McKnight Brain Research Grant Fund Report

with related accounts
Balances through December 31, 2017

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
	$ 29,426,338	2018	$ 520,645	$ (520,645)		$ 260,322
Life-to-date Totals			**$ 16,510,366**	**$ (17,152,435)**	**$ 902,392**	

CAM-CTRP		Fiscal Year Ending	Transferred from F008058 (1/2 of MBRF Grant Income)	Total Expenses / Net Transfers	Additional Investment Revenue[2]	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-CTRP	Actual transfers to CAM-CTRP	Still due to CAM-CTRP
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	$ 520,645	$ (260,322)	$ 781,762	$ 130,161
	Life-to-date Totals		**$ 8,783,186**	**$ (6,025,810)**	**$ 5,895,522**	

[1]The McKnight Brain Research Grant had a spendable account balance of $332,192 as of Dec. 31, 2015. As of July 1, 2014, the UF Foundation changed its practice for transfering spendable funds to UF Peoplesoft accounts. Now all interest earned from the endowment transfers to the MBI Peoplesoft account and MBI then transfers half to the CAM-CTRP.

[2]Distributions 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.

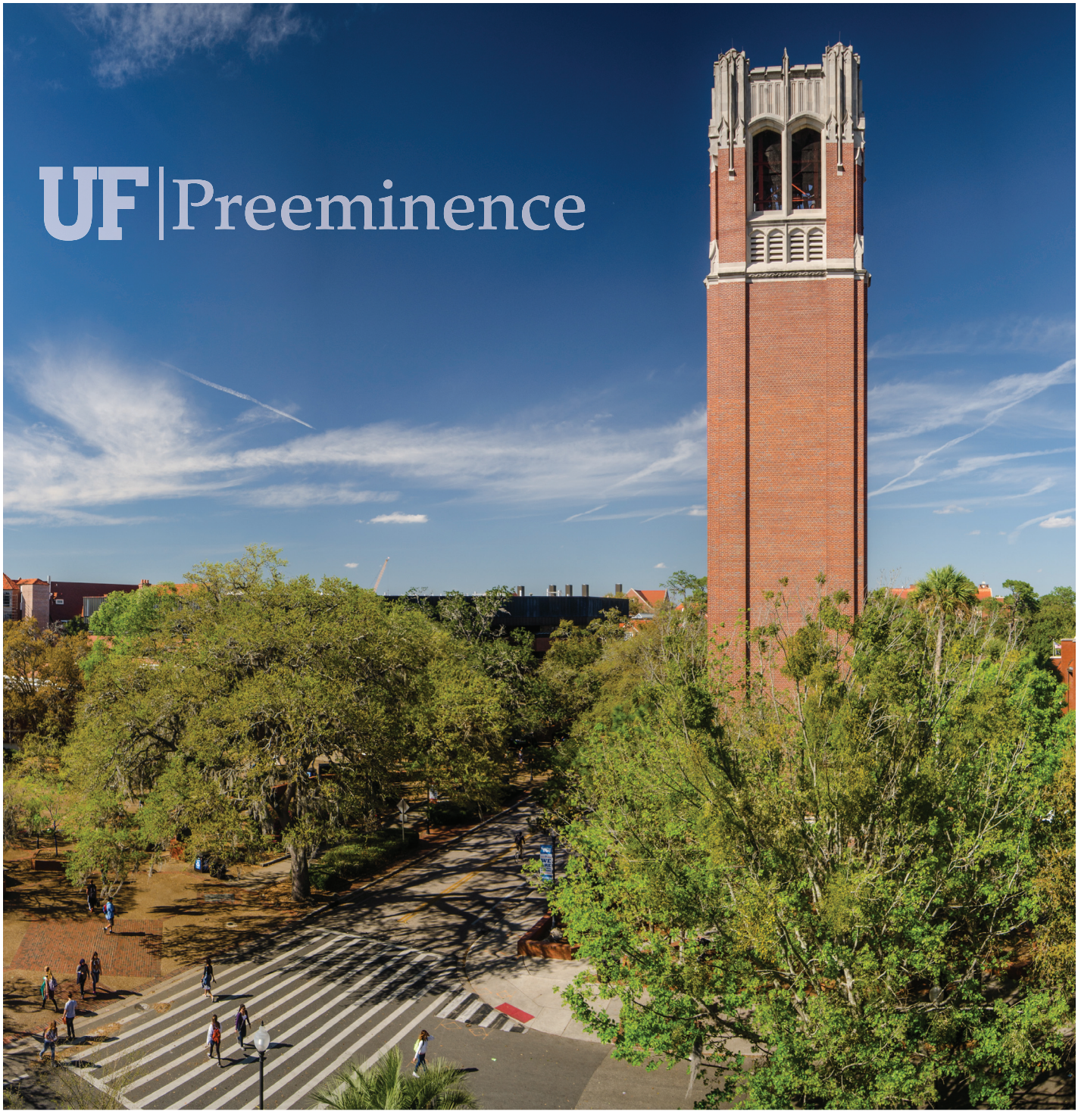
Evelyn F. McKnight Chair Endowments

Balances through December 31, 2017

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
	$ 3,939,277	2018	$ 69,907	$ (69,907)	$ -	$ 34,954
Life-to-date Totals			**$ 2,512,588**	**$ (2,747,416)**	**$ 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
	$ 3,949,366	2018	$ 69,877	$ (69,877)	$ -	$ 34,938
Life-to-date Totals			**$ 353,491**	**$ (318,553)**	**$ -**	

UF Foundation Endowment Reports



UF UNIVERSITY of FLORIDA

FUND IMPACT REPORT

Evelyn F. McKnight Brain Research Grant

Book Value as of 9/30/17	**$25,967,781**
Market Value as of 9/30/17	**$29,686,660**
Projected Spendable Income for 2017/18	**$1,041,290**

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.

UF UNIVERSITY of FLORIDA

FUND IMPACT REPORT

Evelyn F. McKnight Chair for Brain Research in Memory Loss

Book Value as of 9/30/17	**$3,995,677**
Market Value as of 9/30/17	**$3,986,028**
Projected Spendable Income for 2017/18	**$139,814**

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.

UF UNIVERSITY of FLORIDA

FUND IMPACT REPORT

William G. Luttge Lectureship in Neuroscience

Book Value as of 9/30/17	**$250,275**
Market Value as of 9/30/17	**$274,491**
Projected Spendable Income for 2017/18	**$9,628**

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.

UF UNIVERSITY of FLORIDA

FUND IMPACT REPORT

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

Book Value as of 9/30/17	**$4,000,000**
Market Value as of 9/30/17	**$3,984,304**
Projected Spendable Income for 2017/18	**$139,754**

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.

UF 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 2017/2018	$34,953 (09/30/17 YTD)
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	$2,477,635

UF UNIVERSITY of FLORIDA

FUND IMPACT REPORT

McKnight Brain Research Foundation

Evelyn F. McKnight Chair for Brain Research in Memory Loss (008057)

Spendable Fund Transfers since endowment inception

FY 2017/2018	$260,322 (09/30/17 YTD)
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	$16,250,043

UF UNIVERSITY of FLORIDA

FUND IMPACT REPORT

McKnight Brain Research Foundation

William G. Luttge Lectureship in Neuroscience (018093)

Spendable Fund Transfers since endowment inception

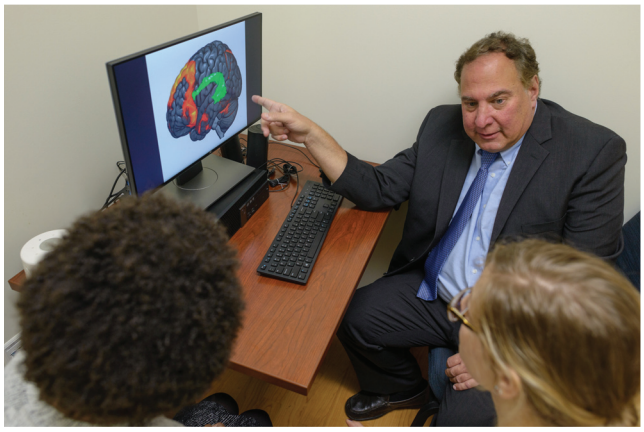
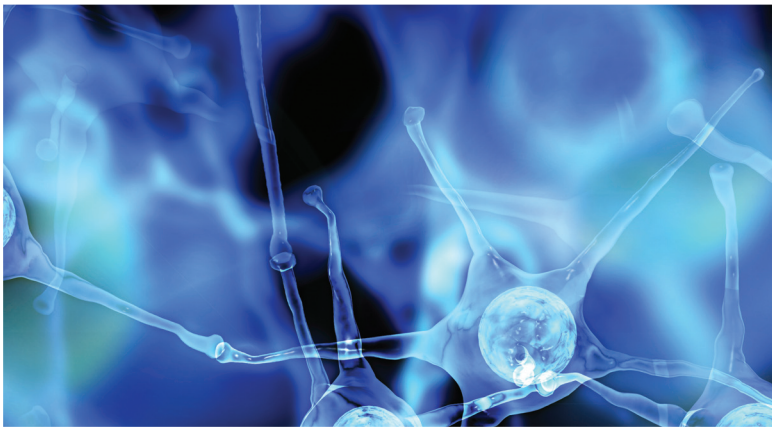
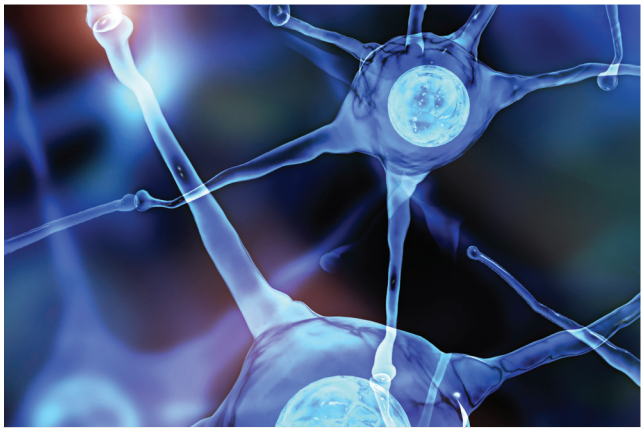
FY 2017/2018	**$2,407 (09/30/17 YTD)**
FY 2016/2017	**$9,627**
FY 2015/2016	**$9,909**
FY 2014/2015	**$9,386**
FY 2013/2014	**$9,074**
FY 2012/2013	**$6,754**
TOTAL	**$47,157**

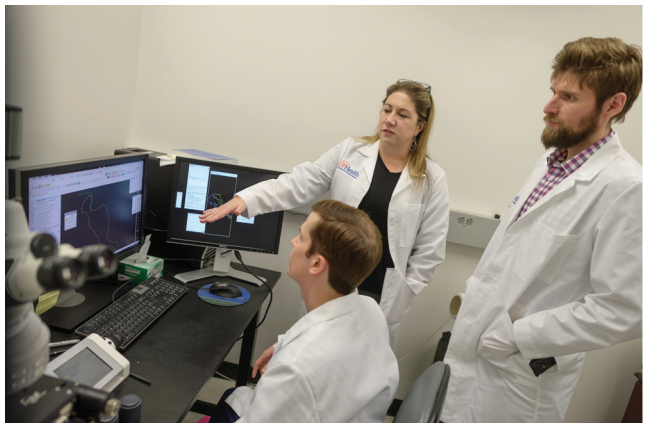
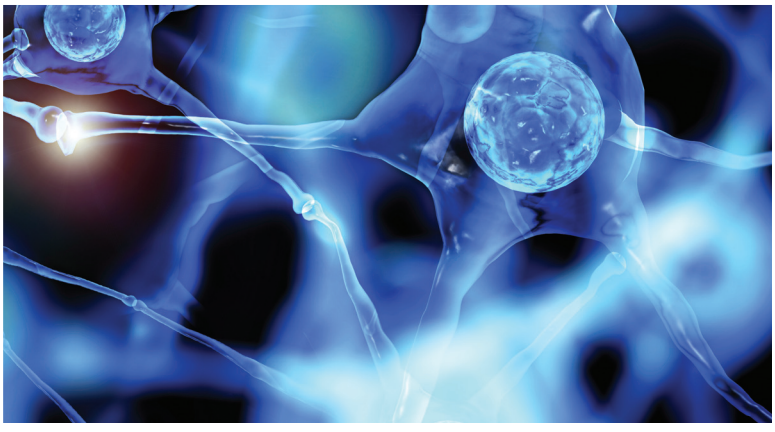
Evelyn F. McKnight Chair for Clinical Translational Research in Cognitive Aging (020105)

Spendable Fund Transfers since endowment inception

FY 2017/2018	**$34,938 (09/30/17 YTD)**
FY 2016/2017	**$139,754**
FY 2015/2016	**$143,861**
TOTAL	**$318,553**

Faculty Biographical Sketches

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 the decline of these functions in aging and disease. Using rodent models, my laboratory employs an integrative approach that combines sensitive cognitive assessments with cellular, molecular, optogenetic and pharmacological methodologies. My laboratory has uncovered disruptions in both glutamatergic and GABAergic signaling in the aged brain (ref a, b) that contribute to impairments in cognitive flexibility, memory and decision making (ref a, d). Moreover, we have demonstrated that pharmacological targeting of GABAergic and glutamatergic signaling reverses working memory impairment in aged rats (ref a, b). In a second line of work, we have demonstrated age-associated alterations in impulsive and risky choice in aged rats (ref c, Simon et al., 2010) that parallel those observed in humans. Using these animal models, we are now using optogenetic tools to dissect the neural circuits that govern decision making in aging (Orsini et al., 2017). In a third line of work, we have identified deficits in olfactory discrimination abilities in aged subjects that strongly predict impairments in hippocampal-dependent memory function (LaSarge et al., 2007, ref d). We hypothesize that these perceptual discrimination deficits reflect impaired function of 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, and are currently probing the neural mechanisms that are influenced by age in this brain region. Our long-term goal is to identify the circuit and cellular alterations in the aged brain that are most relevant to executive dysfunction and maladaptive decision making, and to design strategies that can target these mechanisms to improve cognitive health and life quality in older adults.

