McKnight Brain Research Foundation Report 2021

January 15, 2021

University of Florida

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APPENDICES

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

PO Box 100015
Gainesville, FL 32610-0015
352-273-8500 Office
352-846-0185 Fax
mbi.ufl.edu

1/19/2022

RE: MBRF Annual Report

Dear Trustees of the McKnight Brain Research Foundation,

Wow! This is my thought as I look at the report that has been compiled by Drs. Bizon, Cohen and their colleagues. The MBRF-supported UF Center for Cognitive Aging and Memory: Clinical Translational Research (CAM) is really knocking it out of the park! Even in the face of the COVID pandemic, the trajectory of the science and the output in terms of publications, trainees, and extramural funding secured are impressive. Extramural funding should not be the only measure of success, but it typically does provide a benchmark that is transparent. The current funding of CAM investigators ($15.7M and almost all from the NIH) is over a five-fold increase since 2010. That is truly impressive growth and a great measure of the success of e CAM and the investigators supported by the MBRF.
I imagine when the MBRF made its initial gift to the University of Florida that this is what they would have envisioned – a dynamic, collaborative group of investigators entwined into the fabric of the larger UF research community that is conducting world-class basic, translational, and clinical research on brain aging. Not only are the senior investigators thriving, but largely because of their esprit de corps, they have created an outstanding training environment for undergraduates, graduate students, and postdocs. Further, UF is now attracting outstanding and diverse junior investigators into the aging field. Moreover, Dr. Bizon, in her position as the permanent Chair of Neuroscience, will certainly attract more neuroscience researchers and faculty into the brain aging field. Numerous CAM faculty are regarded as the next generation of leadership within the UF Health Science Center and will no doubt influence new hires and resource allocation over the coming years.

The success of CAM investigators and the larger neuroscience and neuromedicine research programs under the MBI “umbrella” has truly been a team effort. Leadership at the University is well aware that neuroscience, in general, and brain aging research, in particular, are foundational pillars of UF’s research portfolio. Multiple CAM investigators have been recruited elsewhere in recent years. Research leadership has provided highly competitive retention packages, which ensures that these vital members of our brain aging research community stay and advance their careers here at UF. Success is not without its challenges. The growth of success of CAM and our larger neuroscience research community is straining our infrastructure. As the director of MBI I have been leading an effort to address those infrastructure needs (space and equipment) as part of a strategic plan that should be completed this year. I am working closely with the CAM directors and HSC leadership to make sure that the infrastructure needs of CAM investigators will be met so that this priority research can continue to blossom.

Although we still do not know precisely how Scripps Florida will integrate into the larger University landscape, they offer unique strengths in neuroscience research and therapeutic discovery. I will be working with other University leadership to facilitate the integration process, and I am sure that this will

further enhance interest and capabilities int e cognitive and brain aging research. Please reach out to me if there are questions about this process, and I will relay what I know. I imagine that there will be some challenges, but that in the long-run this will further strengthen our neuroscience research.

I would like to personally thank the board for pushing us to integrate our basic, translational, and clinical research supported by MBRF into a single center. Thanks to the efforts of Drs. Bizon, Cohen, Woods, and Burke, this “reintegration” has really helped to achieve the translational integration that the MBRF has long desired. It also helps us strategically within the University, as it really shows the strength and trajectory of the cognitive and brain aging programs and their scientific and institutional impacts. I hope the trustees find the rest of the document as informative and impressive as a I do.

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

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

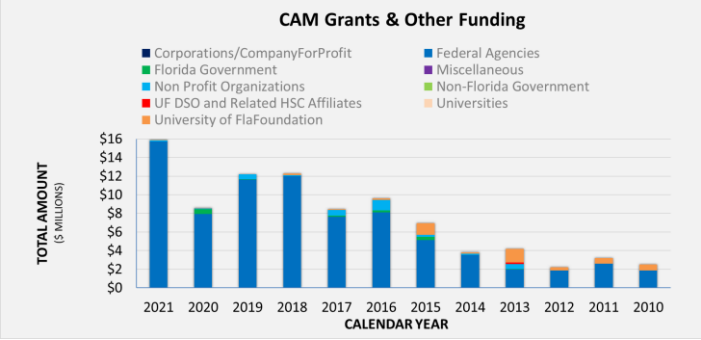
PO Box 100015
Gainesville, FL 32610-0015
352-273-8500 Office
352-846-0185 Fax
mbi.ufl.edu

January 13, 2022

Dear Trustees of the McKnight Brain Research Foundation:

We are pleased to provide this report on the activities and financial status of the Center for Cognitive Aging and Memory: Clinical Translational Research (CAM) for the year ending December 31, 2021. The CAM faculty were very productive with significant accomplishments pursuant to the center's mission to conduct cutting-edge, interdisciplinary clinical neuroscience and translational research on age-associated cognitive, behavioral and emotional functioning. Additionally, our faculty have continued to make important strides in determining how brain structure and function, metabolism, and physiology contribute to cognitive decline associated with advancing age. The overarching objective is to advance human clinical translation of findings from more basic neuroscience studies of cognitive and brain aging that can be used in clinical applications to slow, avert, or restore age-related cognitive decline and memory loss. The academic mission has also expanded to include: 1) education and research training opportunities for students, postdoctoral fellows and young faculty on the neuroscience of cognitive and brain aging, 2) development of improved vehicles for the dissemination of information on cognitive and brain aging to the public, and 3) creating an accessible platform for accessing findings and data to investigators at other institutions. Considerable progress was made in this regard over the past year. As discussed in last year's report, the Center for Cognitive Aging and Memory Clinical Translational Research (the "CAM Center") now encompasses both the Age-Related Memory Loss Core Program ("ARML Core Program") and the Cognitive Aging and Memory Clinical Translational Research Program ("CAM-CTRP"). Our leadership continues to meet weekly and is building the necessary infrastructure to support a successful world-class program on cognitive aging that spans preclinical to clinical translation research. While the pandemic had halted all new hiring in 2020, these restrictions have been eased over the course of 2021. In September, we were very fortunate to bring Kathleen (Katie) McIntyre on to our CAM administrative team. Katie's prior work experience includes time as an administrator in the Pharmacology department in the UF College of Medicine and many years working as a high school English teacher. Her unique background offers the combined organizational, communication, and administrative skills that make her a perfect fit for establishing a top-notch communications plan and offering the administrative support needed to build our CAM community locally, nationally and beyond. She joins Tina Lacy who continues to offer outstanding fiscal and accounting support to the CAM Center. With Katie and Tina's administrative services, we have ambitious goals for increasing our community events and outreach as well as increasing new content our website and social media to better promote CAM researchers and the MBRF mission. Other highlights of CAM's research, education, and outreach activities are summarized below with more detailed information in the body of the report.

RESEARCH PRODUCTIVITY: The CAM faculty continue to be very productive in their research activities with multiple ongoing and new R01 and P01 projects in the past year. Extramural funding this previous reporting period totaled a remarkable $15.7 million. Twenty-six new grants from NIH and other government agencies were awarded to faculty of the CAM.



CTRP: Collaboration of the CAM with the HIV center at UF led to NIAAA awarding us a P01 program project (Cohen, MPI) that focuses on HIV, alcohol use, and aging. A large U24 data science grant was also received that supports the P01 and other neuroHIV studies being conducted by Cohen, Porges, Gullett, Fang, Williamson, and Lamb. Dr. Cohen received funding as a co-I to support two clinical trials focused on enhancing cognitive function and weight reduction in older adults: one examining the benefits of nutritional supplementation with flavanol in a large Boston cohort (R56), the other examining the benefits of mindfulness training in older adults with heart failure (R01, pending). Drs. Cohen and Williamson are also co-Is on VA Merit Award (Rose, PI) that focuses on enhanced motor function and neural plasticity (fMRI) in older VA patients who have had a strong hemiparesis. Dr. Woods was awarded two large R01s for clinical trials focusing on neuromodulation and/or cognitive training in older adults and is MPI with Dr. Marsiske on new T32 grant that supports the training of graduate students using non-pharmacological approached to treat cognitive aging. In addition to his role as a co-I on several of grants already mentioned, Dr. Williamson is PI of a new Department of Defense Grant focusing on TBI and PTSD, as well two foundation grants. Dr. Porges received an R01 to study GABA in aging, along with being PI on research component 2 of the P01.

ARML Core Program: As are detailed in the main report, numerous new funding has been awarded to investigators who affiliate with the ARML Core Program. These include National Institute of Aging (NIA)-supported funding (RF1) grant was awarded (Bizon, Setlow, MPIs, Burke co-I) to support preclinical research investigating mechanisms and therapeutic potential of vagus nerve stimulation (VNS) in aging and Alzheimer's disease. Drs. Bizon and Setlow also received a new R01 from NIA to study the effects of acute and chronic cannabis use on cognitive function in the context of aging. Dr. Burke received a competitive renewal for her R01 (now converted to an RF1) that is aimed at bridging levels of analysis from single cells to networks to understand how functional connectivity is related to cognitive aging. Several other CAM faculty members are co-Is on this award (Lamb, Maurer and Bizon). Drs. Burke and Mauer (MPIs; Bizon and Setlow co-Is) further received a new R01 grant to study assays of hippocampal-prefrontal circuit engagement for future application in therapeutic development. Drs. Ashok Kumar and Tom Foster also received a new R21 award to continue their long-standing work investigating NMDA receptor dysfunction as an underlying cause of age-associated cognitive decline.

A critical mission for the ARML core program is to recruit, train and support a diverse cadre of outstanding individuals into the field of cognitive aging. To this end, the ARML core program has initiated a pathway program (CAM Summer Scholars) this past year. This program supported a research-intensive summer internship in ARML-laboratories for four talented undergraduates. Notably, Dr. Burke has received a fundable score as lead PI on a new undergraduate training grant (R25), which is pending council review at the NIA. This award, entitled: "Neurobiology of Aging to Advance Diversity (NEURON-Aging)," will develop and expand research education and opportunities for underrepresented students interested in aspects of cognitive aging and dementia.

ONGOING LINES OF RESEARCH:

CTRP: Considerable effort was directed at continuing ongoing studies supported by NIH and other agencies (including the MBRF, which was quite successful despite occurring against the background of COVID-19. The ACT study (Woods, Cohen, Marsiske, MPIs) is entering the final months of the clinical trial which will yield a final sample of 300 participants. To date, findings from analyses of baseline data have been published, and analyses of the longitudinal data will occur in the spring after the study blind is broken in early spring of 2022. We anticipate soon being able to examine the cognitive and neuroimaging outcomes then for this study, which is the largest neuromodulation study to date directed at enhancing cognitive aging. The WISE bariatric study (Cohen, PI) is also in the final six months of follow-up assessments. Publications have been published and submitted addressing preliminary findings. Multiple manuscripts are being prepared focusing on improved cognitive and brain functioning associated with marked reductions in body mass and diabetes status (A1C) in morbidly obese adults, including examination of whether effects vary as a function age. The results thus far are intriguing and

consistent with our original hypotheses. Obesity was found to be associated with baseline cognitive performance deficits and abnormalities in cerebral metabolic state (MRS) and functional brain response (fMRI). Three months after surgery, participants have reduced BMI and A1C levels, are exhibiting improvements in executive-attention functioning and processing speed which are associated with neuroimaging changes. Other NIA supported R01 studies were funded at Tufts University and Brown University this year that focus on cognitive aging and related age-associated behavioral functions. At Tufts, Dr. Cohen is a co-Investigator (Roberts, PI) supporting a large study of the effects of nutritional supplementation with flavanol on cognitive functioning in older adults. We will be using the NIH-Toolbox as a primary outcome measure. At Brown, Dr. Cohen is also collaborating with Elena Salmoirago-Blotcher, MD on a clinical trial to examine the effects of mindfulness training on cognitive functioning in older adults. We published preliminary study findings this year "Exploring Effects of Aerobic Exercise and Mindfulness Training on Cognitive Function in Older Adults at Risk of Dementia: A Feasibility, Proof-of-Concept Study".

Multiple R01 projects are in progress or nearing completion addressing HIV, substance use and aging including the NIA funded ROGUE study. This project focuses on gut-brain axis and the impact of the microbiome on cognitive and brain functioning in the context of aging among people living with HIV. A major achievement this year is that funding of P01 and U24 grants from NIAAA on which I am MPI along with Robert Cook, MD. One of the core research components of the P01 is being led by Dr. Eric Porges (CAM faculty) examining the effects of vagus nerve stimulation and probiotic supplementation in people living with HIV who consume large quantities of alcohol. The P01 project was made possible through collaboration of CAM with SHARC center at UF. The U24 is a complementary study which will develop a data science core for the P01 and our other HIV data. Dr. Joseph Gullett (CAM faculty) is leading the study's neuroimaging data core. Dr. Cohen's current research also includes: 1) Analyses of longitudinal cognitive and cytokine outcome data associated stem cell transplantation; 2) Analyses of function imaging findings on cognitive/brain function in older adults without MCI with focus on visual perception and semantic functioning; and 3) Neuroimaging study of age-associated differences in functional brain response during music processing in older adults during discrimination and production of simple and complex (syncopated) rhythm. Talia Seider's dissertation project "An fMRI studies of age-associated changes in basic visual discrimination" were published in Frontiers in Aging Neuroscience and Brain Imaging and Behavior. These analyses show subtle age-associated changes in functional brain response, though overall preservation of neural response during visual perception was evident in older adults. Likewise, in another manuscript submitted to Frontier in Aging Neuroscience, that focuses on neuroimaging findings in the context of semantic processing and aging. We found relatively preserved functional connectivity across neural networks during semantic decision making with in older adults, findings that provide further evidence that age-associated cognitive decline and brain dysfunction are not ubiquitous as people age.

Dr. Woods continues outstanding research focusing on neuromodulation, cognitive training, and neural plasticity in the context of advanced age. Dr. Woods is a tenured Associate Professor and is being reviewed for promotion to Professor in 2022. He is a phenomenal scientist, teacher, and leader. His research portfolio grew last year to 4 concurrent R01's with the addition of two newly funded projects. In the 2021 fiscal year, he was recognized as the top funded investigator in the College of Public Health and Health Professions amassing approximately 3.6 million dollars in total funding for the fiscal year. He is recognized internationally for his research on neuromodulation in the context of aging and is playing a central in the development of the artificial intelligence (AI) initiative within the UF Health Science Center. This includes the recruitment of faculty with expertise in this area, including Aprinda Indahlastari, Ph.D. She is now a Research Assistant Professor in the CAM with salary support through the AI initiative and start-up funding provided across CAM-CTRP, the Health Science Center's Senior Vice Presidents office, the College of Public Health and Health Professions and the Department of Clinical and Health Psychology.

Dr. Porges is being considered for promotion to Associate Professor and tenure in CHP. He has become

a leader in studies of cerebral metabolic function in older adults with a particular focus on GABA in the context of aging. He along with Drs. Williamson, Lamb, and Cohen are involved in multiple studies employing Vagus nerve stimulation (VNS) (a neuromodulation approach) to enhanced cognitive function and neuroinflammatory and other adverse physiological changes occurring with advanced age. Dr. Williamson in collaboration with Dr. Porges, Lamb, and Cohen are employing VNS in funded studies of healthy older adults, MCI, and PTSD/TBI. Dr. Ragu is conducting outstanding research employing AI analytic methods to study brain aging. She received funding from the UF AI initiative to support her salary. Dr. Gullett is also conducting important studies employing machine learning to develop predictive models for cognitive decline.

The CAM-CTRP continues to grow. There are 48 in people now working full time: faculty, study coordinators, an administrator, graduate students, post-doctoral fellows, and undergraduate volunteers. There are also many affiliated faculty and students. As this growth necessitated greater office space, the CTRP has moved to the Communicore Bldg. of the UF Health Science Center, approximately 3200 square feet. This move has been extremely valuable, facilitating collaboration.

ARML Core Program: Major lines of continuing research among the ARML faculty include preclinical studies of the circuitry of the hippocampus, para- hippocampal, and prefrontal cortical areas during attention, working memory, and long-term memory encoding in laboratory animals. Broadly, work in these labs in the past year has encompassed: 1) investigations of cannabis effects on the brain and cognition, 2) eating behavior and nutritional impact of specific lipid containing compounds on brain function and cognition in old rats, 3) VNS effects on the aged brain and cognition and exploration of VNS as a potential therapeutic approach for cognitive aging and Alzheimer's disease, 4) and use of epigenetic techniques to establish epigenetic biomarkers of cognitive function. comorbid conditions), and demographic variables in older adults.

Dr. Burke continues to expand her leading-edge research program and she is recognized as a scientific and academic leader in our college, university and nationally. In the past year, her laboratory continued its work focused on understanding the systems-level mechanisms of age-related cognitive decline as well as developing and testing diet-based interventions for improving cognitive outcomes in old age. She now serves as PI on three major R01 grants from NIA as well as co-I on numerous others. One highlight from this past year includes a *Neurobiology of Aging* publication demonstrating a novel behavioral assessment for rodents that promises to offer increased translational potential across species (Smith, Zequiera et al, 2021). This year Dr. Burke completed the College of Medicine Leadership Program, Mentor Academy, and a Master Mentor Certificate in Culturally Aware Mentoring, in addition to serving as Associate Editor of *Behavioural Brain Research and on the* Editorial Board of *Behavioral Neuroscience.*

Dr. Maurer was successfully promoted in August 2021 to the rank of Associate Professor with tenure in the College of Medicine. This promotion recognizes Dr. Maurer's marked contributions to the field of understanding how activity moves across the brain to support cognition and how this process changes with age. In the past year, Dr. Maurer graduated three Ph.D. students and received an Exemplary Teaching recognition from the College of Medicine. His new R01 with Dr. Burke will relate cortically recorded neurophysiological events with those recorded with an invasive electrode in order to develop methodology that can be used to infer the inner workings of deeper brain regions that are challenging to assess using conventional methods. The long-term goal of this work is to use these methods to investigate activity of deep brain regions within the context of cognitive tasks with high cross-species translatability.

Dr. Foster's research program is described in detail in the letter below. Of particular note, one of his studies from the past year identified microRNA that predicted cognition and that are linked to aging and inflammation, supporting idea that microRNA can act as an epigenetic marker or a mechanism underlying differential ageing that contributes to cognitive decline (Gullett 2020).

As included in the main report, the ARML core faculty have continued to publish in top research outlets

as well as disseminate their work at high-impact venues. Both Drs. Foster and Bizon actively contributed to the Reserve and Resilience Collaboratory sponsored by both the National Institute on Aging and the McKnight Brain Research Foundation. Within the scope of this effort, Dr. Foster led a collaborative review paper offering a perspective on using preclinical models to investigate mechanisms of reserve in animal models. In other notable collaborations, Drs. Burke and Bizon teamed with investigators at University of Alabama to offer several perspective pieces arguing for a more comprehensive approach within the field of aging that integrates the contributions of peripheral health to brain function and cognition (e.g., Hernandez et al., 2021).