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

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

c. Hernandez CM, Vetere LM; Orsini CA; McQuai JA; Maurer AP; Burke SN; Setlow B, **Bizon, JL**. Decline of prefrontal cortical-mediated executive functions but attenuated delay discounting in aged Fischer 344 x Brown Norway hybrid rats. *Neurobiology of Aging*, In press.

d. Yoder WM, Gaynor, L, Burke SN, Setlow B, Smith DW, **Bizon JL**. (2017) Interaction between age and perceptual similarity in olfactory discrimination learning: relationship with spatial learning impairment. *Neurobiology of Aging*. 53:122-137. doi: 10.1016/j.neurobiolaging.2017.01.023.

B. Positions & Employment

1993-1998	Graduate Student Assistant, University of California, Irvine, Laboratory of Dr. Christine Gall
1998-2003	Postdoctoral Fellow, Johns Hopkins University, Laboratory of Dr. Michela Gallagher
2002-2004	Assistant Research Scientist, Dept. of Psychology, Johns Hopkins University
2004-2010	Assistant Professor of Psychology, Texas A&M University
2004-2010	Faculty of Neuroscience, Texas A&M University
2010-2016	Associate Professor of Neuroscience and Psychiatry, University of Florida College of Medicine
2016- present	Full 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 - present	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	Ad hoc member, NIH Chronic Dysfunction and Integrative Neurodegeneration
2013	Ad hoc member, NIH Sensory and Motor Neuroscience, Cognition and Perception Fellowship Study Section (F02B)
2013 - present	Member, NIH Neurodevelopment, Synaptic Plasticity, Neurodegeneration Fellowship Study Section
2014	Member, NIEHS Special Emphasis Panel (ZES1 LWJ-K), Environmental Contributors to Neurodegeneration
2016 – present	Section Editor, Cognition, Behavior and Physiology Section, Neurobiology of Aging
2014 – present	Chair, NIH Neurodevelopment, Synaptic Plasticity, Neurodegeneration Fellowship Study Section
2016 – present	Executive Committee, University of Florida McKnight Brain Institute
2016 - present	Associate Chair, Department of Neuroscience, UF College of Medicine

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, College of Liberal Arts, 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
2017-2020	UF Term Professor

C. Contributions to Science

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

1. A primary focus of my laboratory is to understand how alterations in excitatory/inhibitory (E/I) signaling dynamics in the prefrontal cortex (PFC) contribute to age-related cognitive decline. To date, much of our work has focused on GABA(B) receptors (refs a,b), which contribute to GABA signaling via both pre- and postsynaptic mechanisms. In PFC, we have documented a number of biochemical (refs a,c) and electrophysiological (ref b) changes in GABA(B)R signaling, which together suggest that pyramidal neurons in this brain region are subject to age-related increases in tonic inhibition (refs a, c). Potentially in response to this increased inhibition, GABA(B)R subunit expression is significantly reduced in the aged PFC (refs b, c). We have found that lower PFC GABA(B)R subunit expression strongly predicts better working memory abilities among aged rats (ref a). We have further identified specific excitatory signaling alterations that contribute to dysregulation of the normal balance of excitation and inhibition in PFC and working memory impairments in aging, including reductions in presumptive synaptic NR2A-NMDARs (ref d). Based on these findings, my laboratory has explored the use of GABA(B)R antagonists and positive allosteric modulators of synaptic NMDARs for improving age-related cognitive decline.

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

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

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

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

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

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

    b. Hernandez CM, Vetere LM; Orsini CA; McQuai JA; Maurer AP; Burke SN; Setlow B, **Bizon, JL**. Decline of prefrontal cortical-mediated executive functions but attenuated delay discounting in aged Fischer 344 x Brown Norway hybrid rats. *Neurobiology of Aging*, In press.

    c. Orsini CA, Trotta RT, **Bizon JL**, Setlow B. (2015) Dissociable Roles for the Basolateral Amygdala and Orbitofrontal Cortex in Decision-Making under Risk of Punishment. *The Journal of Neuroscience*. 35(4):1368-79. **PMCID: 4308589.**

    d. 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. Epub ahead of print. *The Journal of Neuroscience.*

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

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

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

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

    d. Yoder WM, Gaynor, L, Burke SN, Setlow B, Smith DW, **Bizon JL**. (2017) Interaction between age and perceptual similarity in olfactory discrimination learning: relationship with spatial learning impairment. *Neurobiology of Aging*. I53:127-134. **PMCID in progress.**

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

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

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

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

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

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

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

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

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

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

D. Current Research Support

Neural mechanisms of age-related cognitive decline
Principal Investigator: Jennifer L Bizon
R01 AG02942 (years 6-11), 2014/05/15-2019/05/19
National Institute on Aging
The goal of this project is to determine how age-related alterations in GABAergic signaling mechanisms in prefrontal cortex contribute to impairments in executive functions, including working memory, behavioral flexibility and decision making.

Risk taking and cocaine use: interactions, mechanisms, and therapeutic targets
Principal Investigator: Barry Setlow, Co-Investigator: Jennifer L Bizon
R01 DA036534, 2015/03/15-2020/03/31
National Institute on Drug Abuse
The goal of this project is to determine neural mechanisms underlying relationships between risk taking behavior and cocaine self-administration.

The contribution of declines in functional connectivity to cognitive aging
Principal Investigator: Sara Burke, Co-Investigator: Jennifer L Bizon
R01 R01AG049722, 2016/01/05-2021/01/15
National Institute on Aging
The goal of this project is investigate how disrupted communication between the prefrontal cortex and hippocampus contributes to age-associated cognitive decline.

Testing and forecasting hippocampal theta wave propagation in learning and memory
Principal Investigator: Andrew Maurer, Co-Investigator: Jennifer L Bizon
R01MH109548, 11/1/16-10/1/21
Agency: National Institute on Mental Health
The goal of this project is to investigate how basal forebrain and entorhinal input to hippocampus regulate brain rhythms in behaving animals.

Impact of perirhinal cortical tau pathology on pre-clinical cognitive decline
Principal Investigator: Jennifer Bizon, Co-Principal Investigator: Sara Burke
Ed and Ethel Moore Alzheimer's Disease Grant, 2/1/17-2/1/19
Agency: Florida Department of Health
This award has provided initial pilot funds to refurbish behavioral equipment and generate pilot data shown in this proposal.

Interactions of Perirhinal Tau Pathology and Aging in Cognitive Dysfunction
1 R21 AG058240-01, Pending Council Review
Role: Bizon PI (Burke MPI)
Agency: NIA
Priority Score: 23, Percentile: 8th

Cognitive augmentation through neuroplasticity
DARPA-TNT Award, 1/1/17-1/1/21
Principle Investigator: Kevin Otto, Project Leader Jennifer L Bizon
Agency: DARPA
The goal of this project is to explore peripheral nerve stimulation as a means to enhance cognition.

Current Mentored Support
Molecular and physiological determinants of age-related working memory decline
Principal Investigator: Joseph A McQuail, Sponsors: Jennifer L. Bizon and Barry Setlow
F32AG051371, 6/1/15-5/31/18
Agency: National Institute on Aging

Neural circuits and mechanisms underlying maladaptive risk-taking following cocaine self-administration
Principal Investigator: Caitlin A Orsini, Sponsors: Barry Setlow and Jennifer L Bizon
K99DA041493, 3/1/16-2/28/20
Agency: Nation Institute on Drug Abuse

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-funded research program is focused on determining the mechanisms that are responsible for the cognitive decline that occurs during aging and early Alzheimer's disease. 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's research is to determine the alterations in network-level interactions that underlie cognitive impairment in advanced age. 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, we are integrating 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 - 2011 Membership Survey Advisory 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 of Council for Undergraduate Research
2015 - Member Faculty for Undergraduate Neuroscience
2016 - Director of the UF Summer Neuroscience Internship Program

Honors

1999 Departmental Honor's in Psychology, University of Oregon
1999 Magna Cum Laude, University of Oregon
1999 Inducted, Phi Beta Kappa
2002 National Institute of Health Training Grant Recipient, University of Arizona
2005 Society for Neuroscience, Travel Award Recipient
2006 Recipient of the Ruth L. Kirschstein National Research Service Award, National Institute of Health
2008 D.G. Marquis Behavioral Neuroscience Award, American Psychology Association
2009 Mentor of the Year Award, Undergraduate Biology Research Program, University of Arizona
2010 D.G. Marquis Behavioral Neuroscience Award , American Psychology Association
2012 Honorable Mention, Mentor of the Year, Undergraduate Biology Research Program, University of Arizona
2014 Best Talk, Department Data Blitz, Department of Neuroscience, University of Florida
2014-2015 Exemplary Teaching Award, University of Florida College of Medicine
2015 Claude D. Pepper Older Americans Independence Junior Scholar
2014-2015 Exemplary Teaching Award, University of Florida College of Medicine
2016 Excellence Awards for Assistant Professors
2017 American Psychological Association Early Career Award for Distinguished Contribution in Cognitive and Behavioral Neuroscience

C. Contribution to Science

1. One aspect of my current research program is to examine the alterations in network-level interactions that underlie cognitive dysfunction in aging and the early stages of Alzheimer's disease. Our rationale is that by elucidating how aging and disease influence systems-level dynamics, we will be better positioned to develop interventions that broadly improve cognition. In support of this objective, we have published a series of experiments that examine the role of prefrontal cortical-medial temporal communication in higher cognition. Specifically, we have shown that performance on a bi-conditional association task (to be used in the current proposal) is highly sensitive to detecting deficits in old age compared to more traditional cognitive tests used to quantify age-related impairments, such as the Morris water maze (a), or spatial non-match to sample test (b). Moreover, we have linked the age-associated impairments on the bi-conditional association task to disrupted communication between the medial prefrontal cortex and the perirhinal cortex (c).

    a. Hernandez AR*, Maurer AP*, Reasor JE, Turner SM, Barthle SE, Johnson SA, **Burke SN** (2015). Age-related Impairments in Object-Place Associations Signify a Decline in Systems-level Neural Communication. *Behavioral Neuroscience*, 129(5):599-610. **PMID: 26413723; PMCID: PMC4945158.**

    b. Johnson SA, Sacks PK, Turner SM, Gaynor LS, Ormerod BK, Maurer AP, Bizon, JL, **Burke SN** (2016). Discrimination performance in aging is vulnerable to interference and dissociable from spatial memory. *Learning & Memory*, 23(7):339-48. **PMID: 27317194; PMCID: PMC4918781.**

    c. Hernandez AR, Reasor JE, Truckenbrod LM, Lubke, K, Johnson SA, Bizon JL, Maurer AP, **Burke SN** (2016). Medial Prefrontal-Perirhinal Cortical Communication is Necessary for Flexible Response Selection. *Neurobiology of Learning and Memory*, 137:36-47. **PMID: 27815215; PMCID: PMC5214530.**