In 2021 the ARML-core program has partnered with several neuro-focused departments, the McKnight Brain Institute (MBI) and the Center for Translational Research in Neurodegenerative Disease (CTRND) to increase access to state-of-the-art microscopy. Specifically, shared costs across these entities are being invested to improve maintenance and increase availability of the latest technologies. All CAM Center faculty now have access to two light sheet microscopes that enable 3-dimensional imaging of large tissue samples, a multi-photon scope that has ex-vivo and in-vivo applications, a scope equipped with Microbrightfield software enabling implementation of cell quantification with design-based stereology, and several fluorescent scopes that offer additional high-throughput analysis options. In addition to investment in software and hardware for this facility, ARML-core funds are helping to support high caliber expertise to facilitate adoption of new technologies in CAM investigator laboratories. These facilities are expected to enhance research related to the cellular mechanisms of cognitive aging and how this relates to large-scale alterations in structure and function of brain circuits across the lifespan.

With the agreement of the MBRF trustees, the ARML Core program has continued to sponsor speakers on topics relevant to cognitive aging. To encourage a robust audience for our cognitive aging speakers, we are inviting the "Luttge" speakers as part two existing seminar series: either the joint MBI-Department of Neuroscience series or as part of a cognitive neuroscience series that is held in the Clinical Health Psychology department. The MBRF-supported honorarium from Luttge lecture funds has enabled us to bring in outstanding outside speakers where we would normally have needed to rely heavily on internal speakers due to funding limitations. In addition, we are now inviting one "Rising Star" speaker each semester. Our goal is identifying a very senior Postdoctoral Fellow or early-career Assistant Professor doing exciting work in the field. As we invite members of each McKnight Center to these talks, we hope that the "rising star" talks will facilitate recruiting the best and brightest in the field to our Institutes and help in showcasing the Evelyn F. McKnight Brain Inter-institutional network.

EDUCATION AND OUTREACH: Significant strides have been made to promote CAM's role in education, research training, and outreach. The faculty currently mentor 28 graduate students who are doing research related to cognitive aging in human and animal models. Several students successfully defended their Master's theses and doctoral dissertations this past year. Our core faculty are highly sought out to serve as primary mentor/advisor for graduate students in the Departments of Clinical and Health Psychology and Neuroscience. As a result, we are very selective and can recruit outstanding trainees.

Three T32 training grants now exist on which the CAM faculty play a major role. These include T32 programs focusing on aging and neuromodulation (Marsiske, Woods, MPIs) NeuroHIV (Cook, PI, Cohen) and Alzheimer's and related dementias (Lewis, Bizon, MPIs).

Beyond graduate students and postdocs, we have made a concerted effort to increase the cadre of junior faculty at UF conducting cognitive aging research. Through interaction and mentorship of individuals who are in the early stages of establishing their research programs, we hope to increase their ability to achieve independent funding in the field of cognitive aging and to inspire a career-long interest and dedication to this research area. Notably, two individuals, Matt Burns, MD. Ph.D. and Aprinda Indahlastari, Ph.D., who began at postdoctoral fellows training in the CAM Center were recently promoted to Assistant Professors in the Departments of Neurology and Clinical Health Psychology,

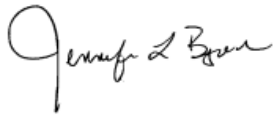
respectively. Dr. Burns received a K08 from the NIA to help launch his independent career. Full biosketches for Dr. Burns and Indahlastari can be found in **Appendix 1**.

We continue to make progress in solidifying and expanding our cognitive aging community at UF. In addition to our primary CAM Center faculty and trainees, we are increasing our connections many more UF faculty conducting research on related topics such as traumatic brain injury, stroke, substance use disorders and neurodegenerative disease. We are also increasing our integration of artificial intelligence (AI) into our research, taking advantage of UF's growth in this arena. Machine learning and AI can offer new insights into predicting declining cognition, as well as facilitate and increase efficiency of numerous analytical approaches such as imaging and genetics. To help build our AI community at UF and spur interactions and collaborations, the CAM Center co-hosted a "local meetup" to view a virtual computational neuroscience event organized that featured prominent speakers from all over the world. By bringing our local community together to view this conference, we were able to foster networking, mentorship between faculty and trainees and visibility of the growing AI community at UF with our online community interactions during this event. Other developments include the implementation of the CAM website which greatly enhanced our presentation to the UF community, faculty and students at other institutions, and the public.

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



Jennifer L. Bizon, Ph.D.
Professor and Chair
Department of Neuroscience
College of Medicine
Co-Director, Center for Cognitive Aging and Memory (CAM Center)

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

PO Box 100015
Gainesville, FL 32610-0015
352-273-8500 Office
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January 13, 2022

Dear Trustees of the McKnight Brain Research Foundation:

This report summarizes my activities as the Evelyn F. McKnight Chair for Clinical Translational Research in Cognitive Aging and in my role as Director of Clinical Translational Research within the Center for Cognitive Aging and Memory: Clinical Translational Research (CAM-CTRP) for the year ending December 31, 2021. I along with the faculty and staff of the Center were extremely productive despite the challenges of COVID-19. Our planned research objectives were met, and we had multiple achievements consistent with the Center's mission.

With respect to my own research activities, multiple funded R01 projects continue with significant progress on several. The ACT study on which I am MPI with Drs. Woods (lead PI) and Marsiske is entering the final months of the clinical trial. To date, we have published findings from analyses of baseline data, and will begin analyses of the longitudinal data and outcomes after the study blind is broken in early spring of 2022. We are excited to determine the results of what is the largest neuromodulation study dataset to date directed at enhancing cognitive aging. The final six months of the WISE bariatric study (Cohen, PI) will also result in multiple manuscripts regarding brain improvements associated with alterations in body mass index (BMI) and diabetes status, including examination of the contribution of aging to outcomes in the cohort. Two papers have been published, two others submitted for publication, and four others being prepared to submission, though the outcome findings will not be available until the formal end of the study. The results thus far are intriguing and consistent with our original hypotheses. Obesity was found to be associated with baseline cognitive performance deficits and abnormalities in cerebral metabolic state (MRS) and functional brain response (fMRI). Three months after surgery, participants have reduced BMI and A1C levels, are exhibiting improvements in executive-attention functioning and processing speed which are associated with neuroimaging changes.

The McKnight Brain Aging Registry (MBAR) study is now complete with respect to recruitment and the assessment of participants. The database has gone through extensive quality control processing and is now largely complete. The MBAR normative data will be posted on the Center for Cognitive Aging and Memory (CAM) website in the coming months. Multiple analyses have been conducted and several manuscripts are ready to be submitted and abstracts presented at scientific meetings. It is not possible to describe the various findings to date in this letter. However, to summarize the most striking overall observation is the degree to which our participants who are over 85 years of age have relatively preserved cognitive functioning and remain highly active in physical activities including aerobic and strength exercise. We have been asked to do another special edition for Frontiers in Aging Neuroscience that focuses on this study, though the interinstitutional investigators felt this was not feasible until perhaps later in 2022.

Other NIA supported R01 studies were funded at Tufts University and Brown University this year that focus on cognitive aging and related age-associated behavioral functions. At Tufts, I am co-Investigator (Roberts, PI) supporting a large study of the effects of nutritional supplementation with flavanol on cognitive functioning in older adults. We will be using the NIH-Toolbox as a primary outcome measure. At Brown I am collaborating with Elena Salmoirago-Blotcher, MD on a clinical trial to examine the effects of mindfulness training on cognitive functioning in older adults. We published preliminary study findings

this year “Exploring Effects of Aerobic Exercise and Mindfulness Training on Cognitive Function in Older Adults at Risk of Dementia: A Feasibility, Proof-of-Concept Study”.

Multiple R01 projects are in progress or nearing completion addressing HIV, substance use and aging including the NIA funded ROGUE study. This project focuses on gut-brain axis and the impact of the microbiome on cognitive and brain functioning in the context of aging among people living with HIV. A major achievement this year is that funding of P01 and U24 grants from NIAAA on which I am MPI along with Robert Cook, MD. One of the core research components of the P01 is being led by Dr. Eric Porges (CAM faculty) examining the effects of vagus nerve stimulation and probiotic supplementation in people living with HIV who consume large quantities of alcohol. The P01 project was made possible through collaboration of CAM with SHARC center at UF. The U24 is a complementary study which will develop a data science core for the P01 and our other HIV data. Dr. Joseph Gullett (CAM faculty) is leading the study’s neuroimaging data core.

I have been author and co-author on multiple manuscripts this past year. One that I am particularly happy about stemmed from the dissertation project of Talia Seider, PhD which was published in Brain Imaging and Behavior, “An fMRI study of age-associated changes in basic visual discrimination”. This study shows some subtle changes in functional brain response, though overall there was preservation of neural response during visual perception. I recently submitted another manuscript to Frontier in Aging Neuroscience with data from Amanda Garcia, PhD dissertation project that focuses on neuroimaging findings in the context of semantic processing and aging to based PhD. Functional brain response on fMRI was also largely preserved during semantic decision making with advanced age. These findings are important as they provide further evidence that age-associated cognitive decline and brain dysfunction are not ubiquitous as people age.

The CAM-CTRP continues to grow. There are 48 in people now working full time: faculty, study coordinators, an administrator, graduate students, post-doctoral fellows and undergraduate volunteers. There are also many affiliated faculty and students. Given this growth it was necessary to acquire greater office space. Consequently, we have moved into the UF Health Science Center Communicore Building occupying approximately 3200 square feet. This move has been extremely valuable, facilitating collaboration. When I arrived at UF in 2012, I was the only faculty member, and for the first two to three years, the CAM-CTRP had two core faculty members (Cohen, Woods), and two graduate students. We have grown exponentially; CAM’s growth is attributable to two factors: 1) the success of our faculty in obtaining funding from NIH with multiple projects in progress, and 2) a significant increase in the number of faculty, students and staff following the merger of the Age-Related Memory Loss program into the Center. Many graduate students and fellows with academic interests in cognitive and brain aging are now part of CAM with several having completed their dissertations and moved on to academic positions at other institutions. Our core faculty is highly sought out to serve as primary mentor/advisor for graduate students in the Departments of Clinical and Health Psychology and Neuroscience. As a result, we are very selective and are able to recruit outstanding trainees. Drs. Williamson and Lamb have received grants from NIH and VA, which has led to additional CAM-affiliated staff and students.

A major initiative was accomplished with merger of the Age-Related Memory Loss (ARML) program into the Center. Collaboration between the faculty of the two programs, including research initiatives and also implementing joint training opportunities. This merger facilitates translating discoveries from animal models to humans. It also enables the integration of resources and expertise, and further strengthens the visibility of the Center. This was achieved in part by the development and implementation of a Center website that is linked to the MBI web site.

I am proud of how the CAM has flourished over the past 10 years, particularly the success of the faculty that I recruited. Several received career development awards from NIH, which they used to catalyze their academic careers. Dr. Woods is a tenured Associate Professor and is being reviewed for promotion to Professor in 2022. He is a phenomenal scientist, teacher and leader. His research portfolio grew last year to 4 concurrent R01’s with the addition of two newly funded projects. In the 2021 fiscal

year, he was recognized as the top funded investigator in the College of Public Health and Health Professions amassing approximately 3.6 million dollars in total funding for the fiscal year. He is recognized internationally for his research on neuromodulation in the context of aging and is playing a central in the development of the artificial intelligence (AI) initiative within the UF Health Science Center. This includes the recruitment of faculty with expertise in this area, including Aprinda Indahlastari, Ph.D. She is now a Research Assistant Professor in the CAM with salary support through the AI initiative and start-up funding provided across CAM-CTRP, the Health Science Center's Senior Vice Presidents office, the College of Public Health and Health Professions and the Department of Clinical and Health Psychology. Dr. Eric Porges has been successful in becoming an independent investigator with NIH funding. He will be reviewed for tenure and promotion to Associate Professor in 2022. His neuroimaging research, particularly with respect to age-associated cerebral metabolic function assessed through magnetic resonance spectroscopy (MRS) is cutting edge. This includes important MRS studies focused on cerebral GABA concentrations of older adults, and also glutathione, a potential biomarker of age-associated oxidative stress in the brain. Dr. Porges has played a key role in supporting and extending my NeuroHIV research and also mentoring graduate students in the CAM. He is also conducting important research on vagus nerve stimulation (VNS) to enhance age-associated cognitive functioning in collaboration with Dr. John Williamson and myself. Drs. Porges and Williamson are MPIs on the renewal proposal of my R01 study of bariatric surgery which will be submitted in 2022. A vagus nerve stimulation pilot study is underway (Williamson, PI) funded by the MBRF. Dr. Williamson is also now funded on Veterans Affairs Merit Award (R01 equivalent) to study VNS in the aging, specifically focusing on its effects on sleep architecture in adults with and without mild cognitive impairment (MCI). He also is conducting important on traumatic brain injury and aging supported by the Veterans Affairs and Department of Defense. Dr. Williamson played a major role in the renewal of Veterans Affairs Brain Rehabilitation Research Center (VA BRRC), and he leads the cognition core. This work is also in collaboration with Dr. Damon Lamb, who was awarded a career development award to study age-associated changes in neural response using fMRI. Dr. Joseph Gullett, a Research Assistant Professor has also been a great addition to our faculty. He recently published an outstanding study employing structural MRI and resting state fMRI to examine conversion to dementia among older adults experiencing mild cognitive impairments. Together these indices were 94% accurate in predicting conversion. Dr. Jennifer Bizon is leading an outstanding core faculty in CAM conducting more neuroscience investigators of aging in animal models, which is described in considerable detail in this annual report. The CAM has clearly matured over the past ten year, with outstanding and students. I am proud to lead the center, providing vision, facilitating research, and mentoring faculty and students. I am certain they will make important scientific contributions for many years to come.

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

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

PO Box 100015
Gainesville, FL 32610-0015
352-273-8500 Office
352-846-0185 Fax
mbi.ufl.edu

January 13, 2022

Dear Trustees of the McKnight Brain Research Foundation:

I am pleased to present the 2021 Annual Report of the Evelyn F. McKnight Chair for Research on Cognitive Aging and Memory. First, I would like to thank the McKnight Brain Research Foundation (MBRF) Board of Trustees for their support in my endeavors.

One of the goals of the MBRF is the promotion of collaborative efforts among research scientists, institutions, and organizations engaged in research in the field of age-related memory loss. I have been active as a catalyst in developing liaison, communication and collaboration, with individuals, units, centers and other entities within the University pursuing research in learning and memory. Below are examples of ongoing collaborations that emphasize the breath of collaborations across departments. I provide expertise on agerelated cognitive decline and deliver cutting edge and innovative techniques for characterizing gene expression and epigenetic modifications. Several of my collaborations provide examples of the translational potential of discoveries and epigenetic techniques developed in my lab.

Promoting Collaboration within the University of Florida

Ongoing collaborations:

Sepsis is a common, expensive, and inadequately managed syndrome and has been labeled 'a disease of the aged,' as 60% of septic patients are older than 65 years. Improved in hospital mortality has yielded a rapidly expanding population of sepsis survivors who develop cognitive impairments. Thus, decreased memory and impaired cognition is common in sepsis survivors. An ongoing collaboration has been established with the Department of Surgery, including Dr. Philip Efron (Director), Dr. Lyle Moldawer, and Dr. Frederick Moore and Dr. Michael Kladde (Department of Biochemistry and Molecular Biology), to examine age and sex differences in response to sepsis as a step toward personalized medicine. Manuscripts have been published that document our collaboration (Barter, Kumar et al. 2019, Stortz, Hollen et al. 2019) and a recent manuscript has been submitted, which examines the epigenetic profile (microRNA) in the brain, that may underlie age and sex differences in response and recovery from sepsis. Due to this collaboration, Dr. Kladde and I Chaired a Plenary Session on *Epigenetics and Exosomes in Shock* for the 43rd Shock Society Annual Conference October 11-15, 2021. In addition, several grant proposals examining age and sex differences in the response and recovery of sepsis have been submitted, including a program project grant (Project 4 Foster PI) to determine the role of cognitive reserve on the trajectory of cognitive function following surgery, which included work on older humans by Dr. Catherine Price (Department of Clinical Psychology). We recently submitted a grant proposal to examine the role of sepsis in contributing to age-related cognitive decline and brain pathology associated with Alzheimer's disease (Efron PI). This proposal also includes individuals from the Department of Neuroscience with expertise on Alzheimer's disease (Dr. Todd Golde, Dr. Paramita Chakrabarty).

Epigenetic techniques from my lab are employed to develop biomarkers to be used as diagnostic and prognostic indicators. In an ongoing collaboration with Dr. Yenisel Cruz-Almeida, from the College of Dentistry, we examine DNA methylation in the blood of older humans, and we currently have a grant (Cruz-Almeida PI) that characterizes DNA methylation in blood as epigenetic biomarker that describes biological age, and predicts cognition function, and the intensity of chronic pain. One paper has been published indicating an association of biological age, determined by DNA methylation, and measures of cognition and pain
(Montesino-Goicolea, Sinha et al. 2020). Two more manuscripts have recently been submitted, which determine the relationship between epigenetic measures of aging and other aging biomarkers (i.e., blood vitamin D levels, frailty, or decreased movement).

New Collaborations:
Considerable progress has been made on a series of collaborations to develop senolytic drug treatments. Senolytic drugs selectively remove senescent cells that chronically release stress signals (e.g., cytokines). I am collaborating with Dr Daohong Zhou (Department of Pharmacodynamics). Dr. Zhou and I share a graduate student (Vivek Budamagunta), and we have published two papers examining the role of cell senescence in contributing to increased chronic inflammation with age (i.e., inflam-aging) (Budamagunta, Foster et al. 2021, Budamagunta, Manohar-Sindhu et al. 2021). This work was featured on the cover of the journal *Aging* and was highlighted in the *Fight Aging! Newsletter*.
A Bidirectional Relationship Between Cellular Senescence and Immune System Aging – Fight Aging!

Arguing for a Central Role of Cellular Senescence in the Age-Related Susceptibility to Inflammatory Conditions – Fight Aging!

Ongoing work is focused on developing and examining the effect of senolytic drugs on brain aging and cognitive decline. A manuscript testing the effectiveness of senolytic drugs that either do or do not cross the blood brain barrier on age-related decline in cognition and motor function is expected next year. Furthermore, an NIH grant to examine effectiveness of senolytic drugs on brain aging and cognition has been submitted in collaboration with Dr. Marcelo Febo (Department of Psychiatry). This proposal will combine brain imaging and gene expression to examine the effects of senolytic treatment on the trajectory of cognitive decline, brain connectivity, and genes involved in brain maintenance and cognitive reserve.

Due to interest in determining if senolytic drugs can improve the outcome of age-related diseases in humans, I have collaborated with several members of the Department of Aging and Geriatric Research (Mankowski, Leeuwenburg, Anton), as well as Dr Zhou. We submitted a proposal for the 2022 Research Opportunity Seed Fund College of Medicine internal competition, for a pilot study to develop a pipeline for the development of senolytic drugs to treat humans. While this proposal was not funded, we continue to seek other funding sources for this intervention pilot study.

Two collaborations have been initiated this past year. Dr. Gemma Casadeus (Department of Pharmacology and Therapeutics) and I have initiated a collaboration to examine the role of sex hormones in mediating the trajectory of cognitive decline and response to inflammation. In addition, my lab has just initiated a new collaboration with Dr. Zhongwu Guo from the Department of Chemistry to examine the brain glycolipids as biomarkers and possible mechanisms contributing to a decline in learning and memory during aging.

Collaborative Projects Outside of the University of Florida:

I am collaborating with Vinay Parikh, PhD, Associate Professor, Psychology and Neuroscience Program, and Head, of the Neurochemistry and Cognition Laboratory at Temple University, Philadelphia, PA to write a review on the role of exosomes in contributing to age-related cognitive decline and as a possible source for treatments. The manuscript has been submitted.

I am a member of an NIH Work Group on Reserve and Resilience, and I am the chief author on a paper discussing method for investigating cognitive reserve in longitudinal studies (McQuail, Dunn et al. 2020). Connected with this endeavor, my lab received funding to study the use of gene expression in defining cognitive reserve, we published a manuscript (Yegla and Foster 2021) and presented the results at the 2021 MBRF annual meeting in Miami and at the Workshop on Research Definitions for Reserve and Resilience in Cognitive Aging and Dementia, October 31 - November 1, 2021, Bethesda, Maryland.

Promoting interest in research on age-related memory decline:

In my role as a scientific advisor, I provide extensive appraisals of information and professional opinion to various cross-functional working groups to support interest and progress on research directed at age-related cognitive decline. I provide expertise on age-related cognitive decline and as the Evelyn F. McKnight Chair; I bring legitimacy to proposals and programs addressing cognitive changes associated with aging. Therefore, I have taken an active and visible role in promoting research on age-related cognitive decline.

As noted above, I am a member of an NIH Reserve and Resilience Collaboratory Working Group. The goal of the Collaboratory is to come to a consensus across the research community on operational definitions to further a cohesive research goal encompassing age-related and disease related cognitive decline.

I am a Member of the Institute of Aging advisory committee, and I am involved in decisions on future research and planning for the renewal of the Older Americans Independence Center, Pepper Center Grant. As such, I am in discussions with all the major stake holders. I have promoted studies in humans and animal models, directed at examining the role of altered circadian rhythms as a biomarker and mechanism for functional decline during aging. In collaboration with Dr Karyn Essor (Department of Physiology and Functional Genomics), we have previously document altered circadian rhythms in predicting the trajectory of cognitive decline (Febo, Rani et al. 2020).

I am on the Scientific Committee for the Winter Conference on Neural Plasticity, where I promote scientific sessions related to cognitive aging. For the next meeting (Feb 2022), I have organized a session on Neural Cellular Senescence: Implication for Aging and Alzheimer’s Disease.

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

Alcohol use is one of the main factors that load for dementia and the aged brain is more sensitive to ethanol. However, previous research has focused on neurodevelopmental effects of ethanol. It is becoming increasingly clear that it is important to understand how ethanol use interacts with advancing age to influence the brain and cognition. Therefore, in collaboration with Katherine Keyes (Columbia University) and Vijay Ramchandani (NIAAA) and Doug Matthews (University of Wisconsin), I have been asked to write a review article focused on how the CNS, particularly the limbic region among others, changes during the aging process, which will serve as a resource for alcohol researchers laboring to

learn how aging impacts the CNS. This review will be published in a special issue on Alcohol and Aging. Currently, there is an April 2022 submission date with publication in later 2022.

Finally, I am actively involved in promoting aging research as a mentor and educator. In addition, to my own students interested in aging and cognition, I am a mentor for Dr. Monika Patel from JAX-ASCENT in Jacksonville, FL, providing expertise on the use of DNA methylation and the methylation clock to examine biological age and possible contributors to biological age (e.g., smoking, drug use, income, education). In addition, I am providing lectures to clinical psychology students on Animal Models of Memory Loss, and I am involved in the Institute for Learning at Oak Hammock supporting students' scholarly investigation and research on issues related to older adults and the aging process.

Again, I would like to thank the MBRF Board of Trustees for their support of my efforts. If there is any other information that I can provide, please feel free to contact me.

Sincerely,

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

Barter, J., A. Kumar, J. A. Stortz, M. Hollen, D. Nacionales, P. A. Efron, L. L. Moldawer and T. C. Foster (2019). "Age and Sex Influence the Hippocampal Response and Recovery Following Sepsis." Mol Neurobiol 56(12): 8557-8572. PMC6834928

Budamagunta, V., T. C. Foster and D. Zhou (2021). "Cellular senescence in lymphoid organs and immunosenescence." Aging (Albany NY) 13(15): 19920-19941. PMC8386533

Budamagunta, V., S. Manohar-Sindhu, Y. Yang, Y. He, D. O. Traktuev, T. C. Foster and D. Zhou (2021). "Senescence-associated hyper-activation to inflammatory stimuli in vitro." Aging (Albany NY) 13(15): 1908819107. PMC8386536

Febo, M., A. Rani, B. Yegla, J. Barter, A. Kumar, C. A. Wolff, K. Esser and T. C. Foster (2020). "Longitudinal Characterization and Biomarkers of Age and Sex Differences in the Decline of Spatial Memory." Front Aging Neurosci 12: 34. PMC7044155

McQuail, J. A., A. R. Dunn, Y. Stern, C. A. Barnes, G. Kempermann, P. R. Rapp, C. C. Kaczorowski and T. C.
Foster (2020). "Cognitive Reserve in Model Systems for Mechanistic Discovery: The Importance of Longitudinal Studies." Front Aging Neurosci 12: 607685. PMC7859530

Montesino-Goicolea, S., P. Sinha, Z. Huo, A. Rani, T. C. Foster and Y. Cruz-Almeida (2020). "Enrichment of genomic pathways based on differential DNA methylation profiles associated with chronic musculoskeletal pain in older adults: An exploratory study." Mol Pain 16: 1744806920966902. PMC7711149

Stortz, J. A., M. K. Hollen, D. C. Nacionales, H. Horiguchi, R. Ungaro, M. L. Dirain, Z. Wang, Q. Wu, K. K.
Wu, A. Kumar, T. C. Foster, B. D. Stewart, J. A. Ross, M. Segal, A. Bihorac, S. Brakenridge, F. A. Moore, S. E. Wohlgemuth, C. Leeuwenburgh, A. M. Mohr, L. L. Moldawer and P. A. Efron (2019). "Old Mice
Demonstrate Organ Dysfunction as well as Prolonged Inflammation, Immunosuppression, and Weight Loss in a Modified Surgical Sepsis Model." Crit Care Med 47(11): e919-e929. PMC6848973

Yegla, B. and T. C. Foster (2021). "Operationally defining cognitive reserve genes." Neurobiol Aging.

FY21 at a Glance

Summary of Major Scientific Accomplishments

Jen Bizon, PhD
Professor and Chair
Department of Neuroscience
Co-Director, CAM center

I am pleased to report a number of significant accomplishments from the Bizon laboratory during the 2021 year. Perhaps most notable, we secured over 5 million in new research funding that includes two new five-year R01 awards from National Institute on Aging and a new grant from the Florida Department of Health. One new award is built upon promising new findings from our laboratory that show vagus nerve stimulation can enhance forms of cognition that decline in preclinical rat models of aging. This initial work was published as part of a special issue in *Neurobiology of Learning and Memory* in October of this year. The second new NIA grant stems from our ongoing collaboration with Dr. Barry Setlow and expands upon preliminary data showing that acute and long-term cannabis use can improve cognition in aged, but not young, rats. We believe these studies are of critical importance given that older adults represent the demographic in which the largest increase of cannabis use has been observed in the past five years. Almost no studies, however, have evaluated effects of this drug in aging. The Florida Department of Health grant will also test effects of extended cannabis use on pathology associated with Alzheimer's disease. We have also continued our work on decision making and how inhibitory signaling dysfunction impacts cognitive function in aging.

We continue to disseminate our research findings, publishing 8 papers during this reporting period. Notably, three of these were a collaborative effort with our MBRF colleagues at the University of Alabama, Birmingham that had the explicit goal of bridging the fields of geroscience and neuroscience to better understand and develop therapies for brain aging. While travel was limited due to the pandemic, my lab presented our findings in a number of virtual venues this year, including Society for Neuroscience and International Behavioral Neuroscience Society meeting. I was fortunate to speak in person at the Cognitive Reserve and Resilience meeting in DC, and personally gave virtual presentations at a number of national and international meetings.

I have been active in mentoring and training individuals in the area of cognitive aging. I am a primary mentor of an MD/PhD Fellow, Dr. Matt Burns, who has received K08 award from the National institution on Aging and recently began a tenure-track assistant professor position in the Department of Neurology. I mentored two CAM Summer Scholars in my lab and graduated Sabrina Zequeira from the Neuroscience Master's Program. Sabrina has received numerous national awards in the past year and has now joined the neuroscience PhD program under my and Dr. Barry Setlow's mentorship. Another PhD student (Wonn Pyon) in my lab recently advanced to candidacy. Earlier this year, Wonn received the Robert Levitt award, a $1000 first-place recognition for his work on aging and decision making and he also received honorable mention in a National Science Foundation fellowship competition. This year, I also recruited a new PhD student (Johleen Seedansingh) whom I will co-mentor with Dr. Sara Burke and a new Master's student (Emely Gazarov) whom I am co-mentoring with Dr. Barry Setlow. All of my trainees are actively working on questions pertinent to cognitive aging. Both Wonn and Sabrina were recently appointed to an NIA-funded Training grant that will provide two full years of support for their graduate studies.

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

As co-director of the University of Florida Center for Cognitive Aging and Memory Clinical Translational Research (CAM) and Professor of Clinical and Health Psychology with joint appointments in the departments of Neurology, and Psychiatry. Currently, my research focuses on a variety of age-associated comorbidities including vascular disease and cerebral hemodynamic function, the effects of obesity and metabolic disturbances on the aging brain, medical disorders and etiological factors that may contribute to accelerated brain aging and cognitive decline, or successful cognitive aging. I was Professor of Psychiatry at Brown University, where I co-directed the Lifespan Memory Disorders Program for many years. My research was an outgrowth of interest and expertise in neuropsychology and cognitive neuroscience, with my early studies focusing on attentional influences on cognitive functions, including studies of the effects of neurological and psychiatric disorders on attentional effort and control. This led to publications focusing on the cingulate cortex, intentional behavior, and emotional processing. This research led to publication of a book, “Neuropsychology of Attention” was among the first on this topic in the field and is now in its second edition. My early clinical research focused on neurodegenerative disease in the elderly, which led to studies of vascular dementia (VaD). As MRI technology progressed, I employed neuroimaging methods to examine structural and functional alterations associated with cerebrovascular disease. As this research progressed, it became evident that it was necessary to study patients with vascular disease and risk factors before they developed dementia. This led to NIMH funded studies of cognitive and neuroimaging abnormalities associated with cardiovascular disease (e.g., heart failure), systemic vascular indices in conjunction with structural and functional neuroimaging measures. We also examine small vessel and blood-barrier disturbances that might link vascular factors with AD. My laboratory made early contributions in 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, cortical and subcortical volumetrics, and fMRI. Besides many research papers, this work led to the publication of three books; one of VaD, another on the cognitive and brain manifestations of cardiovascular disease, and a third “Brain Imaging in Behavioral Medicine and Clinical Neuroscience”, which was among the first to address neuroimaging in the study of medical disorders. My research increasingly focused on risk factors for cognitive decline, including obesity and diabetes, as well as the role of brain reward and inhibitory control systems in obesity. This research resulted in my current ongoing R01 study examining cognitive and brain (neuroimaging) improvements following weight loss and better glucose regulation following bariatric surgery. I have extensively studied other medical conditions occurring in the context of aging, most notably neuroHIV. A major emphasis on my research over the past decade has been translational research on factors that affect the brain and cognition in in the context of normal aging. The Augmenting Cognitive Training R01 (Woods, Cohen, Marsiske, MPIs) which is in final year exemplifies these efforts, as it is one of the largest Phase 3 clinical trials to date examining whether neuromodulation via transcranial direct current stimulation (tDCS) enhances the benefits of cognitive training in older adults. The development of a cognitive and neuroimaging registry of the oldest old who are successfully aging is another example of these efforts, as is research employing Vagus nerve stimulation (VNS) to enhance cognitive and health outcomes

Sara Burke, PhD
Associate Professor
Department of Neuroscience
Associate Director, CAM center

2021 was marked by several scientific achievements for the Burke laboratory. Our research program continues to focus on understanding the systems-level mechanisms of age-related cognitive decline as well as developing and testing diet-based interventions for improving cognitive outcomes in old age. In support of this, I renewed my NIH/NIA R01/RF1 for another 5 years entitled, "The Contribution of Declines in Functional Connectivity to Cognitive Aging." The focus of this grant is to integrate systems-level and cellular analyses of neural activity by combining 3-dimensional cellular imaging using light sheet microscopy with resting sate functional MRI. This award is also supporting a new collaboration with investigators at the MIT Lincoln Laboratory that are develop machine learning approaches to combine different modalities and analyze large imaging datasets.

Integral to the research mission of both my lab and the CAM is the training of graduate and undergraduate students. I have recruited 2 new graduate students this year, Aleyna Ross and Johleen Seedansingh. Johleen will be co-mentored by myself and Dr. Bizon. I also mentored a CAM Summer Scholar (Elena Garcia), who just applied to the UF Biomedical Sciences-Neuroscience PhD program. Moreover, I have also recruited 6 new undergraduate students and I am excited to foster their interest in normal aging. To continue to support undergraduate research opportunities I also submitted and R25 training grant to the NIH/NIA, entitled "Networking and Expanding Undergraduate Research on the Neurobiology of Aging to Advance Diversity (NEURON-Aging)" with Drs. Jeremy McIntyre and Jose Abisambra. We were delighted that this grant received a fundable score, and we hope to be able to provide enhanced research opportunities for underrepresented students both from UF and other colleges/universities starting this summer.

We have also continued to disseminate our research findings regarding mechanisms of cognitive aging both with research publications and with formal seminars and research symposia. This past year, my laboratory has published 7 papers on the topic of cognitive aging. Three of these were a collaborative effort with our MBRF colleagues at the University of Alabama, Birmingham that had the explicit goal of bridging the fields of geroscience and neuroscience to better understand and develop therapies for brain aging. Although the pandemic continued to limit travel, I gave 4 invited seminars (1 international) and my trainees presented at the annual meeting of the Florida Consortium on the Neurobiology of Cognition and the virtual Society for Neuroscience meeting.

Adam J. Woods, PhD
Associate Professor
Department of Clinical Health Psychology
Associate Director, CAM center

The Woods Lab has experienced another year of significant growth with 25 PhD students, postdocs, full time staff and junior faculty in the lab. The lab was awarded 2 new R01s in the past year. With 4 concurrent R01s (ACT trial, REVITALIZE trial, PACT trial, AI tDCS study) and $3.6 million in research funding for the last fiscal year alone, the Woods Lab continues to forge new ground in the remediation of age-related cognitive decline and prevention of dementia. Our most recent

work using artificial intelligence to derive precision dosing approaches for brain stimulation in older adults and predict future cognitive and functional decline has been highlighted in both local and national media over the past year. Our precision medicine work was also featured in the Society for Neuroscience Annual report. In addition, Dr. Woods was recognized for being the top funded investigator in the college of Public Health and Health Professions for the 2020-21 fiscal year. At present, Dr. Woods is training 2 post-doctoral fellows and 9 graduate students. These trainees have accumulated over 15 awards in the past year alone. Graduate student Alejandro Albizu was awarded a prestigious NSF Graduate Research Fellowship during this past year, with only 1000 such awards given across all fields of science and all graduate students across the US in a single year. In addition, Dr. Woods published 26 peer-reviewed manuscripts in 2021 in top-tier journals such as Brain Stimulation, Neuroimaging, GeroScience, etc. Finally, Dr. Woods was able to negotiate ~3200 square feet of continuous office space for the CAM-CTRP arm of the center to bring, for the first time, all 35 core CTRP faculty, trainees and staff under the same roof. This has been a long-term goal over the past 6 years as our group has continued to experience exponential growth. The Woods Lab also continues to work toward further growth, with a $26 million R01 (potentially #5 in the lab) currently under review, playing central roles in the UF Health Artificial Intelligence Initiative, new partnerships with NVIDIA, new clinical trial collaborations with UF Jax, and a growing number of post-docs transitioning to junior faculty in the lab group. 2022 is already on track for a year of record growth within the lab and our expanding portfolio of promising non-pharmacological interventions for remediating age-related cognitive decline.

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

The Foster lab has continued to make strides in three core areas that are fundamental to understanding age-related memory loss: Cognitive reserve, Cellular Senescence, and Inflammation. Regarding the Cognitive reserve, variability in the trajectory of cognitive decline is related to genetic factors and biomarkers of aging that are responsive to the environment and the history of experience (e.g. history of infection). This variability has led to a call for new approaches for understanding how the environment and history of life experiences could mediate “better-than-expected” cognition for a given level of brain aging or pathology (i.e. cognitive reserve). I served on an NIH sponsored committee to define cognitive reserve. I published a review on how to employ longitudinal studies to examine cognitive reserve and (McQuail et al., 2020) and a study demonstrating how gene expression can be used to examine cognitive reserve (Yelga and Foster, 2021). It was concluded that most cognitive reserve genes represent a form of resilience to the stressors of aging, including genes that are anti-inflammatory. Finally, I presented the results of this work at several meetings.