2. My prior publications were the first to demonstrate that age-related deficits in object recognition memory are mediated by perirhinal cortical dysfunction. The perirhinal cortex is an area of the brain that receives sensory information from all modalities and is interconnected with the hippocampus to support memory. Using neurophysiological approaches (ref a) and activity-induced gene expression (ref b), my work showed that perirhinal activity is blunted in aged rats during an object exploration task and that this decline in perirhinal activity is tightly related to behavioral performance. This work demonstrates my experience in linking neural activity to behavioral performance, which is a central feature of the current proposal.

    a. **Burke SN**, Hartzell AL, Lister JP, Hoang LT, Barnes CA. Layer V perirhinal cortical ensemble activity during object exploration: a comparison between young and aged rats. *Hippocampus*. 2012 Oct;22(10):2080-93. **PubMed PMID: 22987683; PubMed Central PMCID: PMC3523702.**

    b. **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.**

3. A long-standing presumption in the field of cognitive aging had been that aged animals have difficulty recognizing stimuli because they "forget" items that have been previously experienced. This idea, however, was difficult to reconcile with other data showing that aged subjects have an increase in false memories. I designed a series of experiments to elucidate the origins

of age-associated recognition memory impairments that led to the novel observation that old animals have recognition memory deficits because they have a reduced ability to discriminate novel stimuli from those that are familiar, which manifests as a false memory (ref a). This work led to foundational insights regarding age-associated declines in recognition memory, which presumably arise from perirhinal cortical dysfunction, and was later replicated in monkeys (ref b) and humans (ref c). We have recently extended this work to show that recognition impairments are due to a reduced ability of aged rats to discriminate between similar stimuli with a LEGO©-object discrimination task (ref d). Moreover, the paper published in 2010, of which I designed and implemented the experimental procedures, analyzed the data, and prepared the manuscript earned the D.G. Marquis Behavioral Neuroscience Award in 2010. This work is indicative of my expertise in the cognitive assessment of rodent cognitive function, which is a core feature of this proposal.

a. **Burke SN**, Wallace JL, Nematollahi S, Uprety AR, Barnes CA. Pattern separation deficits may contribute to age-associated recognition impairments. *Behav Neurosci*. 2010 Oct;124(5):559-73. **PubMed PMID: 20939657; PubMed Central PMCID: PMC3071152.**

b. **Burke SN**, Wallace JL, Hartzell AL, Nematollahi S, Plange K, et al. Age-associated deficits in pattern separation functions of the perirhinal cortex: a cross-species consensus. *Behav Neurosci*. 2011 Dec;125(6):836-47. **PubMed PMID: 22122147; PubMed Central PMCID: PMC3255096.**

c. **Burke SN**, Ryan L, Barnes CA. Characterizing cognitive aging of recognition memory and related processes in animal models and in humans. *Front Aging Neurosci.* 2012;4:15. **PubMed PMID: 22988437; PubMed Central PMCID: PMC3439640.**

d. Johnson SA, Turner SM, Santacroce LA, Carty KN, Shafiq L, Bizon JL, Maurer AP, **Burke SN**. Rodent age-related impairments in discriminating perceptually similar objects parallel those observed in humans. *Hippocampus*. 2017; in press. **PubMed PMID: 28342259.**

4. Although the spatial correlates of hippocampal firing properties have been extensively described, less is known regarding the influence on non-spatial sensory information (e.g., 3-dimensional objects) on the activity patterns of these neurons. The perirhinal cortex is extensively interconnected with the hippocampus and receives sensory input related to non-spatial information. Prior to my research it was believed that this structure supported recognition memory with changes in firing rate as a stimulus goes from novel to familiar. My work produced two foundational insights regarding the perirhinal cortex and its interactions with the hippocampus. First, we showed the perirhinal cortical neurons selectively respond to objects, but that firing rates do not change as a function of novelty (ref a). This observation called for a refinement of standard models of recognition memory. Second, we found that the neurons in the hippocampal subregion receiving direct perirhinal input are robustly modulated by objects (ref b).

   a. **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.**

   b. **Burke SN**, Hartzell AL, Lister JP, Hoang LT, Barnes CA. Layer V perirhinal cortical ensemble activity during object exploration: a comparison between young and aged rats. *Hippocampus*. 2012 Oct;22(10):2080-93. **PubMed PMID: 22987683; PubMed Central PMCID: PMC3523702.**

   c. **Burke SN**, Barnes CA. The neural representation of 3-dimensional objects in rodent memory circuits. *Behav Brain Res*. 2014 Sep 6; **PubMed PMID: 25205370.**

5. In young animals, dynamic hippocampal activity patterns support learning and memory. I have been involved in a series of papers that show how behavior-dependent modulation of hippocampal activity is compromised in aged animals to produce memory deficits. Moreover, we have shown that altering NMDA receptor currents with the Alzheimer's disease therapeutic memantine can restore experience-dependent plasticity in aged memory-impaired rats (ref a). This paper, on which I was first author, received the D.G. Marquis Behavioral Neuroscience Award from the American Psychological Association for the best paper published in Behavioral Neuroscience in 2008. These papers demonstrate my expertise regarding the physiological signatures of hippocampal dysfunction and my commitment to exploring potential therapeutics for treating cognitive aging, both of which are central to the current proposal.

   a. **Burke SN**, Maurer AP, Yang Z, Navratilova Z, Barnes CA. Glutamate receptor-mediated restoration of experience-dependent place field expansion plasticity in aged rats. *Behav Neurosci*. 2008 Jun;122(3):535-48. **PubMed PMID: 18513124; PubMed Central PMCID: PMC2773228.**

b. Gerrard JL, **Burke SN**, McNaughton BL, Barnes CA. Sequence reactivation in the hippocampus is impaired in aged rats. *J Neurosci*. 2008 Jul 30;28(31):7883-90. **PubMed PMID: 18667620; PubMed Central PMCID: PMC2703197.**

c. Hartzell AL, **Burke SN**, Hoang LT, Lister JP, Rodriguez CN, et al. Transcription of the immediate-early gene Arc in CA1 of the hippocampus reveals activity differences along the proximodistal axis that are attenuated by advanced age. *J Neurosci*. 2013 Feb 20;33(8):3424-33. **PubMed PMID: 23426670; PubMed Central PMCID: PMC3711759.**

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

2016/01/01-2020/11/30
1R01AG049722, National Institute on Aging, **Role: PI**
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.

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

2016/08/15-2018/05/31
1R21AG051004, National Institute on Aging, **Role: PI**
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.

2017/02/01-2019/01/31
Florida Department of Health Ed and Ethel Moore Alzheimer's Disease Research Program
Grant: 7AZ06, **Role: co-PI** (contact co-PI Jennifer L. Bizon)
Impact of Perirhinal Cortical Tau Pathology on Pre-Clinical Cognitive Decline
The goal of this proposal is to develop and validate a rat model of human tauopathy.

2017/09/01-2021/05/31
R01MH109548, National Institute of Mental Health (Maurer, PI), **Role: co-I**
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.

2017/04/01-2022/01/31
R01AG055544, National Institute on Aging (Maurer, PI), **Role: co-I**
Title: Age-associated changes in hippocampal circuits and cognitive function
The goal of this award is to determine if age-related changes in hippocampal circuit dynamics is due to synaptic senescence for adaptive compensation.

2017/09/15-2019/08/30
1F31AG058455, National Institute on Aging (Hernandez, PI), **Role: Mentor**
Title: Metabolic Mechanisms for Treating Cognitive Aging
The goal of this mentored training fellowship is test whether dietary ketosis can improve cognitive function in a pre-clinical model of aging.

Completed Research Support

2015/08/15-2017/05/31
1R03AG049411-01A1, National Institute on Aging (Primary), **Role: contact-PI**
Neurogenesis and Memory Network Dynamics during Normal Aging
This proposal seeks to determine the integrity of dentate function in the aged animal.

2015/08/01-2017/3/31
Claude D. Pepper Older Americans Independence Center Junior Scholar Award and Pilot Grant
A Novel Rodent Model of Age-related Motor-Cognition Dual-Task Deficits, **Role: PI**
The goal of this award is to development a rodent model of the association between motor and cognitive frailty in order to test potential interventions for maintaining positive health outcomes in the elderly.

2016/01/01-2017/3/31
AG047266, sub-Award 1Florida Alzheimer's Disease Research Center Pilot Grant, **Role: contact co-PI**
Age-associated functional connectivity declines in the anterior network and memory dysfunction
The goal of this pilot grant is to collect comparable data in rodents and humans that points to the mechanisms of age-related cognitive decline.

BIOGRAPHICAL SKETCH

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

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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-CTRP). 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-CTRP 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-CTRP 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-CTRP.

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 coinfected individuals. *J Neurovirol*. 2014 Aug;20(4):398-411. **PubMed PMID: 24867610; PubMed Central PMCID: PMC4351737.**

4. In addition, to these specific areas of clinical focus, my laboratory continues to conduct studies that address more basic cognitive and behavioral neuroscience questions using neuroimaging as a core component. Some examples are listed below. Studies with Wing, McCaffery, Sweet and me focused on the role of brain reward and inhibitory control systems in obesity. This related to other work on obesity and metabolic effects on the brain and recent R01 funding to use use neuroimaging to study bariatric surgery and weight loss effects on the brain. We continue to also conduct studies to better understand the neural bases of functional neuroimaging responses, including the temporal dynamics of the BOLD response of specific tasks (e.g., Paskavitz et al). I also continue to conduct studies that examine older adults with and 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

1R01AG054077-01 (Woods/**Cohen, PI's**) 09/1/2016-04/30/2021

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.

1R01DK09933401A1 **(Ronald Cohen, PI)** 09/30/2014-08/30/2019

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. 35% effort

2 P01 AA019072 (Monti, PI) 09/01/2015-05/31/2020

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).

Role: Co-1; Research Component-1: PI (20% effort)

U24AA022002 (Cook, PI) 09/01/2013-08/31/2017

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

1U54EB020403-01 (Thompson , PI) 09/29/2014-09/30/2018

ENIGMA: Center for Worldwide Medicine, Imaging and Genomics

The Enigma Center for Worldwide Medicine, Imaging and Genomics is an unprecedented global effort bringing together 287 scientists and all their vast biomedical datasets, to work on 9 major human brain diseases: schizophrenia, bipolar disorder, major depression, ADHD, OCD, autism, 22q deletion syndrome, HIV/AIDS and addictions. Enigma integrates images, genomes, connectomes and biomarkers on an unprecedented scale, with new kinds of computation for integration, clustering, and learning from complex biodata types. Responding to the BD2K RFA, ENIGMA'S Working Groups target key programmatic goals of BD2K funders across the NIH, including NIMH, NIBIB, NICHD, NIA, NINDS, NIDA, NIAAA, NHGRI and FIC. Enigma creates novel computational algorithms and a new model for Consortium Science to revolutionize the way Big Data is handled, shared and optimized, creating new algorithms to handle Big Data from (1) Imaging Genomics, (2) Connectomics, and (3) Machine Learning & Clinical Prediction. **Dr. Cohen is a co-I (10% effort) and director of HIV data initiative.**

R56 HL127175-01 (Williamson, PI) 09/01/2015-08/30/2020

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

R21AG053736-01A1 (Clark; PI) 06/01/2017 -05/31/2019

Combining tDCS and neurorehabilitation to treat age-related deficits of mobility and cognition

This study examines whether brain stimulation is effective in increasing neural plasticity, thereby enhancing motor functions and mobility in older adults. In my role as co-I, I provide support for the neuroimaging conducted as part of the protocol.