In relation to cellular senescence, we have established collaborations (Dr Zhou) and submitted grants directed at the idea that age-related cognitive decline is linked to cell senescence in the periphery, which contributes to an increase in systemic inflammation, sometimes referred to as “inflammaging”. This included a review of aging of the immune system (Budamaguntaet al., 2021a), which was highlighted in the Fight Aging! Newsletter.https://www.fightaging.org/archives/2021/08/a-bidirectional-relationship-between-cellular-senescence-and-immune-system-aging/. Another project tested the hypothesis that senescent cells play a central role in this age-associated pathology due to their expression of the senescence-associated secretory phenotype (Budamaguntaet al., 2021b). We demonstrate that, in response of senescent cells to inflammatory stimulation, senescent cells exhibit hyper-activation, increasing the production of inflammatory cytokines and chemokines. These findings suggest

that senescent cells play an important role in the age-related increases in the susceptibility to developing an exacerbated inflammatory response. Current work and submitted grants will examine the potential to use senotherapeutics to ameliorate the severity of various devastating inflammatory conditions in the elderly, including cognitive decline. This work was highlighted in Fight Aging! Newsletter https://www.fightaging.org/archives/2021/10/arguing-for-a-central-role-of-cellular-senescence-in-the-age-related-susceptibility-to-inflammatory-conditions/. In addition, I have sponsored a session for the Winter Conference on Neuroplasticity, addressing the role of cellular senescence on brain aging.

To further enhance our understanding of the role of inflammation on cognitive aging, grants have been submitted in collaboration with the UF School of Medicine (Dr Efron) to examine the role of systemic infection on brain and cognitive aging (Darden et al., 2021) and I Chaired a session for the annual Shock Society meeting (2021) on this subject. Examination of the mechanisms for inflammation mediated cognitive impairment indicated that the mechanism is not due to activated microglial cells alone (Yegla et al., 2021). Rather peripheral inflammation associated with sepsis or COVID, contributes to the impairment. Concern about the history of inflammation on cognition has increased due to the COVID-19 pandemic and neurological features of the disease, which suggest possible long-term effects. We demonstrate that the history of systemic inflammation is one component of environmental factors that contribute to the susceptibility to age-related brain changes and associated trajectory of cognitive decline that emerges in advanced age (Barter et al., 2021). Other projects are directed at precision medicine, using genomic and epigenetic techniques to understand sexually dimorphic response to inflammation and the trajectory of cognitive decline. Finally, we employed epigenetics to provided evidence that DNA methylation underlies the closing of estrogen's therapeutic window and beneficial effects on cognition (Sinha et al., 2021) and that DNA methylation associated with aging is a marker for pain severity in humans (Montesino-Goicolea et al., 2020).

In the past year, the Foster lab has published 7 papers on the mechanisms of cognitive aging across these topics. Moreover, lab members have continued to disseminate data at both local and national meetings.

Karina Alvina, PhD
Assistant Professor
Department of Neuroscience
Member, CAM center

The Alviña lab was established in the UF Department of Neuroscience in Fall 2020. Our long-term research goal is to understand how cells in the nervous system communicate with each other in normal and pathological conditions, specifically during aging and age-associated neurodegenerative disorders. In support of this goal, I have led projects that range from studying intrinsic properties of single brain cells to *in vivo* studies of behavior and mechanisms underlying neurological disorders. I also have extensive training in neurophysiology, specifically in the use of acute brain slices to study electrophysiological properties of cells and neural circuits using rodents as animal models. As such, my first interest is in understanding neural mechanisms that lead to aberrant responses caused by stress and aging-associated processes of neurodegeneration. My research is also focused on understanding how environmental manipulations such as diet and exercise can be used as resilience agents.

In the short time since I have been at the University of Florida, which has almost exclusively been during the COVID pandemic, I have already been selected as an AlzSTAR Fellow for the 1Florida

Alzheimer's Disease Research Center (1FL ADRC; Mentors: Bizon, Lewis and Tansey) and received an Ed and Ethel Moore Alzheimer's Disease Research Program Pilot grant from the Florida Department of Health. In 2021, we collected new data on the effects of exercise as stress resilience mediator. We have new exciting findings that suggest strong sex-dependent effects. This year we were also able start the lab's colony of CRND8 transgenic Alzheimer's mouse model, which will be used to test exercise-related pathways that can potentially help counteract or treat the effects of neurodegeneration. In addition, we published 3 new research papers, and several students presented at major conferences including the 2021 Society for Neuroscience and ABRCMS.

Matt Burns, MD, PhD
Assistant Professor
Department of Neurology
Member, CAM center

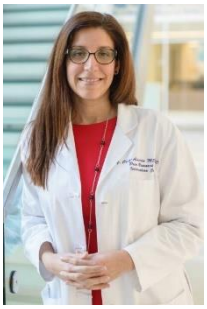
I am a physician-scientist who obtained his MD/PhD in 2014 from the University of Illinois at Chicago. I then completed a residency in Neurology in 2018 at the University of Chicago Medical College. In 2018, I started a postdoctoral position supported by a fellowship on movement disorders from the Fixel Center for Neurological Disorders at the University of Florida. My research is currently focused on the mechanisms of cognitive dysfunction that occur as a consequence of normal aging and age-associated diseases such as Parkinson's disease. My mentored awards are focused on determining how aging and synuclein pathology affect executive functioning and decision-making. I am also further assessing how deep brain stimulation in the prefrontal cortex may be effective at remediating cognitive deficits. Since joining UF, I have been selected as a KL2 Pepper Center awardee and recently transitioned to tenure-track Assistant Professor in the Department of Neurology.

Over last calendar year, I completed my clinical and research fellowship training in movement disorders and neurodegeneration, was awarded Mcknight Brain Institute/Fixel Institute Clinical & Post-doctoral Fellowship, the McKnight Clinical Translational Research Scholarship in Cognitive Aging and Age-related Memory Loss, and a K08 from the NIA on Cognitive and Affective Network Dysfunction and Neuromodulation in Aging and Synucleinopathy. I established my laboratory under the mentorship for Drs. Barry Setlow, Jen Bizon, Ben Giasson, and Marcelo Febo, and trained 5 undergraduates in high field animal MRI imaging, rodent behavioral assessments, and immunohistochemistry. I established two subspecialty clinics at the Norman Fixel Institute for Neurological Diseases in synucleinopathies, dementia, and ataxia. Finally, I presented at several national patient organizations and foundations including the Parkinson's Foundation and the National Ataxia Foundation.

Russell Bauer, PhD
Professor
Department of Clinical and Health Psychology
Member, CAM center

The RR&D Brain Rehabilitation Research Center at the Malcom Randall VA (Russell M. Bauer, Ph.D., Director) completed its 22nd year of continuous funding with an excellent track record of funding (a 5.6:1 leverage ratio) and publications. We have made significant progress on establishing a biomarker and neuroimaging core to be used by all preclinical and clinical investigators that will forge links between studies along the translational continuum. The focus of the BRRC continues

to be to develop, test, and implement novel treatments that harness neuroplastic mechanisms in the rehabilitation of neurological deficits after traumatic brain injury, stroke, and spinal cord injury. We expanded our Career Development Program and our program of outreach to Veterans. Center investigators were responsible for 56 new peer-reviewed publications, 16 in-press articles, 7 chapters in commissioned books, and 48 presentations at 10 scientific conferences. Two of Bauer's doctoral trainees (Leslie Gaynor, Gabrielle Hromas) successfully obtained their Ph.D.'s during the past year.



Yenisel Cruz-Almeida, PhD
Associate Professor
Department of Dentistry
Member, CAM center

As a clinical neuroscientist, my research interests continue to focus on understanding age-related pain perception and modulation in humans. Using multiple interdisciplinary and translational approaches, my research examines nervous system factors contributing to the observed inter-individual differences in pain phenotypes and its functional consequences including cognitive and mobility impairments.

In this reporting period, we have made significant progress on our NIA-funded R01 entitled "*Mechanisms of Oxytocin's Analgesia in Older Adults*" for which we received CAM funds to augment our neuroimaging project. Specifically, have refined our IRB protocol for the study and the IND for the drug compound has been updated. Both the drug and the placebo have been compounded at the Investigational Drug Services at UF and spray supplies (spray bottles and pumps) have been received from collaborating companies (SGD-Pharma and Aptar Pharma). We have fully trained study staff including several trainees from under-represented backgrounds. Related to this project, we have submitted and have had accepted several manuscripts, as well as submitting NIH grants, including receiving a 2% on a 3rd RO1 on pain, brain aging, and mobility. In total, my research group has published 12 papers in 2021 and I am currently organizing a program project grant with CAM researchers to examine how osteoarthritis impacts cognitive outcomes in older adults.

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

My research program spans data, brain and cognitive aging. I focus on how to evaluate brain health, via mining the big medical data, and how to make medical imaging higher quality and lower risk for the broad population. My current research is rooted in the big medical data and brain dynamics understanding in order to develop innovative computational models to understand, diagnose and treat brain disorders in big and complex data. Through productive collaboration with CAM and College of Health and Human Performance, our team has built artificial intelligence (AI) systems for understanding mechanism and individual variability in tDCS for cognitive aging and spinal cord stimulation for chronic pain. We have also developed AI system for diagnosing Alzheimer's Disease and Parkinson's Disease via eye scans (featured by a number of media outlets including Forbes). In 2021, my lab received 7 new extramural awards including PI of $2.9M NIA RF1, Co-PI of $1.2M NSF SCH, Co-I of $7.6M NIAAA P01, $5.3M

NINDS U01, $2.5M NIAAA U24, $2.3M NIMH R01, $1.8M NIAAA P01. My research is also supported by the National Science Foundation (NSF), National Institute of Health (NIH), industry grants, and internal grants. We also published 7 journal papers and 7 conference proceeding/abstracts in this past year. The research of my group related to Artificial Intelligence (AI) for Brain Health has been featured by the Washington Post, Alligator, UF News Front Page, ABC Local, etc. In 2021, my 2nd PhD student graduated with dissertation entitled "Biology and Neuroscience-Inspired Deep Learning".

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

My research uses multimodal neuroimaging, including functional MRI and Diffusion methods to study populations with white matter pathology including older adults, Veterans with mild traumatic brain injury (mTBI), and people living with HIV (PLWH). Currently, I remain clinically-involved in the neuropsychological assessment of various populations, and collaborate as a licensed neuropsychologist both on a weekly clinical service as well as on a number of NIAAA-funded U-01 and R-01 grants focused on aging and PLWH. In the past year I have had a first author publication of an AI manuscript predicting dementia conversion using baseline MRI, which was feature by UF Health: https://m.ufhealth.org/news/2021/uf-study-shows-artificial-intelligence-s-potential-predict-dementia. I also had 3 additional publication, and I have had a promising score on a K23 submission to the National Institute of Aging. Finally, I have obtained Graduate Faculty status and have become an official co-mentor to a graduate student, Brian Ho.

Aprinda Indahlastari, PhD
Research Assistant Professor
Department of Clinical Health Psychology
Member, CAM center

My long-term research goal is to develop personalized medicine using cutting-edge technology such as the state-of-the-art neuroimaging modalities and individualized computational models. For the past eight years, I have been involved in computational-based research, specifically using finite element modeling to predict the effects of biomedical devices. During my postdoctoral training, I was cross trained in cognitive neuroscience methods and clinical trials. I was actively involved in phase 2 and phase 3 clinical trials of tDCS administration paired with cognitive training in older adults to remediate cognitive aging. I further expanded my computational expertise to develop a novel method to compute the accuracy and consistency of electrode location as quality control metrics in tES clinical studies. I managed a modeling project to perform the largest tES computational modeling study to date that investigates age-related effects, such as brain atrophy and white matter hyperintensities, on delivered tES current dose in 587 unique older adult brains. White matter hyperintensities are highly prevalent in older adults over the age of 60. These initial research findings are crucial in constructing a robust platform to use computational models as means of predicting tES treatment effects. Further use of these computational models by pairing it with artificial intelligence methods such as machine learning and deep learning algorithms will enable us to predict treatment outcomes and formulate precision dosing that is tailored to individuals to optimize gains in cognitive performance resulted from tES application, specifically in older adults. These methods can be translated in the future to investigate other domains of brain function as well as

exploring other intervention methods beyond tES/tDCS. Recently, I transitioned to an Assistant Professor position in the Department of Clinical Health Psychology. In 2021, I published four papers (two first-author). In addition, I have attended and presented in six conferences (three in 2020, three in 2021) and received one award) I transitioned from post-doc to research assistant professor in early 2021. In December of 2020, I was featured as an MBI Rising Star.

Ashok Kumar, PhD
Research Associate Professor
Department of Neuroscience
Member, CAM center

Over the past two decades, my research has been focused on delineating the mechanisms contributing to age-related cognitive impairment. Toward this goal, a central focus of this research involves the role of various interventions such as environmental enrichment, exercise, viral vector, and anti-inflammatory compounds in restoring/reversing age-associated impaired cognition, synaptic plasticity, and cell excitability. During 2021, I have published 3 manuscripts. I have also had the privilege of mentoring trainees at all levels. These include Dr. Linda Bean (postdoc), two undergraduate students, and Vevekananda Budamagunta, a graduate student whose committee I serve on. I served as an associate editor for Frontier's in Neuroscience, Frontier's in Aging Neuroscience and Frontier's in Pharmacology. In addition, I have served as an Ad hoc reviewer for 30 publications. Finally, I served in an NIH study section ZRG! FO1A-F (20) Brain Disorders and Related Neurosciences Study Section.

Damon Lamb PhD
Assistant Professor
Department of Psychiatry
Member, CAM center

My research is interested in the complex interaction of autonomics, emotional function and cognition. I currently conduct clinical-translational research and education in human neuroimaging of psychiatric and related disorders in relation to cognitive aging. Despite the continuing challenges of the COVID-19 pandemic for research with human study participants, our research project investigating a putative treatment for age-related memory loss, evaluated in an amnestic mild cognitive impairment cohort, is almost completed. So far, this NIH NIA R21 study has had promising results, with measure of activity in brain regions and networks important for learning memory improved with stimulation, and follow-up grants have been submitted. In 2021, I received funding as a co-I on multiple NIA R01 grants in collaboration with Drs. Burke and Bizon. I have also published 5 papers within the past year, and we applied for and received funding from NIH, International OCD Foundation, and the National Endowment for the Arts this year, with ongoing support from the department of Veterans affairs and the DOD.

Carolina Maciel, MD
Clinical Assistant Professor of Neurology and Neurosurgery; Director of Research, Division of Neurocritical Care
Member, CAM center

I am a neurointensivist with dedicated training in EEG monitoring in critically ill patients. I received my medical degree with honors from Universidade Federal Fluminense in Brazil, and completed a Neurology residency at Weill Cornell Medical College and Memorial Sloan Kettering Cancer Center. I subsequently moved to New Haven, where I underwent Neurocritical Care and ICU EEG fellowship training at Yale-New Haven Hospital. I then obtained a Master's of Science in Clinical Research at Medical University of South Carolina. In 2021, I co-developed and launched a successful virtual shadowing program (Medi-Gators) for UF pre-health undergraduates (now on its 3rd iteration with nearly 2000 students enrolled in this semester) due to the void in such opportunities caused by the pandemic. I also co-authored the American Clinical Neurophysiology Society guidelines for Critical Care EEG terminology. I launched the first pilot study of synergistic GABAergic modulation in post-anoxic status epilepticus. Moreover, I have acquired equipment with CAM funding to begin *in vivo* calcium imaging experiments with the Scientifica Multi-photon microscope that is partially supported by the CAM.

Andrew Maurer, PhD
Associate Professor
Department of Neuroscience
Member, CAM center

My research program continues to focus on understanding how activity moves across the brain to support cognition and how this process changes with age. In the face of the ongoing COVID pandemic, we have managed to make progress on multiple fronts. Notably, I have graduated three students: Drs. Nicholas DiCola (neuroscience), Yu Qin (engineering) and Yuchen Zhou (engineering). Dr. Zhou is currently employed as a post-doc at Yale while Drs. DiCola and Qin are finishing up projects in preparation for publication prior to finding their next opportunity. Finally, we have hosted a SNIP student over the summer, Ms. Pamela Toh. We hope to have more undergraduate opportunities as we leave COVID.

We were also fortunate to be awarded a 5-year R01 from the NIMH titled "Preclinical Assays of Hippocampal-Prefrontal Cortical Circuit Engagement for Application in Therapeutic Development (MPI with Burke; MH126236)." This application is novel in that it will related cortically recorded neurophysiological events with those recorded with an invasive electrode. The intention of the project is that we will be able to provide a method by which to infer the inner workings of deeper brain regions without having to use intracranial electrodes – all in the context of human relevant cognitive tasks. We are currently recruiting new graduate students for this project. Moreover, I am a co-I on the R25 training grant, "Networking and Expanding Undergraduate Research on the Neurobiology of Aging to Advance Diversity (NEURON-Aging)" with Drs. Burke, McIntyre and Abisambra which has received a competitive score.

In terms of disseminating research, I have participated in the virtual UCI Learning and Memory conference and was keynote for the 2021 FCNC conference this summer. We have published 7 papers

and are continuing to explore different avenues by which to understand how the brain organizes and propagates activity "at the speed of thought'.

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

In the past year, we have continued our work in cognitive aging in two primary areas. First, we are exploring both the acute and persistent impacts of non-invasive transcutaneous vagus nerve stimulation in normal aging and other populations to investigate the potential utility of the approach as a neuromodulatory cognitive intervention. The funds from the McKnight Brain Research Foundation have been used to support the collection of a normal aging cohort to complement the NIH/NIA funded study of older adults with mild cognitive impairment. In 2021, our most significant achievements in relation to cognitive aging were the receipt of 2 NIH grants that will allow us to continue our exploration of age-related changes in inhibitory and antioxidant neurometabolites using Magnetic Resonance Spectroscopy (MRS). We currently have 4 students in our lab, all involved in cognitive aging research. One student from a collaborating lab (Katleen Hupfeld) that we trained in the use of MRS methods has accepted a postdoc at Johns Hopkins University to continue applying MRS in the context of aging as well as dementia related cognitive changes. Finally, we published more than 20 peer reviewed manuscripts.

Barry Setlow, PhD
Professor
Department of Psychology
Member, CAM center

There has been considerable progress in the past year on a number of fronts related to our cognitive aging research program. Most significantly, the lab was awarded two new R01 grants from NIA, focused on the application of vagus nerve stimulation and cannabinoids to remediating cognitive decline in aging. In addition, the lab was awarded a grant from the Florida Department of Health to investigate effects of cannabinoids on age-related cognitive decline and Alzheimer's disease-like pathology.

The lab published six peer-reviewed papers in the past year. None of these were specifically focused on cognitive aging, but several of them (listed below) lay the groundwork for future NIH-funded projects. Lab trainees presented their research at local, state, national, and international meetings. In addition, I gave six invited presentations, including two in East Asia.
In terms of training, two undergraduates in the lab completed senior Honors Theses on preclinical aging research, and a third received a University Scholars Program award to support her work on cannabinoids and aging. Two PhD students in the lab (Wonn Pyon and Sabrina Zequeira) were awarded spots on the T32 training grant on Alzheimer's disease and related dementias. Finally, Dr. Matthew Burns (post-doctoral fellow in the lab) was awarded a K08 fellowship from NIA and began a tenure-track faculty position in the UF Department of Neurology.

Alexins Simpkins, MD, PhD, MSCR, FAHA
Clinical Assistant Professor
Department of Neurology
Member, CAM center

I am an Assistant Professor of neurology in the University of Florida College of Medicine. I am an active member in the American Heart Association and Director of the CREST Initiative for stroke trainee and fellow research and career development in the Vascular Neurology Division. The CREST initiative that I created has been a great success. We had a total of 9 abstracts were submitted to the International Stroke Conference, including one oral presentation at the 2021 conference and now have another oral abstract accepted from the group at the 2022 International Stroke Conference and one at the American Academy of Neurology. Several manuscripts are in revision from the working group. I am also collaborating with Dr. Ellis on several research projects focusing on stroke disparities in under-represented groups and women with a manuscript in submission and a grant currently under review. Within the CREST group we now also have a robust collaboration with our rehabilitation colleagues Dr. Geis and Dr. Awosika from the University of Cincinnati. I am also collaborating on two historical stroke projects that focus on stroke health care systems and educational pipelines with Dr. Benson, from NINDS.

John Williamson, PhD
Assistant Professor
Department of Psychiatry
Member, CAM center

Over the past year, my research team has started six new grants (I am PI/site PI on 3). One project I am quite excited about it is a biomarkers study in aging and traumatic brain injury. This DOD funded consortium project (including UF, University of California San Francisco, University of Washington, University of Pittsburgh, and the Seattle VA) incorporates neuroimaging, blood biomarkers, and neuropsychological testing to develop indicators that will assist in identifying those older adults at highest risk post TBI to develop cognitive decline within the AD spectrum. This work complements currently active DOD funding that I have to determine biomarker sensitivities to subphenotypic outcomes in traumatic brain injury.

Further, we have made progress in our developing work using transcutaneous vagus nerve stimulation. Our NIH funded R21 is nearing completion (n =54 MCI, 10 HC, target 64 MCI). We have promising results with respect to during stimulation impacts on functional connectivity relevant to progression of AD. We have submitted these results for publication and presented them at the Alzheimer's Association International Conference. We continue to work on our McKnight Brain Research Foundation supported pilot project pairing tVNS with cognitive training in healthy older adults. This multi-modal neuroimaging and neuropsych study with the University of Arizona, delayed by COVID, is underway. Both sites have IRB approval, and we are enrolling participants with a goal of study completion by October 2022. Eric Porges leads a P01 subproject longitudinally assessing tVNS impacts on microbiome and brain metabolic status in older adults with HIV. Further, we are running a pilot project in undergraduates with anxiety with at-home tVNS longitudinally to assess impacts on sleep quality and anxiety. This complements a lab-based study (Merit Review, Williamson

PI) we are running in veterans with PTSD/TBI in which we are assessing the effects of tVNS on sleep architecture and indicators of hyperarousal.

On the education front, my graduate student, Sarah Bottari, successfully defended her master's thesis. She published her first, first author paper, submitted two grants, and received funding on one (tVNS longitudinal pilot described about), contributed to multiple papers as co-author, presented at an international conference and received notice of acceptance to present at another international conference in the new year. Erin Trifilio, a post-doctoral fellow working with me, submitted a CDA (VA career development mechanism) to determine individual differences in blood biomarker expression in sub-acute TBI relationships to brain metabolic differences and cognitive performance, with a goal of further understanding mechanisms of decline in TBI in older adults. Another graduate student, Aaron Colverson (Ethnomusicology PhD), proposed his dissertation, an evaluation of the ability of older adults to process simple and complex rhythms and changes in brain function in response to these tasks. This fMRI-based study is a CAM work and Dr. Cohen and I are working with Aaron to develop this project, with a completion goal of Fall 2022. Aaron and I have also engaged in outreach, presenting on music and Alzheimer's disease on a nationwide VA podcast earlier in the year, and, more recently, to the Alzheimer's Association via a fundraising outreach program. Further, Alexandria "Lexi" O'Neal was awarded a T32 for Alzheimer's disease work. She is assisting in finishing our tVNS project in MCI as well as our work on paired tVNS and cognitive training in healthy aging.

Summary of Training Achievements and Programs

In the past reporting period, CAM Center faculty have trained 11 postdoctoral fellows, 28 graduate students and numerous undergraduate scholars (See names in Appendix 1). Our trainees are doing exceptionally well, successfully competing in both intramural and national competitions. Currently, over 25 graduate students in CAM laboratories are supported by NIH-funded training programs and/or individual fellowships. In addition, our trainees regularly compete for local and national awards with great success. Just a few highlights include:

- Pre-doctoral fellow, **Alejandro Albizu (Woods Lab)**, received a National Science Foundation (NSF) Graduate Fellowship.
- Pre-doctoral fellow **Cheshire Hardcastle (Woods Lab)** received Dissertation Research Award, sponsored by the Science Directorate of the American Psychological Association
- Pre-doctoral fellow **Nicole Evangelista (Woods Lab)** received the Department of Clinical and Health Psychology Florence Schafer Memorial Award for Excellence in Psychotherapeutic Counseling; awarded Honorable Mention for the 2021 WIN Inclusion, Diversity, Equity & Advocacy Award, and was selected as a member of the American Psychological Association of Graduate Students Advocacy Coordinating Team (ACT) for 2022
- Pre-doctoral fellow **Wonn Pyon (Bizon Lab)** received first place Robert Levitt Award ($1000 prize) after a presentation and question/answer session hosted by the Institute for Learning in Retirement at Oak Hammock (a retirement community associated with the University of Florida); Wonn also received honorable mention in National Foundation Graduate Fellowship competition
- Pre-doctoral fellow **Sabrina Zequeira (Bizon Lab)** received a travel award for the International Behavioral Neuroscience Meeting and was selected in a national competition to attend Summer Neuroscience Program in Excellence and Success (SPINES) program held in Woods Hole, MA.

- Post-doctoral fellow, **Carly Logan, PhD (Burke Lab)** was selected as the College of Medicine Thomas H. Maren Junior Investigator 2021 Postdoctoral Awardee and won the Best Data Blitz presentation at the 2021 Florida Consortium on the Neurobiology of Cognition conference.

CAM Summer Scholar Program: In 2016, Dr. Sara Burke initiated a summer training program in the Department of Neuroscience with the goal of increasing recruitment of individuals underrepresented in science to our research workforce. This program has been immensely successful and has trained over 70 select students from well-over 1000 applications. Last summer, the CAM Center partnered with the SNIP program to spearhead the CAM Summer Scholars program, which is specifically focused on recruiting talented young scholars to the field of cognitive aging. Last summer, our summer scholars included: Adeola Olowokudejo who was mentored by Drs. Bizon and Setlow; Pamela Toh who was mentored by Dr. Andrew Maurer; Elena Garcia who was mentored by Dr. Sara Burke and Johanna Bergstrom who was mentored by Dr. Argyle Bumanglag. More information about the SNIP program can be found: https://neuroscience.ufl.edu/training/summer-neuroscience-internship-program/

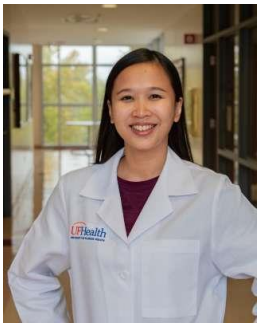
CAM Graduate Scholar Program: This year we also launched a CAM Graduate Scholar's Program which is a logical extension of the CAM Scholar's summer program. Our Graduate Scholar's program identifies individuals who are passionate about cognitive aging research early in their graduate training and provides stipend support and training opportunities to enhance their graduate experience and immersion in the field of cognitive aging (including attendance at multiple national and international meetings). Our inaugural CAM Scholar is Samantha (Samm) Smith who is training in the laboratory of Dr. Sara Burke. Samm was introduced to the field of cognitive aging as a SNIP student in 2020 and then chose to enroll in the neuroscience concentration of the Biomedical Sciences PhD program in the College of Medicine to pursue her graduate training under Dr. Burke's mentorship. She is a talented graduate student who in the past year has successfully advanced to candidacy and published her initial first author paper.

Federal Funding for CAM training programs: Two NIH training (T-) grants which provide specialized curriculum and funding for PhD students training on topics relevant to cognitive aging are held by CAM faculty members. Dr. Bizon is a co-Director of one training grant on Alzheimer's Disease and Related Dementia and Drs. Michael Marsiske and Adam Woods co-Direct a T32 focuses on nonpharmacological interventions for cognitive aging. Dr. Sara Burke submitted and R25 training grant to the NIH/NIA, entitled "Networking and Expanding Undergraduate Research on the Neurobiology of Aging to Advance Diversity (NEURON-Aging)" along with Drs. Jeremy McIntyre and Jose Abisambra. This grant, which received an outstanding (likely fundable) score, will be used to fund the CAM Summer Scholars program focused on increasing research opportunities in the field of cognitive aging for talented students from backgrounds underrepresented in science. Students will be recruited both nationally and from UF. The long-term goal of this program is to increase the talented cadre of researchers passionate about cognitive aging research.

Introductions of New Junior Faculty. Matt Burns, MD. Ph.D. and Aprinda Indahlastari, Ph.D., who began at postdoctoral fellows training in the CAM Center, were recently promoted to Assistant Professors in the Departments of Neurology and Clinical Health Psychology, respectively. Brief summaries of Drs. Burns and Indahlastari are below and full Biosketches can be found in Appendix 1.

Matt Burns, MD, PhD
Assistant Professor
Department of Neurology
Member, CAM Center

Dr. Burns is a physician-scientist who was introduced last year at which time he was a Postdoctoral Fellow supported by a fellowship on movement disorders from the Fixel Center for Neurological Disorders at the University of Florida. He obtained his MD/PhD in 2014 from the University of Illinois at Chicago. He then completed a residency in Neurology in 2018 at the University of Chicago Medical College. In the past reporting period, Dr. Burns received a K08 from National Institute on Aging and has now begun a tenure-track faculty position in the Department of Neurology. Dr. Burns is interested in cognitive dysfunction that occurs as a consequence of normal aging and age-associated diseases such as Parkinson's disease. This mentored award is focused on determining how aging and synuclein pathology affect executive functioning and decision-making. He is further assessing how deep brain stimulation in the prefrontal cortex may be effective at remediating such cognitive deficits.



Aprinda Indahlastari, PhD
Research Assistant Professor
Department of Clinical Health Psychology
Member, CAM Center

Dr. Indahlastari is a Research Assistant Professor who started her faculty appointment in 2021 in the Department of Clinical and Health Psychology at the University of Florida. Dr. Indahlastari received her faculty position in the context of the highly competitive campus wide UF Artificial Intelligence Initiative, an initiative funded by an 80-million-dollar gift to UF and bringing in 100 new experts in AI to the UF faculty. Prior to this, Dr. Indahlastari was a Post-Doctoral Fellow in the Woods Lab and Center for Cognitive Aging and Memory from 2017-2021. She obtained her PhD in 2017 in the field of Biomedical Engineering from Arizona State University. In the past reporting period, Dr. Indahlastari published two papers, one of which was a first author paper published in Brain Stimulation Journal (IF: 8.9). Dr. Indahlastari gave two scientific conference presentations in the topic of brain stimulation, neuroimaging, computational neuroscience, and artificial intelligence. Dr. Indahlastari is interested in personalizing medical devices and non-invasive intervention techniques, particularly in the field of cognitive neuroscience and aging neuroscience with the help of cutting-edge methods such as computational neuroscience and artificial intelligence. She has also submitted KL-2 application in December 2021, with a planned K01 submission in February 2022. In the proposed grant, she is further assessing how transcranial electrical stimulation in the prefrontal cortex may be effective at remediating age associated cognitive decline in healthy older adult population and older adults with mild cognitive impairment. She is planning to use gathered data to further formulate customized treatment that is tailored to each person and optimize the treatment outcomes.

Seminar Speaker Series (Luttge-Sponsored): With the agreement of the MBRF trustees, the ARML Core program has continued to sponsor speakers on topics relevant to cognitive aging. To encourage a robust audience for our cognitive aging speakers, we are inviting the "Luttge" speakers as part two existing seminar series: either the joint MBI-Department of Neuroscience series or as part of a cognitive neuroscience series that is held in the Clinical Health Psychology department. The MBRF-supported honorarium from Luttge lecture funds has enabled us to bring in outstanding outside speakers where we would normally have needed to rely heavily on internal speakers due to funding limitations. In addition, we are now inviting one "Rising Star" speaker each semester. Our goal is identifying a very senior Postdoctoral Fellow or early-career Assistant Professor doing exciting work in the field. As we

invite members of each McKnight Center to these talks, we hope that the "rising star" talks will facilitate recruiting the best and brightest in the field to our Institutes and help in showcasing the Evelyn F. McKnight Brain Inter-institutional network.

At present, some upcoming speakers are planned to visit UF in person, however, the Omicron variant has once again pushed us into an all zoom format. Nevertheless, our zoom seminars have been well-attended, with participant numbers ranging between 70-100 each week. Discussions are lively and we have been excited that the CAM Center has been able to assist in bringing outstanding speakers to our UF Neuromedicine community. Below we have listed our Fall 2021s speakers who were sponsored by the CAM Center (via the Luttge lecture funds), as well as upcoming speakers for the spring.

Fall 2021 CAM-Sponsored Seminar Speakers

Dr. Farah Lubin, PhD (Associate Professor for Comprehensive Center for Healthy Aging and Comprehensive Neuroscience Center, University of Alabama Birmingham) was the CAM sponsored speaker on September 23, 2021. Dr. Lubin's main research work is focused on investigating the molecular and genetic basis of learning, memory, and its disorders. The goal of these studies is to elucidate the role of genetic and epigenetic mechanisms in the on and off regulation of gene transcription during consolidation of memory. These studies will provide novel insights into novel candidate transcriptional mechanism that may be involved in abnormal regulation of genes underlying memory deficits associated with neurological disorders such as epilepsy and Alzheimer's disease.

Dr. Zvinka Zlatan, PhD (Assistant Adjunct Professor in the Department of Psychiatry, University of California, San Diego) was the CAM sponsored speaker on October 20, 2021. Dr. Zlata's lab (Wellness Initiative for Senior Enrichment – WISE Lab) investigates the neural mechanisms by which modifiable risk factors such as physical activity, sedentary time, fitness, diet, and subjective perceptions of cognitive function affect brain plasticity and cognition in healthy aging, with a focus on prevention. Her research seeks to modify risk markers of cognitive decline by developing novel behavioral interventions (exercise, diet) to promote brain health using digital technologies with diverse samples. The WISE Lab also investigates how subjective cognitive decline (an individual's perception of their cognitive functioning) relates to objective performance on neuropsychological testing and risk of future decline in older Hispanics.

Dr. Jonathan Kipnis, PhD (BJC Investigator, Alan A. and Edith L. Wolff Distinguished Professor of Pathology and Immunology, Washington University School of Medicine in St. Louis) was the CAM sponsored speaker on October 21, 2021. Dr. Kipnis's research group focuses on the complex interactions between the immune system and the central nervous system (CNS). The goal is to elucidate the cellular and molecular mechanisms underlying these interactions in neurodegenerative, neurodevelopmental, and mental disorders as well as in physiology (including healthy aging).

Upcoming Spring 2022 CAM-sponsored Seminar Speakers

Dr. Alexis Stranahan, PhD (Associate Professor in the Department of Neuroscience & Regenerative Medicine) will be the CAM sponsored speaker on January 13, 2022. Dr. Stranahan's research focuses on microglial and neurovascular regulation of hippocampal function in metabolic disorder. Her lab studies the regulation of synaptic plasticity and cognition by metabolic stress at the behavioral. Electrophysiological, and cellular levels. They define 'metabolic stress' broadly to encompass responses to exercise and caloric restriction at one extreme, and changes occurring in obesity and diabetes at the opposite end of this continuum. The long-term goal is to understand how neurons, glia, and cerebrovascular cells sense and respond to homeostatic challenges.

RISING STAR Dr. Perla Moreno Castilla, PhD (Postdoctoral Fellow in the Neurocognitive Aging Section, National Institute on Aging) will be the CAM sponsored speaker on February 24, 2022. Dr. Moreno-Castilla's research projects aim to understand inter-individual differences in hippocampal circuit engagement and elucidate the role of extracellular vesicles containing the synaptic protein Arc in the successful neuroadaptation in aging.

Dr. Dan Nicholson, PhD (Associate Professor of Neurological Sciences, Rush University) will be the CAM sponsored speaker on March 3, 2022. Dr. Nicholson's lab is interested in the neurobiology of cognitive aging, Alzheimer's disease and epilepsy. They bring to bear numerous techniques to unveil the events and pathogens that ultimately lead to brain failure, including electron microscopy, patch-clamp physiology, immunofluorescence array tomography, immunoprecipitation assays and mass spectrometry.

Dr. Kirk Erickson, PhD will be the CAM sponsored speaker on March 31, 2022 (Professor in the Department of Psychology, University of Pittsburgh) will be the CAM sponsored speaker on March 31, 2022. Dr. Erickson research interests range from cognitive neuroscience, aging, neuroplasticity, genetics, and molecular mechanisms of cognitive function. He is currently the Principal Investigator of the BACH lab and is continuing his research on how the brain changes in late adulthood and the factors that promote successful aging.

Summary of Clinical-Translation Achievements and Programs

A. **NEW PROGRAMS**

Adam J. Woods, PhD

Preventing Alzheimer's Disease with Cognitive Training (PACT Trial): new R01

In collaboration with 7 trial sites across the country, Dr. Woods and his UF team are leading a trial site for the newly funded PACT trial. PACT will recruit 7600 older adults across the United States in a Phase III trial to determine the efficacy of cognitive training in preventing MCI and Alzheimer's disease in healthy older adults. The UF site will recruit 500 older adults in the Gainesville catchment area. We have already recruited 150 in the past 9 months alone. Dr. Woods is also leading the trial wide magnetic resonance imaging component of the trial, in addition to his duties as the UF site PI.