Role: Co-I

R01DA042069 (Cook, PI) 08/15/2017 – 03/31/2022
Health outcomes and cognitive effects of marijuana use in people living with HIV. 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.
Role: Co-I

U01AA020797 (***Cook***, Cohen, **MPIs**) 09/01/2016 – 06/30/2021
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. Health outcomes and cognitive effects of marijuana use among persons living with HIV/AIDS

R21AG054876 – (Williamson, PI) 09/01/2017 – 05/31/2019
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.
Role: Co-I

Completed Research Support
R01 HL089311 (Gunstad, PI) 09/15/2008 - 05/31/2012
NHLBI/Subcontract from Kent State
Cognitive Benefits of Cardiac Rehabilitation in Heart Failure
The main goal of this project will be to study CVD and its effects on the brain, and particularly how cardiac rehabilitation and the effects of vascular conditioning are influenced by the vascular CVD and systemic vascular disease factors. **Role: PI of Subcontract**

R01 HL084178 (Sweet, PI) 01/25/2007 - 11/30/2012
NHLBI/Subcontract from Butler Hospital
Hemodynamic and Cognitive Function in Cardiovascular Disease
This study aims at characterizing the relationship between cerebral hypoperfusion and abnormalities of BOLD on FMRI in association with working memory and attention performance among patients with heart failure.
Role: PI of Subcontract

R01 MH074368 (Cohen, PI) 09/30/2006 - 08/31/2012
Age Effects on HIV-Associated Brain Dysfunction
The goal of this project was to achieve greater understanding of how HIV infection interacts with aging to cause brain abnormalities that affect neurocognitive functioning. **Dr. Cohen oversees this entire project.**

RO1 NS080655 (Thompson, PI) 08/01/2012-07/31/2016 NINDS
Predicting Brain Changes in HIV/AIDS
This project greatly advances the ability to map, and predict, brain changes in people living with HIV/AIDS. HIV/AIDS is perhaps the greatest threat to public health worldwide in the 21st century. 40 million people are HIV-infected – a shocking 1 out of every 100 people aged 18-45 – and 40% have some neurological or cognitive impairment. This work offers 3 immediate public health consequences: (1) new methods to predict whether a person with HIV/AIDS will show imminent brain decline; (2) enhancing basic neuroscience by identifying brain circuits disrupted by the virus, and (3) a clear method to boost power for clinical trials of drugs to treat the brain in the millions of people now living with HIV/AIDS.
Role: Co-Investigator

P01AA019072 (Monti, PI) 09/30/2010-08/31/2015
Alcohol and HIV: Biobehavioral Interactions and Intervention (ARCH)
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 underling 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's role was the principal investigator of the R01 type project (RC1) overseeing all aspects of the study.**
Role: Co-Investigator; PI: Research Component 1

This is an abbreviated listing of completed grants from NIH over the course of Dr. Cohen's career.

BIOGRAPHICAL SKETCH

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

NAME: Cruz-Almeida, Yenisel

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

POSITION TITLE: Assistant Professor

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	START DATE MM/YYYY	END DATE MM/YYYY	FIELD OF STUDY
University of Florida, Gainesville, FL	BS	08/1996	05/2001	Microbiology & Cell Science, Immunology
University of Miami, Miami, FL	MSPH	01/2002	08/2004	Epidemiology & Public Health, Biostatistics, Pain Research
University of Miami, Miami, FL	PhD	08/2006	12/2011	Neuroscience, Pain Research
University of Florida, Gainesville, FL	Postdoctoral	12/2011	12/2012	Neuroimmunology, Pain Research

A. Personal Statement

I have a longstanding interest in understanding the mechanisms underlying the observed inter-individual variability of the complex, multidimensional pain experience. This area of interest stems from my previous research training in the fields of Epidemiology, Neuroscience, and Immunology within the context of pain research. During my doctoral work, I studied brain metabolites associated with pain phenotype profiles in persons with spinal cord injury combining **MRS** and **QST**. Consistent with animal studies, we showed that greater concentrations of brain metabolites associated with glial activation (or brain inflammation) were specifically associated with greater clinical pain intensity after spinal cord injury, and not due to spinal cord injury alone. During my post-doctoral training, I became familiar with experimental methods to assess endogenous pain modulation, as well as systemic inflammation in older adults. Finally, my K01 Career Development Award has allowed me to set up my laboratory within the University of Florida to study pain in older individuals using interdisciplinary and translational research approaches.

B. Positions and Honors

Positions and Employment

1997 - 1999 Clinical Research Coordinator, Florida Ophthalmic Institute, Gainesville, FL
1999 - 2001 Medical Laboratory Assistant, Shands Hospital, Gainesville, FL
2004 - 2006 Research Associate, University of Miami, Miami Project to Cure Paralysis, Miami, FL
2004 - 2006 Senior Research Associate, University of Miami, Miami Project to Cure Paralysis, Miami, FL
2006 - 2011 PhD Student, University of Miami, Neuroscience Graduate Program, Miami, FL
2011 - 2012 Post-doctoral Fellow, University of Florida, College of Dentistry, Gainesville, FL
2012 - 2014 Research Assistant Professor, University of Florida, College of Dentistry, Gainesville, FL
2014 - Assistant Professor, University of Florida, College of Medicine, Gainesville, FL

Other Experience and Professional Memberships

2003 - Member, American Pain Society
2004 - Member, International Association for the Study of Pain
2004 - 2012 Member, National Neurotrauma Society
2006 - Member, Society for Neuroscience
2009 - Ad-hoc Reviewer, Pain Medicine
2012 - Ad-hoc Reviewer, Journal of Pain
2013 - Member, Gerontological Society of America
2013 - Ad-hoc Reviewer, Clinical Journal of Pain
2013 - Editorial Board, Journal of Geriatrics & Palliative Care
2014 - Ad-hoc Reviewer, Experimental Gerontology
2014 - Chapter Faculty Advisor, Gamma Eta Sorority
2014 - 2016 Elected Chair, American Pain Society, Shared Interest Group: Measurement of Pain

2014 - 2016 Elected Member, American Pain Society, Early Career Forum Planning Committee
2015 - Executive Board Member, ElderCare of Alachua County UFHealth
2015 - Appointed Member, American Pain Society, Membership Committee
2015 - 2016 Appointed Member, American Pain Society, Early Career Advisory Group
2016 - 2019 Elected Senator, University of Florida, Faculty Senate
2017 - 2019 Elected Co-Chair, American Pain Society, Shared Interest Group: Geriatrics
2017 - Early Career Reviewer (ECR), Inaugural Somatosensory and Pain Systems [SPS] Section

Honors

1998 Leadership Award, University of Florida Hispanic Student Association
1999 Outstanding Student Award in Community Service, University of Florida
2004 Award for Academic Merit, University of Miami
2004 Young Investigator Travel Award, American Pain Society
2006 Lois Pope Life Fellowship, University of Miami Neuroscience Program
2006 Predoctoral Training Fellowship, NINDS/NIH
2006 Young Investigator Travel Award, American Pain Society
2007 Florida Graduate Academic Scholar Award, University of Miami
2008 Congress Scholarship, Congress of Spinal Cord Medicine and Rehabilitation
2010 Inductee, Alpha Epsilon Lambda Graduate Honor Society
2010 RR&D Predoctoral Fellowship Award, Department of Veteran Affairs
2011 Top Student Competition Finalist, National Neurotrauma Symposium
2011 Young Investigator Best Clinical Poster Presentation Award, Miami VA Medical Center
2011 Young Investigator Travel Award, American Pain Society
2011 Margaret Whelan Graduate Student Scholarship Award, University of Miami Medical Faculty Association
2012 Postdoctoral Training Fellowship, NIDCR/NIH
2013 Affiliated Junior Pepper Scholar, University of Florida
2013 Young Investigator Travel Award, American Pain Society
2014 Junior Pepper Scholar, University of Florida
2014 Junior Cognitive Aging & Memory Scholar, University of Florida
2014 Scientific Annual Meeting Faculty, Tampa, Florida, American Pain Society
2015 Annual Meeting Faculty, Palm Springs California, American Pain Society
2015 Annual Meeting Faculty, Orlando Florida, Gerontological Society of America
2015 Annual Meeting Best Poster Presentation Award, Washington, DC, Older Americans Independence Centers

C. Contribution to Science

1. A large portion of my research revolves around characterizing profiles explaining the inter-individual differences in persons with chronic pain using multivariable statistical approaches in cross-sectional and longitudinal studies.

    a. **Cruz-Almeida Y**, Riley JL 3rd, Fillingim RB. Experimental pain phenotype profiles in a racially and ethnically diverse sample of healthy adults. *Pain Med*. 2013 Nov;14(11):1708-18. doi: 10.1111/pme.12203. Epub 2013 Jul 24. **PMID: 23889771.**

    b. **Cruz-Almeida Y**, Felix ER, Martinez-Arizala A, Widerström-Noga EG. Pain symptom profiles in persons with spinal cord injury. *Pain Med*. 2009 Oct;10(7):1246-59. **PubMed PMID: 19818035.**

    c. **Cruz-Almeida Y**, Alameda G, Widerström-Noga EG. Differentiation between pain-related interference and interference caused by the functional impairments of spinal cord injury. *Spinal Cord*. 2009 May;47(5):390-5. **PubMed PMID: 19030010.**

    d. **Cruz-Almeida Y**, Martinez-Arizala A, Widerström-Noga EG. Chronicity of pain associated with spinal cord injury: A longitudinal analysis. *J Rehabil Res Dev*. 2005 Sep-Oct;42(5):585-94. **PubMed PMID: 16586184.**

2. Ongoing research interests have been related to the appropriate measurement of pain and its impact across various populations using sophisticated statistical procedures. The examination of the psychometric properties of various self-report measures as well as of experimental pain measures is required in order to perform meaningful clinical research that can be translated into effective therapies.

    a. *Cardoso JS, **Cruz-Almeida Y**. Moving beyond the eigenvalue greater than one retention criteria in pain phenotyping research. *Pain*. 2016 Jun;157(6):1363-4. doi: 10.1097/j.pain.0000000000000520. **PubMed PMID: 27183445; PubMed Central PMCID: PMC4919897.** *Student Mentee

b. **Cruz-Almeida Y**, Naugle KM, Vierck CJ, Fillingim RB, Riley JL. Reliability of pain intensity clamping using response-dependent thermal stimulation in healthy volunteers. *BMC Neurosci*. 2015 Apr 18;16:21. doi: 10.1186/s12868-015-0164-4. **PubMed PMID: 25909597; PubMed Central PMCID: PMC4409722.**

c. **Cruz-Almeida Y**, Fillingim RB. Can quantitative sensory testing move us closer to mechanism-based pain management? *Pain Med*. 2014 Jan;15(1):61-72. doi: 10.1111/pme.12230. Epub 2013 Sep 6. **PMID: 24010588**

d. Soler MD, **Cruz-Almeida Y**, Saurí J, Widerström-Noga EG. Psychometric evaluation of the Spanish version of the MPI-SCI. *Spinal Cord*. 2013 Jul;51(7):538-52. doi: 10.1038/sc.2013.21. Epub 2013 Apr 23. **PubMed PMID: 23608807; PubMed Central PMCID: PMC3803149.**

3. In another line of research, we have investigated factors contributing to individual differences in pain related to knee osteoarthritis. In collaboration with other researchers, we have used sophisticated psychophysical protocols to investigate age-related changes in pain modulation profiles, which may contribute to increased clinical pain among older adults. We have also examined the extent to which demographic factors contribute to individual differences in pain responses, including their interactions with psychosocial variables.

   a. **Cruz-Almeida Y**, *Cardoso J, Riley JL 3rd, Goodin B, King CD, Petrov M, Bartley EJ, Sibille KT, Glover TL, Herbert MS, Bulls HW, Addison A, Staud R, Redden D, Bradley LA, Fillingim RB. Physical performance and movement-evoked pain profiles in community-dwelling individuals at risk for knee osteoarthritis. *Exp Gerontol*. 2017 Aug 24;98:186-191. doi: 10.1016/j.exger.2017.08.026. *Student Mentee

   b. *Cardoso JS, Riley JL 3rd, Glover T, Sibille KT, Bartley EJ, Goodin BR, Bulls HW, Herbert M, Addison AS, Staud R, Redden DT, Bradley LA, Fillingim RB, **Cruz-Almeida Y**. Experimental pain phenotyping in community-dwelling individuals with knee osteoarthritis. *Pain*. 2016 Sep;157(9):2104-14. **PubMed PMID: 27340911; PubMed Central PMCID: PMC4988907.** *Student Mentee

   c. **Cruz-Almeida Y**, Sibille KT, Goodin BR, Petrov ME, Bartley EJ, Riley JL 3rd, King CD, Glover TL, Sotolongo A, Herbert MS, Schmidt JK, Fessler BJ, Staud R, Redden D, Bradley LA, Fillingim RB. Racial and ethnic differences in older adults with knee osteoarthritis. *Arthritis Rheumatol*. 2014 Jul;66(7):1800-10. **PubMed PMID: 24729357; PubMed Central PMCID: PMC4077911.**

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

4. Ongoing research efforts address the utility of biomarkers including those associated with endocrine and immune function in humans.

   a. **Cruz-Almeida Y**, Aguirre M, Sorenson HL, Tighe P, Wallet SM, Riley JL 3rd. Age differences in salivary markers of inflammation in response to experimental pain: does venipuncture matter? *Journal of Pain Research*, In Press.

   b. Riley JL 3rd, **Cruz-Almeida Y**, Dasilva Ribeiro MC, Simon CB, Eckert NR, Aguirre M, Sorenson HL, Tighe PJ, Edwards RR, Wallet SM. Age Differences in the Time Course and Magnitude of Changes in Circulating Neuropeptides After Pain Evocation in Humans. *J Pain*. 2017 Apr 29;**PubMed PMID: 28461253.**

   c. **Cruz-Almeida Y**, Aguirre M, Sorenson HL, Tighe P, Wallet SM, Riley JL 3rd. Age differences in cytokine expression under conditions of health using experimental pain models. *Exp Gerontol*. 2015 Dec;72:150-6. **PubMed PMID: 26456458; PubMed Central PMCID: PMC4664177.**

   d. **Cruz-Almeida Y**, King CD, Wallet SM, Riley JL 3rd. Immune biomarker response depends on choice of experimental pain stimulus in healthy adults: a preliminary study. *Pain Res Treat*. 2012;2012:538739. **PubMed PMID: 23213513; PubMed Central PMCID: PMC3508574.**

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

Ongoing Research Support

R01DE019456, National Institute of Dental and Craniofacial Research
Luciana Shaddox (PI)
06/01/14-05/31/19
Mechanisms and treatment response of aggressive periodontitis in children
The primary goal of this award is to determine the inflammatory mechanisms accounting for the inter-individual variability in

periodontitis and treatment outcomes in children
Role: Co-Investigator

K01AG048259, National Institute on Aging
Yenisel Cruz-Almeida (PI)
05/15/15-05/14/20
Neuroimaging age-related changes in pain modulation
The primary goal of this award is to provide the necessary training and mentoring for Dr. Cruz-Almeida to determine the neurobiological mechanisms underlying abnormal pain modulation in older adults that may account for increased clinical pain in this population.
Role: PI

UL1TR000064, PRICE-IOA ARG, University of Florida CTSI
Yenisel Cruz-Almeida (MPI)
08/01/16-12/31/17
Neurobiological Mechanisms of Oxytocin's Pain-Modulatory Role in Aging
The goal of this project is to determine the neurobiological mechanisms of chronic oxytocin nasal administration in aging.
Role: MPI

Completed Research Support
R01AG039659, National Institute on Aging
Joseph L. Riley III (PI)
06/01/13-05/31/17
The effects of aging on experimental models of pain inhibition and facilitation
The overall aim of the research project is to characterize alterations in pain perception and endogenous pain modulation associated with aging.
Role: Co-Investigator

P30AG028740, National Institute on Aging
Yenisel Cruz-Almeida (PI)
04/01/15-03/31/17
Pain and mobility function in older adults
The overall aim of the present study is to examine the associations between pain-related brain network reorganization and complex walking function in older persons with musculoskeletal pain.
Role: PI

UL1TR000064, University of Florida CTSI
Yenisel Cruz-Almeida (PI)
06/01/14-05/31/16
Cortico-striatal connectivity in predicting clinical OA-related pain
The overall aim of the research project is to obtain pilot data to characterize nervous system function in older adults with and without knee OA pain.
Role: PI

ULTR000064, University of Florida CTSI
Yenisel Cruz-Almeida (PI)
06/01/12-12/31/13
Saliva as an alternative to plasma to measure biomarkers associated with pain mechanisms
The goal of this pilot study is to delineate and quantify the standard basal and pain-evoked changes in saliva concentrations of relevant biomarkers and validate their analysis with plasma samples in the context of experimental pain stimulation across various age groups in a sample of healthy adults.
Role: PI

n/a, VA RR&D Office of Academic Affiliations
Yenisel Cruz-Almeida (PI)
09/01/10-08/31/11
Utility of thalamic metabolites and sensory testing in neuropathic pain conditions after spinal cord injury using Magnetic Resonance Spectroscopy and Quantitative Sensory Testing
The goal of the study was to assess the diagnostic utility of thalamic biomarkers in predicting clinical pain phenotypes in persons with pain after spinal cord injury used for Dr. Cruz-Almeida's dissertation.
Role: PI

BIOGRAPHICAL SKETCH

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

NAME: Thomas C Foster

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

POSITION TITLE: Professor and Evelyn F. McKnight Chair for Research on Cognitive Aging and Memory

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Arizona, Tucson AZ	BS	1981	Psychology
Bowman Gray, School of Medicine, W-S, NC	Ph.D.	1987	Physio/Pharm
University of Colorado, Boulder CO	Postdoctoral	1991	Neurophysiology and behavior

A. Personal Statement

My research focuses on understanding the relationship 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. Reviews related to our work:

a) **Foster, TC**. (2012) Dissecting the age-related decline on learning and memory tasks in rodent models: N-methyl-D-aspartate receptors and voltage-dependent Ca2+ channels in senescent synaptic plasticity. *Prog Neurobio*l 96:283-302. **PMID: 22307057.**

b) **Foster TC**. Role of estrogen receptor alpha and beta expression and signaling on cognitive function during aging. *Hippocampus* 2012; 22(4):656-669. **PMCID: PMC3704216.**

c) Bean, LA, Ianov, L, **Foster, TC**. Estrogen receptors, the hippocampus, and memory. *The Neuroscientist*, 2014, 20, 534-545. **PMCID: PMC4317255.**

d) **Foster, TC**, Kyritsopoulos, A., and Kumar, A., Central role for NMDA receptors in redox mediated impairment of synaptic function during aging and Alzheimer's disease. *Behav Brain Res*, 2017. 322, 223-232. **PMID: 27180169.**

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. In general, my research has focused on understanding mechanisms for modifying synaptic transmission and their relationship to memory, particularly in the context of cognitive decline during aging. My early work employed in vivo recording and showed that neuronal discharge activity in the hippocampus, a brain structure involved in memory, could represent the history of experience and the association of sensory-motor information.

    a) **Foster, TC.**, Christian, EP., Hampson, RE., Campbell, KA. and Deadwyler, SA. (1986) Sequential dependencies regulate sensory evoked responses of single units in the rat hippocampus. *Brain Research* 408:86-96. **PMID: 3594233.**

    b) **Foster, TC.**, West, MO., Hampson, RE. and Deadwyler, SA. (1988) Control of sensory activation of granule cells in the fascia dentata by extrinsic afferents: Septal and entorhinal inputs. *Journal of Neuroscience* 8:3869-3878. **PMID: 3193182.**

    c) **Foster, TC.**, Castro, CA. and McNaughton, BL. (1989) Spatial selectivity of rat hippocampal neurons: Dependence on preparedness for movement. *Science* 244: 1580-1582. **PMID: 2740902.**

2. Synaptic plasticity is thought to mediate the associative and information storage properties of neurons. I employed electrophysiological techniques to determine the mechanisms for altered synaptic strength (quantal analysis) and provide illumination on age-related changes in mechanisms, which regulate the induction and expression of synaptic plasticity associated with cognitive decline.

    a) McNaughton, B.L. and **Foster, T.C.** (1990) The cellular basis of memory. *Science* 249:1487. **PMID: 2271062.**

    b) Norris, C.M., Korol, D.L. and **Foster, T.C.** (1996) Increased susceptibility to induction of long-term depression and long-term potentiation reversal during aging. *Journal of Neuroscience* 16: 5382-5392. **PMID: 8757251.**

    c) Bodhinathan, K., Kumar A., **Foster, T.C.** Intracellular redox state alters NMDA receptor response during aging through Ca2+/calmodulin-dependent protein kinase II. *Journal of Neurosciences* 2010; 30(5):1914-1924.**PM:20130200.**

    d) Guidi, M., Kumar, A., and **Foster T.C.** Impaired attention and synaptic senescence of the prefrontal cortex involve redox regulation of NMDA receptors. *Journal of Neuroscience* 2015, 35(9) 3966-3977. **PMCID: 434819.**

3. To examine the molecular mechanisms for altered synaptic plasticity and determine how synaptic plasticity contributes to transcription and cell health, I have developed molecular techniques including next generation sequencing, DNA methylation, and viral mediated gene expression. The results indicate that during aging expression of neural activity-dependent genes and synaptic genes declines. Transcriptional changes likely result from impaired synaptic plasticity, a decline in hormone mediated transcription, and epigenetic mechanisms. In some cases, we have been able to alter synaptic function and cognition using gene delivery.

    a) **Foster, T.C.**, Rani, A., Kumar, A., Cui, L. and Semple-Rowland, S.L. (2008) Viral vector mediated delivery of estrogen receptor-alpha to the hippocampus improves spatial learning in adult estrogen receptor-alpha knockout mice. *Molecular Therapy* ,16: 1587-1593, **PMID: 18594506.**

    b) Lee WH, Kumar A, Rani A, Herrera J, Xu J, Someya S, **Foster TC.** Influence of viral vector-mediated delivery of superoxide dismutase and catalase to the hippocampus on spatial learning and memory during aging. *Antioxid Redox Signal* 2012; 16(4):339-350. **PMCID: PMC3246419.**

c) Ianov, L., Rani, A., Beas, B. S., Kumar, A., and **Foster, T.C.** Transcription profile of aging and cognitive-related genes in the medial prefrontal cortex. *Front Aging Neurosci*, 2016, 8, 113. **PMCID: 4868850.**

d) Ianov, L., Riva, A., Kumar, A., **Foster, T.C.** DNA methylation of synaptic genes in prefrontal cortex is associated with aging and age-related cognitive impairment. *Front. Aging Neuroci.* 2017, 9, 249. **PMCID: 5539085.**

4. Much of my work has focused on the mechanisms for the closing of the therapeutic window for E2 treatment. This body of work combines behavior, electrophysiology, and molecular studies, including gene delivery. My work demonstrates a critical window for effective E2 treatment in aging female rats, and reveals a differential role for various estrogen receptors in regulating estrogen effects on cognition, synaptic function, and the maintenance of neuronal health.

a) **Foster, TC.**, Sharrow, K.M., Kumar, A. and Masse, J. Interaction of age and chronic estradiol replacement on memory and markers of brain aging. *Neurobiology of Aging*, 2003, 24: 839-852, **PMID 12927766.**

b) Han, X., Aenlle, K.K., Bean, L.A., Rani, A., Semple-Rowland, S.L., Kumar, A., and **Foster, TC**. Role of estrogen receptor alpha and beta in preserving hippocampal function during aging. *Journal of Neuroscience* 2013, 33: 2671-2683. **PMID: 23392694.**

c) Bean, L.A., Kumar, A., Rani, A., Guidi, M., Rosario, A., Cruz, P., Golde, T., **Foster, TC**. Re-opening the critical window for estrogen therapy. *Journal of Neuroscience*, 2015, 35 16077-1693. **PMCID: 4682778.**

d) Ianov, L., Kumar, A., and **Foster, TC**. Epigenetic regulation of estrogen receptor α contributes to age-related differences in transcription across the hippocampal regions CA1 and CA3. *Neurobiology of Aging*, 2016, 49, 79-85. **PMCID: 5479492.**

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

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.
OVERLAP: None.
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.
OVERLAP: None.
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.
OVERLAP: None.
Role: PI

NIA P30AG028740 (PI Pahor) 7/1/2006-3/31/2017
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.
OVERLAP: None.
Role: advice on animal models of aging and age-related cognitive decline

Completed Research Support

NIA R01 AG037984 (PI: Foster) 9/15/2010 to 7/31/2016
Estrogen and cognition over the lifespan

NINDS R37 NS040389 (PI Ranum) 8/1/2015 – 7/31/2017
The purpose of this project is to use molecular genetic approaches to better understand the pathophysiology of spinocerebellar ataxia type 8. As part of this effort we have developed and are characterizing two distinct SCA8 transgenic models.
OVERLAP: None.
Role: advice on synaptic physiology and plasticity in transgenic animals

R21NS091435 (PI Notterpek) 9/1/2017 – 8/31/2017
This projects targets chaperone pathways for myelin repair in hereditary neuropathies
OVERLAP: None.
Role: advice on statistical analysis of behavior and transcription

BIOGRAPHICAL SKETCH

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

NAME: Todd E Golde

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

POSITION TITLE: Professor of Neuroscience
Director, Center for Translational Research in Neurodegenerative Disease

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	B.A.	05/1985	Biology/Immunology
Case Western Reserve University	Ph.D.	05/1991	Pathology
Case Western Reserve University	M.D.	05/1994	Medicine

A. Personal Statement

I have recently been appointed Director of the Evelyn F. and William L. McKnight Brain Institute at the University of Florida where I am charged with overseeing, championing, and facilitating our neuroscience and neuromedicine research programs. I previously directed 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 be surrounded by outstanding scientists and physicians, and the track record of scientific advances made by faculty in these groups has been, and continues to be, outstanding. Although I believe the field as a whole has dramatically increased our understanding of the triggers of AD and other neurodegenerative conditions, we have yet to translate these into successful disease modifying therapies. Thus, I remain committed to opportunistically develop "proof of concept" for therapeutic strategies such as γ-secretase modulators and anti-amyloid as opposed to anti-Aβ immunotherapy. Though there is reasonable consensus that misfolded protein accumulation triggers neurodegenerative cascades, the downstream steps in the cascade are much less well understood. Thus, in addition to an "amyloid β protein centric" focus, my laboratory has recently been focusing on factors that may drive the downstream neurodegenerative cascade in various diseases with a major focus on innate immunity and its role in protecting and driving neurodegeneration. My lab has been at the forefront of utilizing rAAV somatic brain and spinal cord transgenic technology to accelerate translational research in preclinical models of neurodegenerative a disorders and we continue to enhance our rAAV-based tool-kit and have now successfully applied this technology to disease modifying studies in models of amyloid deposition, tauopathy, SOD1 mediated ALS, and α-synucleinopathy. We continue to innovatively use this technology and have been applying it not only to models of amyloid deposition but other mouse models of CNS proteinopathy. Indeed, our studies using rAAV somatic brain and spinal cord transgenesis demonstrate that this is a major technology accelerator that can greatly reduce the cost and other resources required to explore disease modifying strategies in preclinical settings. Indeed, it is this rAAV toolkit which can support some of the studies proposed.