Leveraging machine learning/artificial intelligence to predict treatment response to tDCS and cognitive training in older adults and design precision dosing approaches: ***New R01/RF1.*** Central to artificial intelligence efforts in the CAM, Drs. Woods and Fang were awarded a new R01/RF1 grant from NIA to perform a secondary data analysis project leveraging the ACT trial data to derive optimized precision dosing for tDCS paired with cognitive training to remediate age-related cognitive decline and prevent dementia. This project combines computational neuroscience, multimodal neuroimaging, clinical trials, and artificial intelligence approaches to not only understand neural mechanisms of tDCS efficacy, but generate a personalized approach for dosing tDCS in older adults. This technology is part of a patent submitted to the US patent office over the summer, has received significant media coverage – including being featured in the Society for Neuroscience Annual report, and has led to new collaborations with NVIDIA to accelerate AI approaches within the project.

UF Jacksonville Collaboration/Trial Site
Over the past year, Dr. Woods has worked to develop a strong collaborative relationship with the UF Jax leadership and clinical trial partners throughout COM Jax. A recent R01 submission from Dr. Woods will serve to establish the first CAM led clinical trial actively recruiting older adults across both UF Gainesville and Jacksonville campuses, with plans to expand to the UF Villages campus. This new UF wide distributed aging clinical trial approach will open multiple new avenues for large scale clinical trials through CAM and the broader UF aging community.

UF Artificial Intelligence Initiative
UF received an $80-million-dollar gift from the co-founder of NVIDIA, a UF alum, to establish one of the fastest AI Super-computers in academia around the globe and create 100 new AI faculty positions on campus. Over the past year, Dr. Woods has served on both the UF Health AI Steering committee and led one of three search committees tasked with hiring 32 new faculty across the UF Health Colleges specializing in diagnostics and therapeutics applications of AI in the health sciences. As part of the leadership team directing the UF Health arm of the AI Initiative, Dr. Woods has solidified a central role for the CAM in UF's ever expanding AI-centric interests. With a recent faculty hire into the CAM through the AI Initiative, and an additional hire under consideration, the CAM is well positioned to make a significant contribution to the application of trustworthy AI in cognitive aging and dementia diagnoses, treatment and prevention.

Tom Foster, PhD

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

Natalie Ebner, PhD

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

B. UPDATE ON EXISTING CLINICAL STUDIES

Adam J. Woods, PhD

Augmenting Cognitive Training in Older Adults COVID Study (NIH Supplement)
We have completed data collection on almost 200 older adults from the ACT trial in our 9 month follow-up COVID supplement funded study from NIA. We are currently in the process of performing data analyses on these complex asynchronous longitudinal data and hope to have results ready for publication in the near future.

Augmenting Cognitive Training in Older Adults: ACT (R01)
ACT is a multisite phase III randomized clinical trial testing the benefits of transcranial direct current stimulation for cognitive training gains in older adults across the University of Florida and University of Arizona. This is the largest tDCS trial in history and the first multi-McKnight site clinical trial. Randomization is complete in the trial, with 379 participants randomized in ACT. The data are currently scheduled for unblinding in April of 2022 following the final one year follow-up visits in participants, barring COVID Omicron delays.

REVITALIZE: Revitalizing Cognition in Older Adults at Risk for Alzheimer's Disease with Near-Infrared Photobiomodulation (R01)
This five-year R01 multisite Phase II randomized clinical trial will investigate the impact of near-infrared (NIR) photobiomodulation, a form of non-invasive brain stimulation, on cognition and mitochondrial function in older adults at risk for Alzheimer's disease. University of Florida (parent site) and the University of Arizona will perform a six-week intervention using NIR and assess changes in cognition, functional brain response and mitochondrial function (31P magnetic resonance spectroscopy) before, immediately post-intervention, and 3 months post-intervention in a population of 168 older adults. 86 older adults have been randomized across the UF and UA sites.

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

PROACT: Understanding Pain and Limitations in Osteoarthritic Disease (R37)
The goal of this project is to evaluate transcranial direct current stimulation and mindfulness-based stress reduction, alone and in combination, as treatments of chronic osteoarthritic knee pain in older adults in a two site phase II clinical trial. The project started in April of 2019, 360 participants at the University of Florida and University of Alabama at Birmingham will participate. Enrollment is underway at both sites.

Planning an adaptive clinical trial of cognitive training to improve function and delay dementia (U01/R01)
This two-year U01 project will develop the infrastructure for a large Phase II/III clinical trial investigating the impact of various forms of cognitive training on functional abilities and dementia conversation in patients with mild cognitive impairment. Dr. Woods led the UF site on this trial and will also lead the neuroimaging and data management for the pilot trial and in the subsequent full trial submission. This grant involves sites at University of South Florida (parent site), University of California San Francisco and the University of Florida. All participants have been randomized and are completed training and follow-up visits. We recently resubmitted a $26 million 4 site Phase II R01 clinical trial to continue this study. Our initial application missed the funding payline by 2 points. We anticipate our new scores in February/March and are hopeful to restart this trial and new 1700 person cohort in summer of 2022.

This study has provisions for both a trial site at UF main campus Gainesville and UF Jacksonville, both under the oversight of Dr. Woods.

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

Neuromodulation of Cognition in Older Adults: The Stimulated Brain Study (K01)
This study was funded off of a K01 awarded to Dr. Woods and builds on the prior Stimulated Brain study funded as a CAM pilot. This study served 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. Dr. Woods K01 funded trial has been completed in the past year. Initial findings have been published and follow-up papers are underway. In addition, several new technologies current under consideration for patents were created as a result of this project.

Mechanism and dosimetry exploration in transcranial electrical stimulation using magnetic resonance current mapping methods (RF1)
This project is an NIMH Brain Initiative funded RF1 (4 year R01) that will pioneer an objective measure of current flow in the brain using state of the art magnetic resonance imaging methods combined with in scanner application of tDCS and tACS. This project will also assess the relationship between activation in working memory related regions from an NBACK fMRI task and correspondence of change following F3-F4 in scanner tDCS. This project will provide an invaluable tool for titrating tDCS dose in our clinical interventions. This project is in its final no cost extension year.

Tom Foster, PhD

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

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

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

John Williamson, PhD

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

Further, related to my VA work, Drs. Kevin Wang and I have submitted a grant through the DOD (currently pending) to determine biomarkers associated with cognitive decline/accelerated aging in people with history of traumatic brain injury. In collaboration with Drs. Cohen and Porges, we continue work on aging and cognitive changes associated with microbiome differences in patients with HIV.

Most Important Research Achievements 2021

Jen Bizon, PhD

Over this past year, we have obtained multiple new grants from NIH/NIH, including large grants to investigate efficacy and mechanisms of vagus nerve stimulation and cannibas on cognition in aging. Our initial work on vagus nerve stimulation on cognition was published earlier this year in a special edition of *Neurobiology of Learning and Memory.* I presented initial findings from our work at the *3rd Workshop on Reserve and Resilience in Cognitive Aging* held in Bethesda, MD in October. Our initial findings suggest that daily vagus nerve stimulation can influence expression of excitatory and inhibitory signaling proteins that are altered in aging, restoring expression to levels akin to young subjects. In addition, we have shown that acute vagus nerve stimulation can enhance cognitive flexibility in young rats when paired with new stimuli. We are now poised to test the effects of stimulation in aged subjects. It is notable that the technical challenges of these studies are significant, particularly with respect to developing the approaches that enable long-term implantation of vagus cuffs in aged rats. Our success to date in this project has been possible due to fruitful collaboration with numerous CAM center members including Drs. Barry Setlow, Sara Burke, Damon Lamb. With others in the CAM Center (Drs. Porges and Williamson) also investigating vagus nerve stimulation in older adults, this is one intervention for which our preclinical work could assist directly in translational efforts. In addition to our work with vagus nerve stimulation, also made substantial progress on initial studies investigating the impact of cannibas on cognition in aging which is described in more detail by our collaborator on this work, Barry Setlow, PhD.

Ron Cohen, PhD

I have been author and co-author on multiple manuscripts this past year. One that I am particularly happy about stemmed from the dissertation project of Talia Seider, PhD which was published in Brain Imaging and Behavior, “An fMRI study of age-associated changes in basic visual discrimination”. This study shows some subtle changes in functional brain response, though overall there was preservation of neural response during visual perception. I recently submitted another manuscript to Frontier in Aging Neuroscience with data from Amanda Garcia, PhD dissertation project that focuses on neuroimaging findings in the context of semantic processing and aging to based PhD. Functional brain response on fMRI was also largely preserved during semantic decision making with advanced age. These findings are important as they provide further evidence that age-associated cognitive decline and brain dysfunction are not ubiquitous as people age.

Sara Burke, PhD

Over this past year, we established a new cognitive task in rats, which was reverse translated from neuropsychological testing in humans, that is sensitive to detecting age-related cognitive decline. This task, called the Paired-Associated Learning task, was first used as part of the Cambridge Automated Neuropsychological Testing Assessment Battery and it can be administered using touchscreens in humans and rodents. Notably, funding for purchasing the Rat Touchscreen Chambers was generously

provided by the endowment funds from the MBRF support. We published our findings in the Neurobiology of Aging (Smith*, Zequeira* et al., 2021, *shared first-author), and are now using this task to test the efficacy of diet-based interventions for improving cognition in old animals. While we are excited about this, I feel that most important scientific accomplishment made by the Burke Lab was the collaboration with University of Alabama, Birmingham MBRF faculty that resulted in a new collaborative grant and 3 publications that established a foundation for bridging geroscience and neuroscience. The 3 publications include a perspective that outlines why historically these two fields are disparate (AR Hernandez et al., 2021), a primer that explains the basics of geroscience to neuroscientists (Hoffman et al., 2021), and another primer that explains the basics of the neurobiology of aging to geroscientists (CM Hernandez et al., 2021). I am the senior/corresponding author on the latter paper. I feel that is interdisciplinary work has the potential to lead to transformative discoveries for understanding and treating brain aging. We have already shown that a 12-month diet intervention, involving intermittent fasting initiated in middle-age, had the ability to both lead to better cognitive performance and a healthier microbiome composition in old age, compared to the consumption of a standard diet. These findings are currently being prepared for submission.

Adam J. Woods, PhD

Over the past year, with the funding of a new R01/RF1 project focused on leveraging neuroimaging, computational neuroscience and artificial intelligence to derive precision dosing strategies for electrical brain stimulation treatments in older adults, we have begun to implement and deploy an advanced technology for precision medicine that bordered on science fiction merely 5 years ago. Combining the expertise of neuroscientists, clinical trialists, cognitive aging experts, and biomedical engineers, we now have a patent pending technology that has the ability to optimize dosing strategies person by person when electrical brain stimulation techniques, like transcranial direct current stimulation, are applied in older adults to remediate cognitive decline. The application of this technology is also being expanded to encompass electrical brain stimulation treatments for depression, chronic pain and other relevant conditions. My team has partnered with NVIDIA through the UF AI Initiative to accelerate the computational implementation and clinical accessibility of this new approach. We are poised to initiate the first phase I/II clinical trial directly testing the superiority of this technology for remediating cognitive decline in older adults in 2022.

Tom C. Foster, PhD

We hypothesized that senescent cells (SnCs) play a central role in age-associated pathology, in part due to their expression of the senescence-associated secretory phenotype (SASP), and SnCs may be primed to respond to inflammatory stimulation. To test this hypothesis, we examined the expression of various inflammatory cytokines and chemokines at the levels of gene transcription and protein production in various SnCs in vitro in response to lipopolysaccharide (LPS), interleukin-1β (IL1β), and tumor necrosis factor α (TNFα) stimulation. We found that SnCs not only expressed higher basal levels of various inflammatory cytokines and chemokines as a manifestation of the SASP, but more importantly exhibited hyper-activation of the induction of a variety of inflammatory mediators in response to LPS, IL1β and TNFα stimulation as compared with non-SnCs. This senescence-associated hyper-activation is likely mediated in part via the p38MAPK (p38) and NFκB pathways because LPS stimulation elicited significantly higher levels of p38 phosphorylation and NFκB p65 nuclear translation in SnCs when compared to their non-senescent counterparts and inhibition of these pathways with losmapimod (a p38 specific inhibitor) and BMS-345541 (a selective NFκB inhibitor) attenuated LPS-induced expression of IL6, TNFα, CCL5, and IL1β mRNA in SnCs. These findings suggest that SnCs may play an important role in the age-related increases in the susceptibility to developing an exacerbated inflammatory response and highlight the potential to use senotherapeutics to ameliorate the severity of various devastating inflammatory conditions in the elderly.

A longitudinal study examined the long-term effects of systemic inflammation, in order to distinguish inflammation-induced changes in baseline cognitive function from changes that interact with aging to

influence the trajectory of cognitive decline. Lipopolysaccharide (LPS; 1 mg/kg) or vehicle was administered to young adult (6 months) male rats via intraperitoneal injections, once a week for 7 weeks. Longitudinal effects on cognitive decline were examined 6 and 12 months after the initial injections. Repeated LPS treatment, in adults, resulted in a long-term impairment in memory, examined in aged animals (age 18 months), but not in middle-age (age 12 months). At 12 months following injections, LPS treatment was associated with a decrease in N-methyl-D-aspartate receptor-mediated component of synaptic transmission and altered expression of genes linked to the synapse and to regulation of the response to inflammatory signals. The results of the current study suggest that the history of systemic inflammation is one component of environmental factors that contribute to the resilience or susceptibility to age-related brain changes and associated trajectory of cognitive decline.

Karina Alvina, PhD

In 2021 my lab continued collecting data on the effects of exercise as stress-counteracting agent in mice. In particular, we are studying pathways associated with skeletal muscle (i.e., myokines) that can be potentially used as therapeutics in aging or neurodegenerative disorders. In addition, we are focused on sex-dependent differences as female mice seem less affected by these myokines. Stress leads to anxiogenic behaviors and hippocampal-dependent memory impairment. Exercise induces the release of myokines such as Irisin from skeletal muscles which can have neuroprotective effects. We previously showed that exercise reverses the effects of acute stress in male mice. However, whether exercise can counteract stress-induced anxiety behaviors and memory impairment in female mice has not been tested. Our results so far show that stressed sedentary female mice showed more anxiety-like behaviors compared to unstressed sedentary groups. Furthermore, exercised mice showed increased rearing behavior, which coupled with more time in the center of the Open Field suggests reduced anxiety. Overall, our study suggests that exercise does have anxiolytic effects in female mice when subjected to acute stress.

Russell Bauer, PhD

We completed work on the validation of a test of unique object processing and recognition (Object Recognition and Discrimination Test) which we are trying to develop as an early behavioral marker of Alzheimer's disease, as it taps a neuropsychological function performed by the perirhinal cortex, a site of early AD pathology. We found that ORDT performance in cognitively normal, MCI, and early AD patients was related to functional connectivity of the hippocampus to entorhinal and perirhinal cortex as well as medial temporal cortical thickness and amyloid positivity. This established the sensitivity of the ORDT to pathological features of early AD. Mediation models further showed that cortical thinning in the medial temporal lobe of amyloid positive patients diagnosed with amnestic MCI or dementia drives the reduction in ORDT performance seen in these groups. The next step is to establish the predictive validity of the ORDT collected at baseline to portend development of MCI or dementia later in life. We also completed work on an important study showing that immediate post-injury exercise is safe in a group of young participants immediately after concussion, opening the door to further studies of early exercise as a means to promote concussion recovery. This is important in debunking the persistent myth that extended rest is important in concussion recovery.

Matt Burns, MD, PhD

I have a.) established a rat model of cognitive and affective dysfunction in synucleinopathy, b.) advanced a multimodal imaging approach to anatomic, functional, and pathologic characterization of synuclein pathology in the intact rodent brain, and c.) tested an non-invasive and potentially disease modifying neuromodulatory therapy in a rodent model of Parkinson's disease dementia and Dementia with Lewy Body.

Ruogu Fang, PhD

AI for precision intervention in cognitive aging and dementia. Drs. Fang and Woods teams built the first AI system for precising dosing in non-invasive electrical brain stimulation by tailoring the treatment to personal anatomical differences like skull thickness and the amount of age-related brain atrophy in each person. This work has been funded by an MPI (with Dr. Adam Woods) $2.9M NIH RF1 (R01-equivalent) award (2021) and published in Brain Stimulation, a leading journal in this field, as well as covered by Alligator, UF News, ABC Local. This work directly leverages Dr. Woods' soon to be completed ACT trial data, a multi-MBI study.

Joseph Gullett, PhD

The most important scientific achievement of the past year in my lab relates to a recent paper that I led demonstrating the ability of artificial intelligence-based approaches to predict with 94% accuracy future decline towards Alzheimer's disease based on commonly acquired neuroimaging data administered through standard neurological assessment of older adult patients with thinking and memory concerns. Leveraging ADRC data from UF and UMiami ADRC, we have established a possible tool for better determining which older adults require more aggressive treatment strategies for prevention of future dementia. This work is also relevant to my recently submitted K23 application to NIA, which will leverage some of these same AI tools to determine treatment efficacy and outcomes for cognitive training interventions in older adults with and without MCI. At present, I am pursuing one of the coveted UF AI Initiative positions, in the hopes of moving onto the tenure track in the Department of Clinical and Health Psychology.

Aprinda Indahlastari, PhD

I published a total of seven scientific papers (2020-2021, three first-author) with average impact factor 4.5 (four of which are published in Brain Stimulation with 8.9 impact factor). I am a co-I in recently awarded NIA RF1 totaling of $2.9M. I was invited to give a talk at the INS 2020, the CEN seminar, and my first AI conference DAISY 2021. I was also invited as a panelist in the APA meeting 2020. I was featured as the MBI Rising Star in Dec 2020 and awarded Best Poster at the 4th International Brain Stimulation conference (2021).

Ashok Kumar, PhD

In the past year, I published three manuscripts and submitted two RO1 grant application to NIH for funding. I started new collaboration with Dr. James Wynn, M.D., Department of Pediatrics and Pathology, and submitted an LOI for UF-SEED funding, which was accepted for 2nd phase. Currently, I am MPI on a R01 with Dr. Foster and received a new R21 as PI.

Damon Lamb, PhD

VNS & tVNS impacts on cognition, memory and autonomic systems – we found VNS to be an effective tool for enhancing neuroplasticity as assessed by learning and memory and parsed the contribution of neurotransmitter systems through pharmacological manipulation during the same suite of behavioral tasks. In humans, with transcutaneous VNS, we found impacts on language learning/memory and have ongoing studies further studying this tool.

PTSD/TBI – we identified preliminary evidence of relationships between blood biomarkers, advanced MRI measures, and neuropsychological testing in the context of accelerated cognitive aging and TBI. We also found brain structural correlates of PTSD symptoms of particular interest in our theoretical framework related to sleep, a critical factor in chronic PTSD. Chronic PTSD and concomitant sleep disruption is associated with increases risk of dementia.