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)
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- AAIC planning committee
2012- Alzheimer's Association National Medical And scientific Advisory Board
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

C. Contribution to Science

1. As a MD PhD student and postdoc with Dr. Steven Younkin, I played a pivotal role in studies showing that the amyloid β protein (Aβ) was a normal metabolite and that mutations that cause AD alter Aβ production in a manner that promote Aβ aggregation. These studies provided pivotal support for the Aβ aggregate (amyloid) hypothesis of AD and enabled drug discovery programs aimed at altering Aβ 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 Aβ42 production and that this effect was attributable to direct alteration of γ-secretase activity. These data were significant as epidemiologic studies showed an association between NSAIDs use and reduced risk for development of AD. We reasoned that the Aβ42 lowering action of certain NSAIDs could account for this association. Subsequently we identified compounds that lowered Aβ42 but lacked cyclooxygenase activity. These data provided the rationale for many other pharmaceutical companies to develop and test what we now refer to as γ-secretase modulators (GSMs) as potential therapeutics for AD. We have also identified compounds that increased Aβ42; thus, mimicking the effect of AD causing mutations and raising the possibility that small molecules could modulate γ-secretase cleavage in a way that might increase one's risk for AD. Finally, we demonstrated that the target of NSAID-like γ-secretase modulators was not the enzyme but 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 γ-secretase modulator.

    a. 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. **PMCID: 3752532.** *Co-corresponing authors

    b. 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.

    c. Eriksen JL, Sagi SA, Smith TE, Weggen S, Das P, McLendon DC, Ozols VV, Jessing KW, Zavitz KH, Koo EH, **Golde TE**. NSAIDs and enantiomers of flurbiprofen target gamma-secretase and lower Abeta 42 in vivo. *The Journal of clinical investigation*. 2003;112(3):440-9. **PMCID: 166298.**

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 γ-secretase. In work conducted in collaboration with Drs. Osborne (UMASS), Miele (LSU/Tulane), and Greenbaum (U Penn), we are evaluating targeting these proteases in cancer, immunologic disease, and malaria. We have recently published proof of concept studies that malarial signal peptidase is a superb anti-malarial drug target.

   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. Roderick JE, Gonzalez-Perez G, Kuksin CA, Dongre A, Roberts ER, Srinivasan J, Andrzejewski C, Jr., Fauq AH, **Golde TE**, Miele L, Minter LM. Therapeutic targeting of NOTCH signaling ameliorates immune-mediated bone marrow failure of aplastic anemia. *The Journal of experimental medicine*. 2013;210(7):1311-29. doi: 10.1084/jem.20112615. **PubMed PMID: 23733784; PubMed Central PMCID: PMC3698520.**

   c. 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/journal.pone.0128619. **PubMed PMID: 26046535; PubMed Central PMCID: PMC4457840.**

   d. 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.**

4. Another focus of my laboratory has been to try to understand how anti-Aβ immunotherapy works. These studies have led to a number of publications that demonstrate many of the assumptions about how this form of AD therapy works are not likely to be correct. Based on these data, we are currently developing anti-amyloid based antibodies and amyloid based vaccines.

   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-Abeta 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-Abeta42- and anti-Abeta40-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 FcRgamma-/- knock-out mice. The Journal of Neuroscience: the official journal of the Society for Neuroscience. 2003;23(24):8532-8.

5. Most recently, 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 Aβ deposition. Recently published studies also reveal a potential novel role of interferon-γ 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. Chakrabarty P, Jansen-West K, Beccard A, Ceballos-Diaz C, Levites Y, Verbeeck C, Zubair AC, Dickson D, **Golde TE**, Das P. Massive gliosis induced by interleukin-6 suppresses Abeta deposition in vivo: evidence against inflammation as a driving force for amyloid deposition. *FASEB journal* : official publication of the Federation of American Societies for Experimental Biology. 2010;24(2):548-59. **PMCID: 3083918.**

Complete List of Published Work in my Bibliography
http://www.ncbi.nlm.nih.gov/myncbi/1PYpZnZ1P9V5n/cv/10576/

D. Research Support

Ongoing Research Support

1P01CA166009 01A1 (Osborne, PI, **Golde P**L) 09/01/2009 – 08/31/2015 2.4 calendar
NIH/NIA $200,000 direct/yr
P01 Title: Targeting Multiple Diseases through Gamma Secretase
Project 2: Profiling Y-Secretase activity and inhibition
Major Goals are to understand why different GSI have different biological activities.
Overlap: None

U01AG046139 **(Golde Contact MPI)** 12/01/2013 -11/30/2018 2.4 calendar
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

R01 AG018454-12A1 **(Golde, PI)** 05/15/2014 – 02/28/2019 2.4 calendar
NIH/NIA $290,762 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-Aβ immunotherapy , and (Aim 3) the pharmacokinetics of antibody exposure in the brain.

P50 AG047266-01A1 **(Golde, Director and Project Leader)** 08/01/2015 -05/31/2020 3.0 calendar
One Florida ADRC $996,381 direct/yr
The UF-MSMC ADRC will be 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.

T32 NS082168 (Bowers, Vaillancourt, MPI, **Golde Co-I**) 05/01/2015 – 04/30/2020 0.0 calendar
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.

Completed Research Support

5P01 AG025531-04 Osborne (PI) 7/15/06 – 06/30/12
P01 Title: TARGETING MULTIPLE DISEASES THROUGH GAMMA SECRETASE
Project 1: Abeta and beyond gamma secretase a drug target for CNS disease
Consortium with Dr. Barbara Osborne, University of Massachusetts
The major goals of the program project are to explore the potential therapeutic benefits and possible adverse effects of γ-secretase inhibitors in AD, MS, immune regulation and cancer.
Role: Project PI

2P01 AG020206-06A1 Koo (PI) 9/01/03 – 6/30/15
P01 Title: NOVEL MECHANISMS OF NSAID ACTION IN ALZHEIMER'S DISEASE
Project 2: Aβ42 Altering Compounds: Mechanisms of Action
Identify target and in vivo mechanisms of action of gamma-secretase modulators.
Role: Project PI

ALSA 286 **(Golde, PI)** 08/01/2015 - 12/31/2016 0.25 calendar
ALS ASSOCIATION $80,000 direct
Exploring the positive effect of rAAV-IL-10 in an ALS mouse model
Major Goals: Evaluate the effect of peripheral delivery of IL-10 to an ALS model.

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 amnestic mild cognitive impairment (aMCI) to enhance cognition both in healthy individuals as well as amnestic mild cognitive impairment. tVNS is an exciting approach based on our understanding of the neurophysiological basis of memory and cognitive function, as well as pilot data. I look forward to extending our knowledge of this mechanistic impact of this innovative tool, laying a foundation for future clinical applications. I also have DARPA funding to further elucidate the neural circuit impacted by vagal nerve stimulation, providing complementary animal model data for the development of this approach. Apropos the mission of the Cognitive Aging and Memory Clinical Translational Research Program, my funded work on novel potential preventative treatments for aMCI (i.e., prodromal Alzheimer's) continues to show translational promise.

B. Positions and Honors

Positions and Employment

2001 - 2001 Product Engineer, Hughes Network Systems, 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 - Research Health Science Specialist, Malcom Randall VAMC, Gainesville, FL
2013 - Assistant Professor, University of Florida, Gainesville, FL

Other Experience and Professional Memberships

Member, Society for Neuroscience
Member, American Association for the Advancement of Science
Member, Organization for Computational Neurosciences

Honors

2005 Computer Science Faculty Commendation, University of Chicago
2007 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 11 times over the past two years since its publication and extensions of the work 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 postraumatic stress disorder and mild traumatic brain injury**
   Postraumatic 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
1IK2RX000707, 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

BIOGRAPHICAL SKETCH

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

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

NAME: MAURER, ANDREW

eRA COMMONS USER NAME (agency login): DREWMAURER

POSITION TITLE: Assistant Professor

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Pittsburgh, Pittsburgh, PA	BS	12/2003	Neuroscience
University of Arizona, Tucson, AZ	PHD	12/2009	Neuroscience
University of Arizona, Tucson, AZ	Postdoctoral Fellow	06/2014	Neurobiology of Aging

A. Personal Statement

Throughout my scientific career, I have been focused on trying to understand the 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. Much of my research focus was on combining neuron spiking data with local-field potentials in order to determine how spike timing is altered as a consequence of both location and time (i.e., theta phase precession). This research track was extended under the supervision of Dr. Carol A. Barnes, in which I continued to develop and implement high-level analyses to reveal novel computations of the CA1 subregion of the hippocampus (ref 1). This expertise will be applied to the analysis of oscillatory data in the current proposal.

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. Many of these people will suffer age-related impairments, either through pathology or normal age-related cognitive decline, necessitating long-term in-home or assisted living care. This outcome comes at a loss of dignity for both the elderly and a financial strain on their children and community. Therefore, it is both timely and necessary to explicitly test the competing hypotheses, "synaptic senescence" versus "adaptive plasticity", in order to determine whether age-related medial temporal lobe change is the result of general decline or the consequence of compensatory dynamics. Our proposal examines the interactions between regions of the medial temporal lobe in young and aged animals, while they perform tasks requiring high-level cognitive function. By taking an innovative cross-regional approach, it will be possible to view aging in the context of larger dynamic processes and potentially identify specific loci of dysfunction.

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). I am also enthusiastic to be joined by Dr. Kamran Diba, an expert in analytical tools for defining microcircuits, Dr. Stephen Blackband, expert in MRI and DTI technology, and Dr. Alexandru Sheremet, nonlinear physicists with an immense knowledge on cross-frequency coupling. Dr. Sheremet, Burke and I have recently published a manuscript using bicoherence, also implemented in the current proposal to investigate oscillatory coupling and nonlinearities in the hippocampus (ref 3). Finally, I have published a unique review providing new insights to the nonlinear nature of the entorhinal cortex (ref. 4). Collectively, this demonstrates that I have successfully achieved research independence.

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. While I have made a complete recovery, the simultaneous combination of these two events kept me out of the laboratory for an extended period of time, effectively delaying my research progress. While I could not manage to push my own projects forward during this time, I did remain active in research and data analysis, co-authoring multiple manuscripts.