Carolina Maciel, MD

In the past year, we made significant progress addressing two major threats to favorable outcomes in patients who suffered hypoxic-ischemic brain injury: address the self-fulfilling prophecy bias that challenges accuracy of outcome predictions and take an initial stab at a novel therapeutic to post-anoxic status epilepticus-- a condition with nearly 100% mortality. We launched the VIGAB-STAT phase IIa study and started enrolling patients to demonstrate that early GABAergic modulation in post-anoxic status epilepticus is feasible in the post-cardiac arrest setting. We also demonstrated that different end-of-life practices driven by cultural differences across countries allow for an opportunity to determine the true prognostic performance of commonly used neuroprognostic tools, and thus mitigate the bias of self-fulfilling prophecy.

Andrew Maurer, PhD

Using the touch screens generously funded by endowment funds from the MBRF support – and in collaboration with the Burke laboratory- we have collected preliminary data to reverse translate a neuropsychological assessment used in humans to rats. This task, the Paired-Associated Learning task, was first used as part of the Cambridge Automated Neuropsychological Testing Assessment will be used in rats to determine cross regionals interactions to understand the basic interaction underlying higher cognitive processes, how this may go awry in normal aging, and explore potential avenues of therapeutic interventions.

I have served as co-author on six manuscripts published in the past year. Notably, one is a theoretical advancement in which we propose that cognition arises through activity "chasing its own tail" through the larger loops of the brain (Maurer and Nadel, 2021). From this perspective, activity in the region like the hippocampus would be formed, propagated out to a downstream region like the cortex, and eventually relayed back to the hippocampus a timestamp later. In this manner "new" sensory input can be integrated and superimposed upon "what happened a moment before". Thus, the brain has a mechanism by which to stitch contiguity together. This novel framework provides testable hypotheses by which to understand age-related cognitive decline.

We explored one critical aspect of this theory in Zhou et al. (2012) in which the brain is always active and propagating activity through these loops. Large amplitude, low frequency activity would engage larger loops (e.g., conversations between the cortex and hippocampus) while high frequency, low amplitude activity reveals bouts of activity between small populations on a local level. Over the course of euthanasia, we found that the smaller circuits are the most vulnerable, with their ability to engage each other collapse prior to the larger loops. We will apply this information to understand neurophysiology of the aging brain.

Eric Porges, PhD

Our two most significant achievements were 1) the publication of a meta-analysis in eLife that characterized the trajectory of cortical GABA (the principal inhibitory neurotransmitter in the brain) across the lifespan. In this manuscript, aggregated individual participant datasets, integrated into a Markov chain Monte Carlo (MCMC) analysis, revealed a steep early life increase, stability during midlife and a gradual reduction during aging of cortical GABA. A follow-up to this manuscript is currently in preparation integrating the data collected as part of the McKnight Brain Aging Registry of adults 85 and older. 2) A second manuscript, published in Cerebral Cortex, demonstrated increased cortical glutathione (the most plentiful endogenous brain antioxidant) concentrations during normal aging as compared to a younger cohort. Additionally, greater glutathione was associated with poorer functional outcomes, likely reflecting and responding to increased oxidative stress.

Barry Setlow, PhD

Aside from obtaining substantial new funding for the lab, we have made substantial progress in two new directions. Although neither is yet published, they have been presented at several national/international meetings, and we believe they will play a large part in our research directions for years to come.

In the first, we are collaborating with Dr. Jen Bizon to investigate the effects of acute and chronic exposure to cannabis and cannabinoids on cognitive performance in aging. Older adults are the fastest-growing group of cannabis users, yet essentially nothing is known about the health, and particular cognitive health, impacts of cannabis use in this population. Using a rat model of cognitive aging, we have found that acute exposure to cannabis smoke produces enhanced performance on a working memory task (notably, the same exposure regimen impairs performance of young adult rats in the same task). In addition, preliminary data indicate that daily oral consumption of THC has similar cognitive enhancing effects in aged rats, suggesting that the effects of cannabis are limited neither to inhalation nor acute administration.

The second line of work addresses the effects of reproductive experience on decision making and cognition. Preclinical research with rodents is conducted almost exclusively with reproductively naïve subjects, whereas almost the entire adult human population has some reproductive experience. Effects of reproductive (particularly maternal) experience on hippocampal/medial temporal lobe-dependent cognition are well documented, but almost nothing is known about the effects of such experience on executive functions and decision making. In initial studies, we find that reproductive experience in female rats leads to lasting (months later) changes in cognitive performance, particularly a decrease in sensitivity to punishment in tests of risky decision making. Ongoing studies are following up these findings and expanding them to male subjects as well. Given the long duration of these effects on cognition and behavior, as well as the fact that these aspects of change across the lifespan, it seems likely that reproductive experience could alter the trajectory of cognitive aging, and thus that future studies should consider this variable.

Alexis Simpkins, MD, PhD, MSCR, FAHA

I have developed a working group, which includes medical students, collaborations with ER researchers, and Dr. Kevin Wang to evaluate CNS biomarkers of CNS disease and determine which serum biomarkers can predict neurologic outcomes and neurologic diseases such as stroke and long-term outcome variables like “long-COVID-19.” Our IRB has been approved and we will have conducted an initial pilot biomarker analysis to look at differences in patients with cognitive deficits and stroke. I have also participated in a multicenter COVID-19 and cerebrovascular epidemiology studies led by Dr. Yaghi Shadi from Brown University, for which 2 manuscripts are being written (1 in revision and 1 to be submitted soon).

John Williamson, PhD

We have an article currently under review, which I think is quite interesting, demonstrating tVNS enhancements of semantic network function in patients with amnestic MCI. The abstract follows:

Better treatments are needed to improve cognition and brain health in patients with mild cognitive impairment (MCI) and Alzheimer’s disease (AD). Transcutaneous vagus nerve stimulation (tVNS) may impact brain networks relevant to AD through multiple mechanisms including, but not limited to, projection to the locus coeruleus, the brain’s primary source of norepinephrine. Neuropathological data suggest that the locus coeruleus may be an early site of tau pathology in AD. Thus, tVNS may modify the activity of networks that are impaired and progressively deteriorate in patients with MCI and AD. Thirty-six patients with MCI (seventeen women) confirmed via diagnostic consensus conference (sources of info: Montreal Cognitive Assessment Test [MOCA], Clinical Dementia Rating scale [CDR], Functional Activities Questionnaire [FAQ], Hopkins Verbal Learning Test – Revised

[HVLT-R] and medical record review) were assessed during rest using functional magnetic resonance imaging (fMRI) on a Siemens 3T scanner during tVNS (left tragus, n = 18) or sham control conditions (left ear lobe, n = 18). During unilateral left tVNS, patients with MCI showed increased functional connectivity between regions of the brain that are important in semantic and salience functions including regions of the temporal and parietal lobes. Further, connectivity between the Default Mode Network (DMN) and other functional networks decreased with tVNS. In conclusion, tVNS modified the activity of brain networks in which disruption correlates with deterioration in AD. These findings suggest afferent target engagement of tVNS, which carries implications for the development of noninvasive therapeutic intervention in the MCI population.

Financial Summary

Cognitive Aging & Memory

Age Related Memory Loss Program

Financial Summary

January 1 to December 31, 2021

Foundation Spendable Account			**Total**
Endowment income transferred to the UF Side			
	1/4/21	$272,360	
	4/1/21	$298,497	
	7/1/21	$304,452	
	10/1/21	$323,924	
Total endowment income transferred in			$599,616
UF Peoplesoft Accounts			
Beginning balance, January 1, 2021			$608,654
Received from the Foundation spendable account			$599,616
Expenditures			
Faculty, Research Staff, Staff Earnings, Graduate Assistant & Post Doctoral		$157,062	
Research equipment, supplies, and services		$66,921	
Tuition Waivers/Assistance		$1,300	
Foster Development Fund		$200,000	
Yegla Development Fund		$50,000	
Other Miscellaneous		$69	
Total Expenditures			$475,351
Ending balance, Dec. 31, 2021			**$732,919**

McKnight Endowed Chair for Brain Research in Memory Loss

Tom Foster, PhD

Financial Summary
January 1 to December 31, 2021

Foundation Spendable Account			**Total**
Endowment income transferred in:			
	1/4/21	$ 36,570	
	4/1/21	$ 40,079	
	7/1/21	$ 40,879	
	10/1/21	$ 43,493	
Total endowment income transferred in			$ 161,021
UF PeopleSoft Accounts			
Beginning balance, January 1, 2021			$ 57,824
Received from the Foundation spendable account			$ 161,021
Expenditures			
Faculty Compensation		$ 125,180	
Total Expenditures			$ 125,180
Ending Balance, December 31, 2021			$ 93,665

Cognitive Aging & Memory

Clinical Translational Research Program

Financial Summary

January 1 to December 31, 2021

Foundation Spendable Account			**Total**
Endowment income transferred to the UF Side			
	1/4/21	$272,360	
	4/1/21	$298,497	
	7/1/21	$304,452	
	10/1/21	$323,924	
Total endowment income transferred in			$599,616
UF Peoplesoft Accounts			
Beginning balance, January 1, 2021			$1,709,114
Received from the Foundation spendable account			$599,616
Expenditures			
Faculty, Research Staff, Staff Earnings, Graduate Assistant & Post Doctora		$209,225	
Research equipment, supplies, and services		$51,258	
Tuition Waivers/Assistance		$17,524	
Publications		$12,553	
Office Infrastructure		$11,356	
Travel		$126	
Total Expenditures			$302,043
Ending balance, Dec. 31, 2021			**$2,006,688**

McKnight Endowed Chair for Clinical Translational Reseach in Cognitive Aging

Ron Cohen, PhD

Financial Summary

January 1 to December 31, 2021

Foundation Funds Transferred			**Total**
Endowment income transferred to the UF Side			
	1/4/21	$36,554	
	4/1/21	$40,062	
	7/1/21	$40,861	
	10/1/21	$43,474	
Total endowment income transferred to the UF Side			$160,951
UF PeopleSoft Accounts			
Beginning balance, January 1, 2021			$59,471
Received from the Foundation spendable account			$160,951
Residual Funds Transferred from Department of Aging and Geriatric Research			$18,579
Expenditures			
Faculty Compensation		$143,117	
Total Expenditures			$143,117
Ending Balance, December 31, 2021			$95,885

Dr. William G. Luttge Lectureship in Neuroscience

Financial Summary
January 1 to December 31, 2021

Foundation Spendable Account			**Total**
Endowment income transferred into the UF Side			
	1/4/21	$2,582	
	4/1/21	$2,761	
	7/1/21	$2,815	
	10/1/21	$2,995	
Total endowment income transferred in			$11,152
UF PeopleSoft Accounts			
Beginning balance, January 1, 2021			$81,312
Received from the Foundation spendable account			$11,152
Expenditures			
Lecture Series Expenditures (Honoraria for zoom seminars)		$2,500	
Total Expenditures			$2,500
Ending Balance December 31, 2021			$89,902

McKnight Brain Research Grant Fund

with related accounts

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	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	$ 1,110,205	$ (709,769)	$ 169,626	$ 1,238,539
	$ 28,270,285	2016	$ 1,118,010	$ (1,713,121)	$ 167,343	$ 810,770
	$ 27,773,120	2017	$ 1,042,879	$ (212,000)	$ -	$ 1,641,650
	$ 30,479,220	2018	$ 1,041,290	$ (1,094,629)	$ -	$ 1,588,310
	$ 30,570,658	2019	$ 1,044,801	$ (892,764)	$ -	$ 1,740,347
	$ 32,042,328	2020	$ 1,059,436	$ (1,594,429)	$ 62,230	$ 1,267,584
	$ 39,272,079	2021	$ 1,110,622	$ (1,788,044)	$ -	$ 590,163
Life-to-date Totals			$ 20,286,176	$ (18,872,591)	$ 964,621	

AMENDED GIFT AGREEMENT - reconciliatic		Fiscal Year Ending	Endowment Transfers from Principal	1/2 allocated to CAM	Actual transfers to CAM	Still due to CAM
Initial Transfer	9/17/09	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	$ 1,110,205	$ (555,103)	$ 415,567	$ 276,036
		2016	$ 1,118,010	$ (559,005)	$ 684,727	$ 150,314
		2017	$ 1,042,879	$ (521,440)	$ -	$ 671,753
		2018	$ 1,041,290	$ (520,645)	$ 781,762	$ 410,636
		2019	$ 1,044,801	$ (522,401)	$ 390,484	$ 542,553
		2020	$ 1,059,436	$ (529,718)	$ 921,957	$ (0)
		2021	$ 1,110,622	$ (555,311)	$ 555,311	$ (0)
	Life-to-date Totals		$ 12,558,996	$ (7,358,404)	$ 7,763,274	

Evelyn F. McKnight Chair Endowments

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	$ 160,673	$ (151,549)	$ -	$ 51,917
	$ 3,729,097	2017	$ 140,027	$ (140,027)	$ -	$ 51,917
	$ 4,092,445	2018	$ 139,814	$ (139,814)	$ -	$ 51,917
	$ 4,104,722	2019	$ 140,285	$ (69,907)	$ -	$ 122,295
	$ 4,302,323	2020	$ 142,250	$ (69,907)	$ -	$ 194,639
	$ 5,273,062	2021	$ 149,123	$ (69,907)	$ -	$ 273,855
Life-to-date Totals			**$ 3,031,118**	**$ (2,887,230)**	**$ 269,781**	

Evelyn F. McKnight Chair for Clinical Transl. Research in Cognitive Aging	Market Value Balance of Endowment	Fiscal Year Ending	Annual Endowment Transfers from Principal	Total Expenses / Net Transfers	Additional Investment Revenue	Ending Spendable Fund Balance
	F020105		F020106			
F020105 / 06	$ 3,794,210	2016	$ 143,861	$ (108,709)	$ -	$ 35,152
	$ 3,727,485	2017	$ 139,967	$ (139,967)	$ -	$ 35,152
	$ 4,090,675	2018	$ 139,754	$ (139,754)	$ -	$ 35,152
	$ 4,102,948	2019	$ 140,225	$ (69,877)	$ -	$ 105,500
	$ 4,300,463	2020	$ 142,189	$ (69,877)	$ -	$ 177,812
	$ 5,270,782	2021	$ 149,059	$ (69,877)	$ -	$ 256,994
Life-to-date Totals			**$ 855,054**	**$ (598,060)**		

UF UNIVERSITY of FLORIDA
ADVANCEMENT

FUND IMPACT REPORT

Evelyn F. McKnight Cognitive Aging and Memory Research Fund

Book Value as of 09/30/2021	$25,967,781
Market Value as of 09/30/2021	$39,272,079
Spendable Income Generated for 2020/2021	$1,110,622

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 Investment Officer who reports to the a volunteer Board of Directors and President of the University of Florida

UNIVERSITY of FLORIDA
ADVANCEMENT

FUND IMPACT REPORT

Evelyn F. McKnight Chair for Brain Research in Memory Loss

Book Value as of 09/30/2021	3,995,677
Market Value as of 09/30/2021	5,273,062
Spendable Income for 2020/2021	149,123

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UNIVERSITY of FLORIDA
ADVANCEMENT

FUND IMPACT REPORT

William G. Luttge Lectureship in Neuroscience

Book Value as of 09/30/2021	$250,300
Market Value as of 09/30/2021	$363,162.27
Spendable Income Generated for 2020/2021	$10,269.27

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 Investment Officer who reports to the a volunteer Board of Directors and President of the University of Florida

UF UNIVERSITY of FLORIDA
ADVANCEMENT

FUND IMPACT REPORT

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

Book Value as of 09/30/2019	$4,000,000.00
Market Value as of 09/30/2020	5,270,782.18
Spendable Income Generated for 2020/2021	$149,058.76

Endowment Management

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UF UNIVERSITY of FLORIDA
ADVANCEMENT

FUND IMPACT REPORT

McKnight Brain Research Foundation

Evelyn F. McKnight Cognitive Aging and Memory Research Fund

Spendable Fund Transfers since endowment inception

FY 2020/2021	$ 1,110,622
FY 2019/2020	$ 1,059,436
FY 2018/2019	$ 1,044,801
FY 2017/2018	$ 1,041,290
FY 2016/2017	$ 1,042,879
FY 2015/2016	$ 1,118,010
FY 2014/2015	$ 1,110,205
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
	$20,286,176

UF UNIVERSITY of FLORIDA
ADVANCEMENT

FUND IMPACT REPORT

McKnight Brain Research Foundation

Evelyn F. McKnight Chair for Brain Research in Memory Loss

Spendable Fund Transfers since endowment inception

FY 2020/2021	$ 149,123
FY 2019/2020	$ 142,250
FY 2018/2019	$ 140,285
FY 2017/2018	$ 139,814
FY 2016/2017	$ 140,027
FY 2015/2016	$ 160,673
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
	$3,031,118

UF UNIVERSITY of FLORIDA ADVANCEMENT

FUND IMPACT REPORT

McKnight Brain Research Foundation

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

Spendable Fund Transfers since endowment inception

FY 2020/2021	$ 149,059
FY 2019/2020	$ 142,189
FY 2018/2019	$ 140,225
FY 2017/2018	$ 139,754
FY 2016/2017	$ 139,967
FY 2015/2016	$ 143,861
	$ 855,054

UF UNIVERSITY of FLORIDA ADVANCEMENT

FUND IMPACT REPORT

McKnight Brain Research Foundation

William G. Luttge Lectureship in Neuroscience

Spendable Fund Transfers since endowment inception

FY 2020/2021	$ 10,269
FY 2019/2020	$ 9,869
FY 2018/2019	$ 9,678
FY 2017/2018	$ 9,628
FY 2016/2017	$ 9,627
FY 2015/2016	$ 9,909
FY 2014/2015	$ 9,386
FY 2013/2014	$ 9,074
FY 2012/2013	$ 6,754
	$ 84,194

UF | UNIVERSITY of FLORIDA INVESTMENT CORPORATION

Quarterly Performance Report

UF Foundation – Endowment Pool
September 30, 2021

UF Foundation – Endowment Pool

Endowment Pool

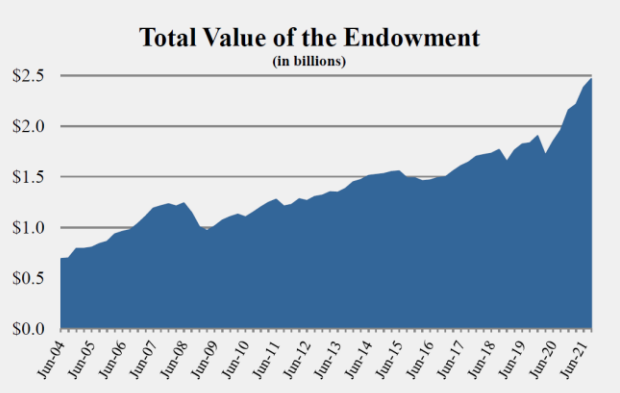
Since the founding of the University of Florida (UF) in 1853, generous alumni, corporations, foundations, parents and friends have contributed financial resources to assist UF in achieving its long-term mission of providing a superb education for undergraduates while maintaining excellent graduate programs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

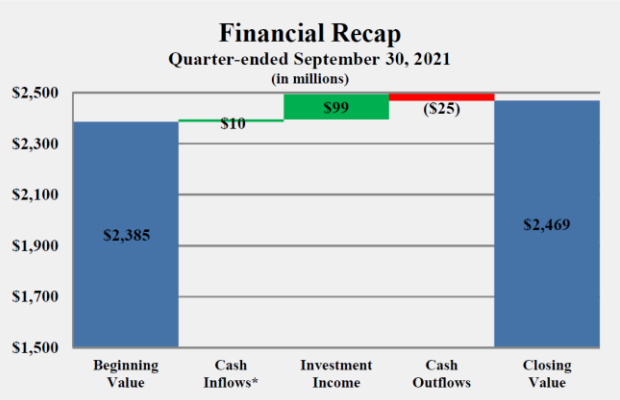
The UF endowment assets reside with the University of Florida Foundation (UF Foundation). The UF Foundation is a private, not-for-profit, 501(c)(3) direct support organization of the University that raises and manages all gift money for the benefit of the University of Florida. The management of the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

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

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

For the first quarter of the 2022 fiscal year, the Endowment Pool started with a balance of $2.4 billion. During the quarter, there was $10 million of cash inflows to the Endowment Pool thanks to the generous support of donors. Endowment investments resulted in a net gain of $99 million during the quarter and there was $25 million of cash paid out during the quarter in support of the University of Florida and its programs. The quarter ended with an Endowment Pool balance of $2.5 billion.