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, Unviersity of Pittsburgh
2007 Recipient of Conference Travel Award, Society for Neuroscience
2008 Recipient of the D.B. Marquis Behavioral Neuroscience Award, Behavioral Neuroscience Journal
2011 Recipient of the Ruth L. Kirschstein National Research Service Award, National Institute of Health

C. Contribution to Science

1. Prior to my thesis research, only two studies investigated hippocampal dynamics in the posterior/ventral region of the hippocampus. Therefore, I sought out to determine the firing rate characteristics of neurons in the intermediate portion of the hippocampus compared to the dorsal. We found that place field size was larger in more posterior regions, associated with a decreased rate of phase precession and a decreased sensitivity to velocity. 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 in not critical for theta phase precession.

    a. **Maurer AP**, McNaughton BL. Network and intrinsic cellular mechanisms underlying theta phase precession of hippocampal neurons. *Trends Neurosci*. 2007 Jul;30(7):325-33. **PubMed PMID: 17532482.**

    b. **Maurer AP**, Lester AW, Burke SN, Ferng JJ, Barnes CA. Back to the future: preserved hippocampal network activity during reverse ambulation. *J Neurosci*. 2014 Nov 5;34(45):15022-31. **PubMed PMID: 25378167; PubMed Central PMCID: PMC4220031.**

3. One of the prominent characteristics of hippocampal pyramidal cell activity is their firing correlates with short-term predictions of future locations. Of course ambulatory characteristics will modulate both the future location and the distance covered. We have determined how ambulation alters firing patterns as well as tested models of hippocampal updating by training rodents to walk backwards on a linear track and found that when rodents walk backwards, hippocampal activity patterns continue to predict future locations regardless of head direction.

    a. **Maurer AP**, Burke SN, Lipa P, Skaggs WE, Barnes CA. Greater running speeds result in altered hippocampal phase sequence dynamics. *Hippocampus*. 2012 Apr;22(4):737-47. **PubMed PMID: 21538659; PubMed Central PMCID: PMC3367321.**

    b. **Maurer AP**, Lester AW, Burke SN, Ferng JJ, Barnes CA. Back to the future: preserved hippocampal network activity during reverse ambulation. *J Neurosci*. 2014 Nov 5;34(45):15022-31. **PubMed PMID: 25378167; PubMed Central PMCID: PMC4220031.**

4. While the size of hippocampal spatial receptive fields increases along the dorsal to ventral longitudinal axis, we asked the additional question on whether non-spatial factors could influence the firing rate charachteristics. By placing objects on the track, we showed that the spatial metric of hippocampal receptive fields can be reduced. This work produced new insights regarding the impact of sensory information along the hippocampal longitudinal axis and highlights the productive collaborative efforts of Dr. Burke and myself.

    a. Burke SN, **Maurer AP**, Nematollahi S, Uprety AR, Wallace JL, et al. The influence of objects on place field expression and size in distal hippocampal CA1. *Hippocampus*. 2011 Jul;21(7):783-801. **PubMed PMID: 21365714; PubMed Central PMCID: PMC3314262.**

    b. Burke SN, **Maurer AP**, Hartzell AL, Nematollahi S, Uprety A, et al. Representation of three-dimensional objects by the rat perirhinal cortex. *Hippocampus*. 2012 Oct;22(10):2032-44. **PubMed PMID: 22987680; PubMed Central PMCID: PMC3447635.**

    c. Burke SN, **Maurer AP**, Nematollahi S, Uprety A, Wallace JL, et al. Advanced age dissociates dual functions of the perirhinal cortex. *J Neurosci*. 2014 Jan 8;34(2):467-80. **PubMed PMID: 24403147; PubMed Central PMCID: PMC3870932.**

5. Interneurons have been hypothesized to provide the "scaffold" by which neuronal activity is structured within neural networks. In this sense, they can both govern the rate that information propagates through neural circuits as well as perform computational operations on the information. In light of these theories, we were enthusiastic to discover that putative basket cells exhibted theta phase precession, plausibly inherited from afferent pyramidal cell activity.

    a. **Maurer AP**, Cowen SL, Burke SN, Barnes CA, McNaughton BL. Phase precession in hippocampal interneurons showing strong functional coupling to individual pyramidal cells. *J Neurosci*. 2006 Dec 27;26(52):13485-92. **PubMed PMID: 17192431.**

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/myncbi/andrew.maurer.1/bibliography/43942059/public/?sort=date&direction=ascending

D. RESEARCH SUPPORT

2016/01/01-2020/11/31
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. 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.**

    b. 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 May 2;8:94. **PubMed PMID: 27199740; PubMed Central PMCID: PMC4852201.**

    c. **Porges Eric C**, Woods AdamJ, Edden RA, Harris AD, Huaihou H, Garcia AM, Lamb DG, Williamson JohnB, Cohen RA. Frontal GABA concentrations are associated with cognitive performance in older adults. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*. 2016; in press.

    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 Aug 25; 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. Falchook AD, **Porges EC**, Nadeau SE, Leon SA, Williamson JB, Heilman KM. Cognitive-motor dysfunction after severe traumatic brain injury: A cerebral interhemispheric disconnection syndrome. *J Clin Exp Neuropsychol*. 2015;37(10):1062-73. **PubMed PMID: 26340588.**

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 imagining (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

I am a Research Health Scientist with the VA RR&D Brain Rehabilitation and Research Center of Excellence, Malcom Randall VA Medical Center and an Assistant Professor with the University of Florida Departments of Neurology and Neuroscience. I am affiliated with the Center for Cognitive Aging and Memory Clinical Translational Research (CAM). I have conducted clinical neuroscience research that has incorporated neuroimaging, cognitive and autonomic data in the study of cerebrovascular disease (vascular cognitive impairment and vascular dementia), heart failure and traumatic brain injury. I have over 50 peer-reviewed research articles. 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.

Current funded research includes NIH support to understand the role of improvement in cardiac output in patients with heart failure on brain healthy, cerebral hemodynamics, and cognitive function, NIH support to determine the effects of Transcutaneous Vagal Nerve Stimulation (tVNS) on cognition in people with amnestic mild cognitive impairment in the Alzheimer's spectrum, VA funding to determine autonomic mechanisms in the impact of mild traumatic brain injury on the development and presentation of Post Traumatic Stress Disorder (PTSD), and VA funding to determine the effects of tVNS on sleep architecture and daily emotional functioning in people with PTSD.

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. **Williamson JB**, Lewis G, Grippo AJ, Lamb D, Harden E, Handleman M, Lebow J, Carter CS, Porges SW. Autonomic predictors of recovery following surgery: a comparative study. *Auton Neurosci*. 2010 Aug 25;156(1-2):60-6. **PubMed PMID: 20451468; PubMed Central PMCID: PMC4801019.**

B. Positions and Honors

Positions and Employment

2012- Research Psychologist, Dept of Veteran Affairs, Gainesville FL
2008-2012 Research Health Scientist. Dept of Veteran Affairs, Gainesville FL
2009-2012 Research Assistant Professor, Department of Neurology University of Florida
2012- Assistant Professor (tenure track), Department of Neurology, University of Florida
2016- Assistant Professor, Department of Neuroscience, 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, that 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.
   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 WMHs in VCI to cognition and also Dr. Williamson's early work on the use of DTI 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 mechanism to study the relationship of regional white matter disease in stroke patients on mobilization of autonomic resources to perform cognitive and motor tasks.
   a) **Williamson JB**, Nyenhuis DL, Pedelty L, Byrd S, Jhaveri M, Wang C, deTeledo-Morrell L, Sripathirathan K, Gorelick P. Baseline differences between Vascular Cognitive Impairment No Dementia reverters and nonreverters. *Journal of Neurology, Neurosurgery, and Psychiatry* 2008;79:1208-1214.
   b) **Williamson JB**, Nyenhuis Dl, Stebbins GT, Gorelick PB. Regional differences in apparent white matter integrity, cognition and mood in patients with ischemic stroke. *Journal of Clinical and experimental Neuropsychology* 2010, 32, 673-681.
   c) **Williamson JB**, Lewis GF, Grippo A, Lamb D, Harden E, Handleman M, Lebow J, Carter CS, Porges SW. Autonomic predictors of recovery following surgery: A comparative study. *Autonomic Neuroscience* 2010:156, 60-66.
   d) **Williamson JB**, Lewis GF, Nyenhuis DL, Stebbins GT, Murphy C, Handelman M, Harden E, Heilman KM, Gorelick PB, Porges SW. The effects of cerebral white matter changes on cardiovascular responses to cognitive and physical activity in a stroke population. *Psychophysiology* 2012; 49:1618-1628.

3. *Elucidated impact of chronic lateralized stroke on spatial cognition as well as normal perturbations of sensory performance on laterality of spatial cognition and autonomic support.* These efforts led to several related lines of investigation to examine risk factors contributing to the development of spatial performance deficits in patients with cerebrovascular disease.
   a) **Williamson JB**, Haque S, Harciarek M, Burtis DB, Lamb D, Zilli E, Heilman KM. The influence of stimulus proximity on judgments of spatial location in patients with chronic unilateral right and left hemisphere stroke. *Journal of Clinical and Experimental Neuropsychology* 2014; 36:787-793.
   b) Finney G, **Williamson JB**, Burtis DB, Drago V, Mizuno T, Jeong Y, Crucian G, Haque S, Heilman KM. Effects of chronic right hemisphere damage on the allocation of spatial attention: Alterations of accuracy and reliability. *Journal of the International Neuropsychological Society* 2015; 21:1-5.
   c) Burtis DB, Heilman KM, Mo J, Wang C, Lewis GF, Davilla MI, Ding M, Porges SW, **Williamson JB**. The effects of constrained left and right monocular viewing on the autonomic nervous system. *Biological Psychology* 2014; 100:79-85.
   d) **Williamson JB**, Lamb DG, Burtis DB, Haque S, Kesayan T, Heilman K. Right hemispatial ipsilesional neglect with chronic right hemisphere strokes. *Journal of Clinical and Experimental Neuropsychology* 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

NIH 1R56HL127175-01 09/01/2015-08/31/2018

Brain and cognition effects of cardio resychronization 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

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

PI: Williamson

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

Completed Research Support

VAMC Merit Review 10/2012-10/2016

Vertical Neglect

The goal of this funding is to examine the impact of unilateral stroke and aging on dorsal and ventral streams in vertical attention.

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

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 Career Development Award 1 2013-2015
Traumatic Brain Injury and Motor Disorders
This career developmental award was designed to assess lateralized motor disorder presentations in patients with TBI. The central hypothesis was that corpus callosal injury would result in different forms of apraxia at the left and right hand driven by the laterality of motor control and communication deficits induced by the injury preventing normal performance of motor activities. The primary findings of this study did demonstrate laterality differences and this work is currently under review at a high impact factor journal.
Role: Co-I (PI = Adam Falchook, MD).

VAMC BRRC 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

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 a cognitive neuroscientist with expertise in non-invasive brain stimulation and neuroimaging. 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 700 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 cognitive aging interventions, multi-disciplinary cognitive neuroscience methodologies (MRI/fMRI, electrophysiology, non-invasive brain stimulation), extensive experience with aging-related disorders, and past research with neurological diseases. 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), and one of the largest phase II tES trials, the Stimulated Brain Study (K01AG054077, n=80). Dr. Woods is also PI and Co-I on 3 other NIH funded tES projects (1 R01, 2 R21s).

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. Szynkowicz, 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. Szynkowicz, 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, RA, 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 health 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 K01AG050707-A1 **(Woods; PI)** 09/30/16-05/31/21
NIH
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: PD/PI

NIMH R21MH112206 (Woods/Ding, MPIs) 11/1/17-10/31/19
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: PI

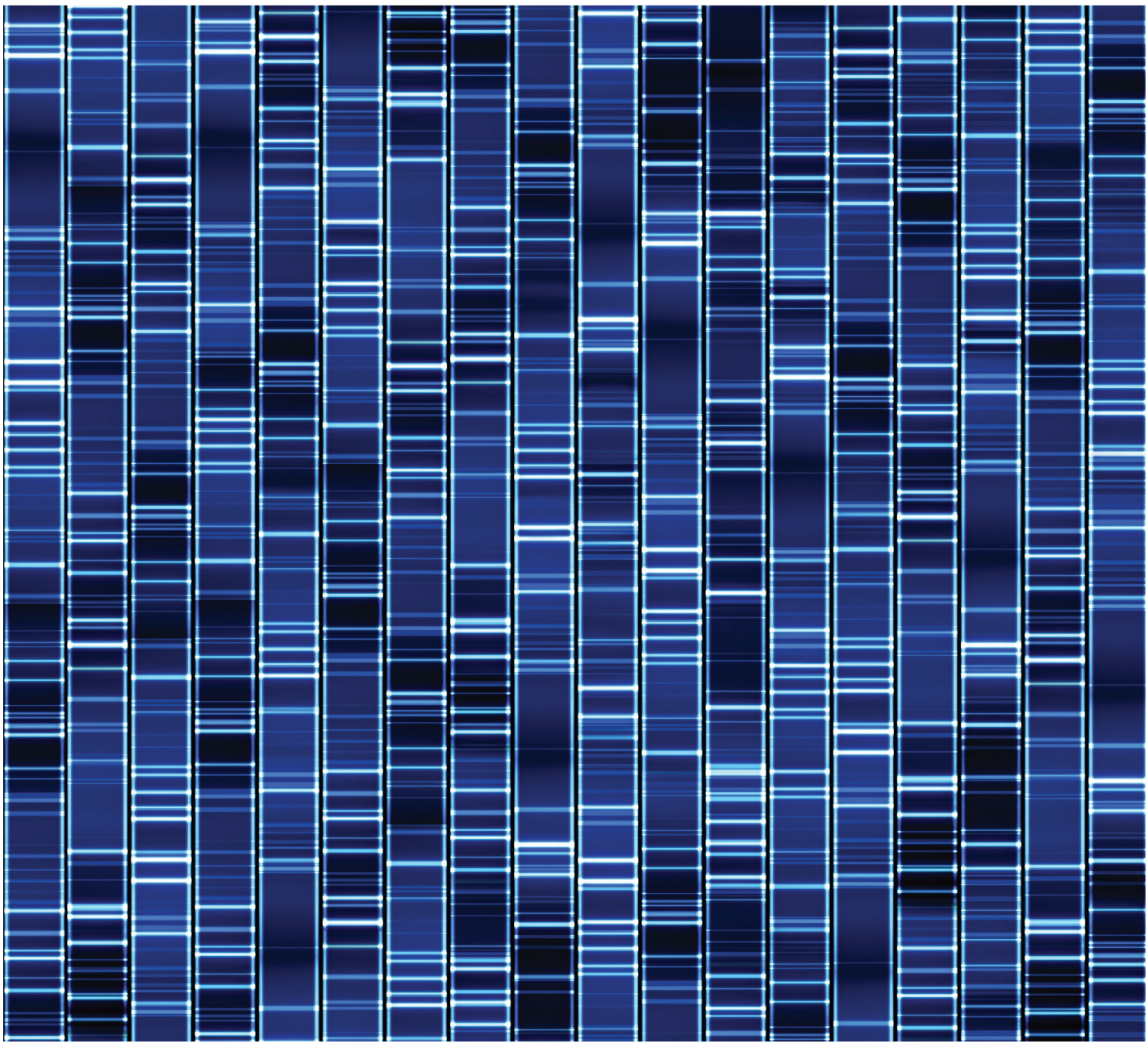
NIMH RF1MH114290-01 (Sadlier; PI) 07/19/17-07/18/21
National Institutes of Health
Mechanism and dosimetry exploration in transcranial electrical stimulation using magnetic resonance current mapping methods
The goal of this project is to pioneer an objective measure of current flow in the brain using 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; 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)

Industry Sponsored Trial **(Woods; PI)** 07/01/16-06/31/18
Osato Research Institute
Impact of Fermented Papaya Product on brain energetics, neuroinflammation, and cognition: The Efficient Brain Study
The goal of this study is to perform a pilot clinical trial investigating the influence of Fermented Papaya Product on brain energetics, neuroinflammation, and cognition in older adults with elevated systemic inflammation using multimodal neuroimaging (fMRI, DWI) and spectroscopy (31P, 1H-MRS), as well as assessment of systemic inflammation and cognition. The project specifically focuses on enhancement of working memory function in older adults.
Role: PI

Affiliate Faculty Biographical Sketches

In addition to primary faculty, the CAM-CTRP maintains a broad network of active cross-college affiliated faculty. These collaborations are central to the mission of the CAM-CTRP in understanding cognitive aging and identifying new approaches to combating the cognitive aging process. The affiliate faculty's research areas represent important lines of investigation for shedding light on underlying brain-based changes that occur with aging. These faculty collaborate closely with the primary CAM-CTRP faculty on funded and pending research projects focused on cognitive aging. In combination, the primary and affiliate faculty of the CAM-CTRP provide a broad base of knowledge and expertise for studying cognitive aging and memory.



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 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 Gingko 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, as Chair of the Alzheimer's Association Med-Sci Advisory Council, and Chair of 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 was a member of the NIH Council of Councils (overseeing the Common Fund), and served previously on the NCCAM (now NCCIH) Council. I maintained an NIH-funded wet lab for over 30 years, and served as 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 and Pitt has facilitated my re-entry into research and research administration. I have trained four PhD or MD/PhD students, seven postdocs, in addition to being a member on over ten graduate student dissertation committees, and I will draw on this experience when mentoring Hunter. In Returning to my graduate and medical school alma mater, the University of Florida, in July 2015, I now am Deputy Director of the McKnight Brain Institute, the center of neuroscience research and teaching at UF, as well as Associate Director of the newly NIA-funded 1Florida ADC, a collaboration among UF, Mt. Sinai Hospital in Miami Beach, and several other Florida universities. I take great pride in mentoring students and I believe I am now in an ideal position to serve as a clinical, research, and leadership mentor.

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 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. Contributions 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, that 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, S.T. and Scheff, S.W. Synapse loss in frontal cortex biopsies in Alzheimer's disease: Correlation with cognitive severity. *Annals of Neurology* 27:457-464, 1990.

   DeKosky, S.T., Harbaugh, R.E., Schmitt, F.A., Bakay, R.A.E., Chui, H.C., Knopman, D.S., Reeder, T.M., Shetter, A.G., Senter, H.J., Markesbery, W.R., and the Intraventicular Bethanecol Study Group. Cortical biopsy in Alzheimer's disease: Diagnostic accuracy and neurochemical, neuropathological and cognitive correlations. *Annals Neurology* 32:625-632, 1992.

   DeKosky, S.T., Ikonomovic, M.D., Styren, S.D., Beckett, L., Wisniewski, S., Bennett, D., Kordower, J.H., and Muston, E.J. Up-regulation of choline acetyltransferase activity in hippocampus and frontal cortex of elderly subjects with mild cognitive impairment. *Annals of Neurology* 51:145-155, 2002.

   Ikonomovic, M.D., Klunk, W.E., Abrahamson, E.E., Wuu, J., Mathis, C.A., Scheff, S.W., Mufson, E.J. and **DeKosky, S.T.** Precuneus amyloid burden is associated with reduced cholinergic activity in Alzheimer disease. *Neurology* 77:39-47, 2011. **PMCID: 3127332**

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.

   Mintun, M.A., LaRossa, G.N., Sheline, Y.I., Dence, C.S., Lee, S.Y., Mach, R.H., Klunk, W.E., Mathis, C.A., **DeKosky, S.T.**, and Morris, J.C. [11C] PIB in a nondemented population: Potential antecedent marker of Alzheimer disease. *Neurology* 67:446-452, 2006.

   Ikonomovic, MD, Klunk, WE, Abrahamson, EE, Mathis, CA, Price, JC, Tsopelas, ND, Lopresti, BJ, Ziolko, S, Bi, W, Paljug, WR, Debnath, ML, Hope, CE, Isanski, BA, Hamilton, RL and **DeKosky, ST** Post-mortem correlates of in vivo PiB-PET amyloid imaging in a typical case of Alzheimer's disease. *Brain* 131:130-1645, 2008. **PMCID:PMC2408940.**

   Cohen, A., Price, J., Weissfeld, L., James, J., Rosario, B., Bi, W., Nebes, R., Saxton, J., Snitz, B., Aizenstein, H., Wolk, D., **DeKosky, S.T.**, Mathis, C. and Klunk, W. Basal cerebral metabolism may modulate the cognitive effects of Aβ in mild cognitive impairment: An example of brain reserve. *Journal of Neuroscience* 29:14770-14778, 2009. **PMCID: 2810461.**

   Wolk, D.A., Price, J.C., Madeira, C., Saxton, J.A., Snitz, B.E., Lopez, O.L., Mathis, C.A., Klunk, W.E. and **DeKosky, S.T.** Amyloid imaging in dementias with atypical presentation. *Alzheimer's and Dementia* 8:389-398, 2012. **PMCID: 3517915.**

   Snitz, B.E., Weissfeld, L.A., Lopez, O.L., Kuller, L.H., Saxton, J., Singhabu, D.M., Klunk, W.E., Mathis, C.A., Price, J.C., Ives, D.G., Cohen, A.D., McDade, E. and **DeKosky, S.T.**Cognitive trajectories associated with β-amyloid deposition in the oldest-old without dementia. *Neurol* 80:1378-1384, 2013. **PMCID: PMC3662268.**

3. **Experimental Brain Trauma:**

   I began experiments utilizing controlled traumatic brain injury as a way to study cascades that I thought were similar to Alzheimer's disease in the early 1990s (before transgenic mouse models were available). My lab demonstrated up-regulation of NGF and its control by IL1β, elevation of APP and Aβ in trauma, and a number of interventions to stop elevation of Aβ 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 Ikonomovic, 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., Ikonomovic, 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 Aß peptide: Implications for clinical outcome. *Experimental Neurology* 197:437-450, 2006.

   Abrahamson, E. E., Ikonomovic, M.D., Dixon, D.E. and **DeKosky, S.T.** Simvastatin therapy prevents brain trauma-induced elevations in ß-amyloid peptide levels. Annals of Neurology 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, Aβ and Aβ plaques (within 2 hours), a possible risk factor for subsequent cognitive decline, suggesting acute post-TBI interventions and bringing the study of AD and TBI together. We are now studying tau as a potential biomarker of CTE in living subjects.

Ikonomovic, M.D., Uryu, K., Abrahamson, E.E., Ciallella, J.R., Trojanowski, J.Q., Lee, V. M.-Y., Clark, R.S., Marion, D.W., Wisniewski, S.R., and **DeKosky, S.T.** Alzheimer's pathology in human temporal cortex surgically excised after severe brain injury. *Experimental Neurology* 190:192-203, 2004.

DeKosky, S.T., Abrahamson, E.E., Ciallella, J.R., Paljug, W.R., Wisniewski, S.R., Clark, R.S.B., and Ikonomovic, M.D. Association of increased cortical soluble Aß42 levels with diffuse plaques after severe brain injury in humans. *Archives of Neurology* 64:541-544, 2007.

Omalu, B.I., **DeKosky, S.T.**, Minster, R.L., Kamboh, M.I., Hamilton, R.L. and Wecht, C.H. Chronic traumatic encephalopathy in a National Football League (NFL) player. *Neurosurgery* 57:128-134, 2005.

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

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

5. **Mild Cognitive Impairment and Prevention of Dementia**

I chaired the AAN practice parameter review that first defined MCI for research and subsequently clinical practice, showed multiple ways neuroplastic responses 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 et al and **DeKosky, ST** (2001) Practice parameter: Early detection of dementia: Mild cognitive impairment (an evidence-based review). *Neurology* 56:1133-1142.

Albert, M.S., **DeKosky, S.T.**, Dickson, D., Dubois, B., Feldman, H.H., Fox, N.C., Gamst, A., Holtzman, D.M., Jagust, W.J., Petersen, R.C., Synder, P.J., Carrillo, M.C., Thies, B. and Phelps, C.H. The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement* 7:270-279, 2011. **PMCID: 3312027.**

DeKosky ST, Williamson JD, Fitzpatrick AL, Kronmal RA, Ives DG, Saxton JA, Lopez OL, Burke G, Carlson MC, Fried LP, Kuller LH, Robbins JA, Tracy RP, Woolard NF, Dunn L, Snitz BE, Nahin RL, Furberg CD. (2008) Ginkgo Evaluation of Memory (GEM) Study Investigators. Ginkgo biloba for prevention of dementia: a randomized controlled trial. *JAMA*. 19;300:2253-62. **PMCID: PMC2823569.**

Gandy, S. and **DeKosky, S.T.** (2013) Toward the treatment and prevention of Alzheimer's disease: Rational strategies and recent progress. *Annual Review of Medicine* 64:367-383. **PMCID: PMC3625402.**

D. Research Support

Ongoing Research Support

1RF1 AG051593-01 Catalano (PI) 09/15/2016-06/30/2018 NIA

"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

1RF1 AG054176-01 Catalano (PI) 08/15/2016-07/31/2018 NIA

"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 Ib trial in early AD.

Role: Clinical Advisor

P50 AG047266-01A1 Golde (Director & Project Leader) 08/15/2015-05/31/2020 NIH/NIA

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

Major goals. The UF-MSMC ADRC focuses on 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. We recruit & train junior investigators to participate in research.

Role: Associate Director (Assoc. PL, Administrative Core)

529-13-0046-00001 Shenkman (PI) 03/01/2015-08/31/2019
Texas Health & Human Serv.-HRSA
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

6AZ05 Cottler (PI) 02/23/2016-01/31/2018
FL Dept. of Health Ed & Ethel Moore Alzheimer's
Linking Older Adults from the Community in Florida to Memory Screening and Related Health Research
This project determines best ways to screen & direct subjects to a Memory Clinic & research studies.
Role: Co-Investigator

1R01AG054077-01 Woods (PI) 09/01/2016-4/30/2021 NIH / NIA
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.

Completed Research Support
1P01 AG025204 Klunk (PI) 06/15/2011-04/30/2015 NIH
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

5 P50 AG005133 Lopez (PI) 04/01/2010-03/31/2015 NIH
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

2 P01 AG14449 Mufson (PI) 09/01/2007-03/31/2013 NIA
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

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

Evelyn F. and William L. McKnight Brain Institute of the University of Florida
P.O. Box 100015 • Gainesville, FL 32610-0015
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