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

UF Foundation – Endowment Pool

Investment Objectives

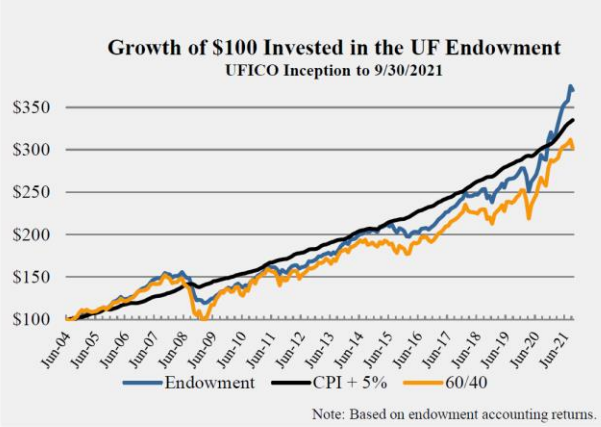
Since the inception of the University of Florida Investment Corporation (UFICO) in June 2004, the investment of the Endowment Pool has been managed by UFICO. Through UFICO's management of the Endowment Pool, the UF Foundation seeks to achieve an annualized real rate of return of at least 5% net of fees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

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

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

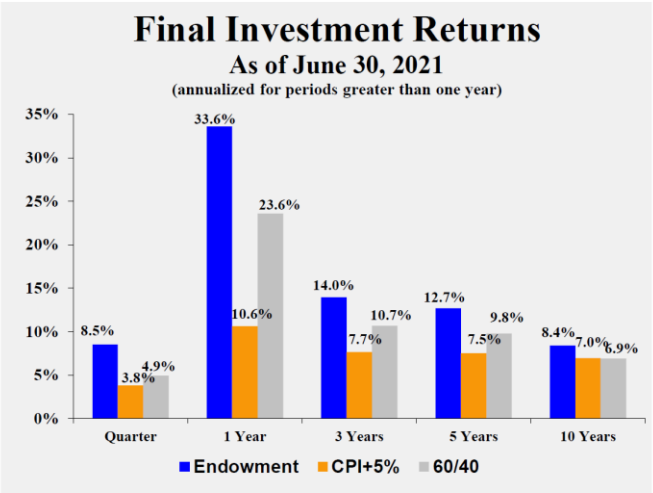
UFICO manages the Endowment Pool based on the objectives for the endowed assets as established by the Finance Committee of the UF Foundation Board of Directors. UFICO has constructed a long-term strategic asset allocation for the endowment portfolio based on the prioritization of these requirements including:

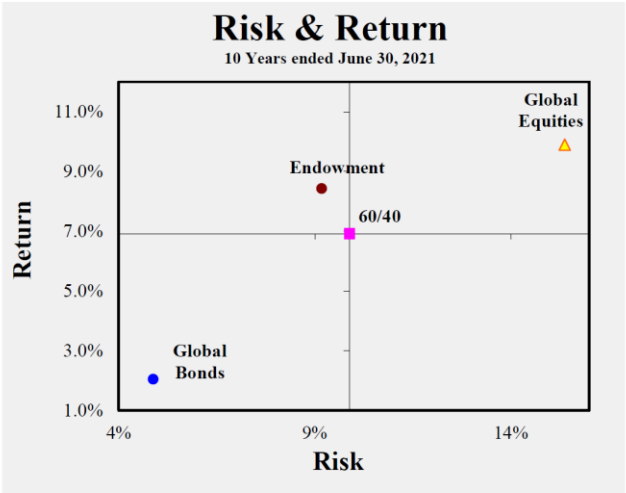
- **Positive Real Returns** – Intergenerational equity and maintaining the real purchasing power of the assets
- **Liquidity** – Retaining the ability to fund endowment obligations in all market conditions
- **Good Stewardship** – Maximizing *risk adjusted* returns
- **Growth** – Increasing the endowment's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



Strategic Asset Allocation
As of 9/30/2021

Strategy	Asset Classes	Target Allocation	Actual Allocation
Growth	Public Equities Hedged Strategies Private Equity	80.0%	80.7%
Diversifying	Hedged Strategies	10.0%	9.8%
Liquidity	Fixed Income Cash	10.0%	9.5%





Collaborative Programs

Inter-Institutional McKnight Collaborations

UF-UAB Collaborations: Throughout 2021, Drs. Bizon and Burke have been working with Drs. Burford and Carter (UAB) on a collaborative project to examine the impact of peripheral interventions (that is, vagus nerve stimulation and the ketogenic diet) on cognitive and peripheral health. A key principle of this collaboration is the reciprocal nature of peripheral and brain health. As such, it is critical to integrate geroscience and the neurobiology of aging in order to improve overall health and behavioral outcomes of older adults. Importantly, both vagus nerve stimulation and the ketogenic modify metabolism and alter the expression of genes in the brain that modulation the balance between excitation and inhibition (E/I). Disruptions in this E/I balance are a key feature of cognitive aging that have been linked to deficits in memory and executive functions. This collaborative project resulted in the submission of a MBRF Cognitive Aging and Memory Intervention Core Inter-Institutional Pilot grant entitled, *"Reuniting the Brain and Body to Understand Cognitive Aging: The Nexus of Geroscience and Neuroscience."* This grant, which was awarded at the start of 2021, aims to examine how interventions that may improve cognitive aging alter the gut-brain axis and the expression of genes that are critical for synaptic transmission as well as E/I balance. This collaboration also led to the publication of 3 papers in the *Journals of Gerontology, Series A Biological Sciences and Medical Sciences* (Hernandez, AR et al., Carter, 2021; Hernandez, CM et al., Burke, 2021; Hoffman et al., Buford, 2021). Moreover, the MBRF pilot award was instrumental in providing funding for Dr. Abbi Hernandez (a UF PhD graduate that trained in the CAM and current postdoc in the Carter/Buford labs) to acquire pilot data on the impact of the ketogenic diet on the gut microbiome and gene expression in the brain for a K99/R00 grant that was submitted on October 12, 2021. This proposal will be reviewed in February and may help to launch an independent research career for a talented young scientist that has been trained with support of the MBRF since the beginning of her PhD.

Dr. Woods continues to collaborate with NIA funded PROACT trial teams across UF and UAB, leading non-invasive brain stimulation efforts on an R37 funded trial investigating the effects of tDCS and mindfulness meditation on chronic knee pain in older adults.

UF-UA Collaborations: Dr. Natalie Ebner is collaborating with members of the University of Arizona and University of Miami to develop novel paradigms for understanding decision-making and susceptibility to scamming in older adults. In addition to publishing several collaborative studies, Dr. Ebner and her collaborators have received a new R01 to the National Institute on Aging on this topic. Supported by an MBRF pilot grant, Dr. John Williamson is collaborating with Dr. Gene Alexander at the University of Arizona to conduct a cross-institution study investigating vagus nerve stimulation in older adults.

Dr. Woods continues his long-standing collaboration with the University of Arizona in the context of 3 ongoing NIA funded clinical trials.

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

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

PACT Trial The NIA funded PACT trial for cognitive training, led by Dr. Woods, involves collaboration across University of South Florida, Clemson University, University of North Florida, University of Arizona/Banner, Duke University, and University of Florida.

UF-UA-UAB-UM Collaborations: The McKnight Brain Aging Registry (MBAR) study has completed all recruitment and assessments with over 200 participants who are over 85 years. Extensive quality control and validation of the database has occurred with one manuscript under review, three others to be submitted soon, **and multiple** others in the works. MBAR cognitive data will be posted on the Center for Cognitive Aging and Memory (CAM) website in the coming months. The extent to which many cognitive functions are preserved in MBAR participants is noteworthy, and over 60% continue to engage in physical exercise (aerobic and/or strength exercises). We have been asked to do another special edition for *Frontiers in Aging Neuroscience* focusing on findings from this study.

Collaborations Beyond McKnight Institutes

Dr. Woods has ongoing collaborations in his areas of expertise in tDCS and other non-invasive brain stimulation methods as well as neuroimaging and cognitive aging at Duke University, Clemson University, University of New Mexico, University of Miami, University of Arizona, Arizona State University, City College of New York, University of Michigan, Brown University, University of South Florida, University of California San Francisco, University of Arkansas for Medical Sciences (UAMS), Imperial College London, Istanbul University, Leibniz Research Center (Germany), and Catholic University of Korea. In addition, Dr. Woods continues to collaborate with a large number of investigators at the University of Florida outside the MBI, including Alex Parker (UF Jax), Fern Webb (UF Jax), David Clark (VA Merit grant), Mingzhou Ding (BME), Christiaan Leeuwenburgh (IOA), Roger Fillingim (Dentistry), etc.

Drs. Burke and Maurer and have ongoing collaborations with investigators at the University of Michigan and Rice University (Diba and Kamere) to examine aging impacts the organization of hippocampal neuronal activity in awake and sleep states. Additionally, Dr. Maurer collaborates with a researcher at Vanderbilt University (Hoffman). Drs. Burke, Lamb and Bizon collaborate with MIT Lincoln laboratory to develop machine learning approaches for quantifying neuron activity in large 3-D brain images obtained with light sheet microscopy through the CAM-supported shared microscope facility. Together, Drs. Burke and Bizon collaborate with Dr. Rapp at the NIH to examine the impact of aging of Tau pathology. Finally, Dr. Burke is also collaborating with researchers in the Institute of Aging (Anton) and UF ADRC (Smith) to develop dietary interventions to improve cognition in older adults with metabolic dysfunction.

Honors

Awards and Recognitions

Jen Bizon, PhD

Appointed Chair of the Department of Neuroscience in College of Medicine at University of Florida
2021 Fellow, Hedwig van Amerigen Executive Leadership in Academic Medicine
Executive Board Member of the Florida Consortium on the Neurobiology of Cognition

Ron Cohen, PhD

Reviewer for the following NIH extramural grant proposals:

R01-R21 review IRG of grant proposals related to cognitive-brain effects of drug use in the context of HIV and Aging
R01 review IRG of grant proposals on cognitive neuroscience of Aging and HIV
R01-R21 review of grant proposals on the topic of cognition and brain alterations in context of depression and aging in older adults
Review of P30 center grant proposal for new center focusing on neuroHIV in context of aging, women and also transexual populations.
T32 training programs focusing on HIV and aging
R01 grant review: Aging-associated cognitive decline in older adults.

Sara Burke, PhD

College of Medicine Leadership Program University of Florida
Mentor Academy, and Master Mentor Certificate in Culturally Aware Mentoring
Associate Editor, *Behavioural Brain Research*
Editorial Board Member, *Behavioral Neuroscience*
Executive Board Member of the Florida Consortium on the Neurobiology of Cognition

Adam J. Woods, PhD

Multiple students funded on Aging-related T32s in the lab for 2021 (n=5) appointed to ADRD T32 led by Bizon and the Non-pharm interventions in aging T32 led by Woods and Marsiske
Top Funded PI for Fiscal Year 2020-2021in College of Public Health and Health Professions with over 3.6 million in funding for the year.
Dr. Woods' research featured in the Society for Neuroscience 2021 Annual Report
Associate Editor, *Frontiers in Aging Neuroscience*
Editorial Board, *Contemporary Clinical Trials*
Standing NIH Study Section Member, CSR Human Cognition and Mental Function (HCMF) Study Section

Tom C. Foster, PhD

Invited to give lecture on "Molecular Markers to Operationally Define Cognitive Reserve. Workshop on Research Definitions for Reserve and Resilience in Cognitive Aging and Dementia, October 31 - November 1, 2021, Bethesda, Maryland.
Editorial Board Member, *Aging Brain*

Karina Alvina, PhD

Invited as member of the Molecular and Cellular Neuroscience (MCNP) NIH study section

Yenisel Cruz-Almeida, PhD

Elected to the US Association for the Study of Pain Board of Directors

Aprinda Indahlastari, PhD

MBI Rising Star, December

Best Poster Award at the 4th International Brain Stimulation conference

Carolina Maciel, MD

American Heart Association Innovative Project Award

Andrew Maurer, PhD

UF Exemplary Teacher 2020

Received tenure and promotion to Associate Professor

Alexis Simpkins, MD, PhD, MSCR, FAHA

College of Medicine Exemplary Teacher Award for academic year 2020-21, University of Florida
Fastest Door To Needle time for administration of thrombolysis to acute stroke patients of 2020 of 17 minutes, UF Shands
Named one of the 1,000 Inspiring Black Scientists in America by The Community of Scholars, in the Cell Press Blog, http://crosstalk.cell.com/blog/1000-inspiring-black-scientists-in-america

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New Grants

RF1AG067429 (NIH-NIA) $1,715,806 05/01/2021-04/30/2024
Mechanisms and therapeutic potential of vagus nerve stimulation in aging and Alzheimer's disease
MPIs: Jennifer Bizon, Barry Setlow (co-Is: **Burke**, Frazier, McIntyre, Dale)

R01AG072714 (NIH-NIA) $604,355 08/15/2021-05/31/2022
Effects of cannabis on age-related cognitive decline and Alzheimer's disease pathology
MPIs: Jennifer Bizon, Barry Setlow (co-Is: Lewis, McCurdy, Frazier)

21A11 FL Dept. of Health $200,000 05/012021-02/012023
Effects of cannabis on Alzheimer's disease-related pathology and cognitive decline
MPIs: Jennifer Bizon, Barry Setlow (co-Is: Lewis, McCurdy)

1R56AG065236-01A1 (NIH-NIA) $1,189,438 08/01/2021- 7/31/2022
Novel food-based approach for prevention of age-associated cognitive decline in older adults with obesity
PI: Robert Cook, **Co-I: Ron Cohen**

3U01AA020797-10S2 (NIH-NIAAA) $147,272 07/01/2021- 06/30/2022
Effects of experimentally-induced reductions in alcohol consumption on brain cognitive, and clinical outcomes and motivation for changing drinking in older persons with HIV infection
PI: Ron Cohen

VA Merit Award
Brain and Behavioral Responses to Backward Walking Training Post-Stroke
PI: Dorian Rose, **Co-I: Ron Cohen**

1RF1AG049722 (NIH-NIA) $2,005,695 04/01/2021-03/31/2026
The Contribution of Declines in Functional Connectivity to Cognitive Aging
PI: Sara Burke, co-I: Damon Lamb, Andrew Mauer, Jennifer Bizon

R25AG076396 (NIH-NIA) *Pending* 04/01/2022-03/31/2027
Networking and Expanding Undergraduate Research on the Neurobiology of Aging to Advance Diversity (NEURON-Aging) The goal of this award it to develop and expand research opportunities for underrepresented undergraduate students interested in aspects of cognitive aging and dementia. Score: impact of 36 (fundable)
PI: Sara Burke (contact), Joe Abisambra, Jeremy McIntyre

1R016236-01A1 (NIH-NIMH) $727,091 09/10/2021-06/30/2026
Preclinical Assays of Hippocampal-Prefrontal Cortical Circuit Engagement for Application in Therapeutic Development (MPI with Burke; MH126236)

MPIs: Sara Burke, Andrew Mauer

5R01AG054077-05 (NIH-NIA) $1,051,712 09/01/2016-04/30/2022
Augmenting Cognitive Training in Older Adults - The ACT Grant
PI: Adam Woods (Ron Cohen, Michael Marsiske), Co-I: Gene Alexander, Steve DeKosky

RF1AG071469 (NIH-NIA) $2,925,577 06/01/2021-05/31/2025
Mechanisms, response heterogeneity and dosing from MRI-derived electric field models in tDCS augmented cognitive training: a secondary data analysis of the ACT study
PI: Adam Woods (MPI: Ruogu Fang), Co-I: Aprinda Indahlastari

R01AG070349 (NIH-NIA) $2,617,287 02/01/2021-01/31/2026
Preventing Alzheimer's Disease through Cognitive Training (the PACT trial)
PI: Adam Woods (Site) co-I: Joseph Gullett, Steve DeKosky

5T32AG020499-17 (NIH-NIA) $279,713 05/01/2003-04/30/2022
Research Training in Non-Pharmacological Interventions for Cognition in Aging, MCI, and Alzheimer's Disease
PI: Michael Marsiske (Glenn Smith, **Adam Woods)**

National Science Foundation-IIS $840,000 (Fang: $301,176) 2021-2025
Collaborative Research: SCH: Trustworthy and Explainable AI for Neurodegenerative Diseases
Co-PI: Ruogu Fang

1P01AA029543-01 (NIH-NIAAA) $1,411,489 09/10/2021-08/31/2022
Interventions to improve alcohol-related comorbidities along the gut-brain axis in persons with HIV infection
PI: Robert Cook (MPI: Ronald Cohen, Varan Govind), Co-I: Rugo Fang, Damon Lamb

P01AA029547 (NIH-NIAAA) $1,755,506 (Fang: $102,301) 09/10/2021-8/21/2022
SHARE Program: Innovations in Translational Behavioral Science to Improve Self-management of HIV and Alcohol Reaching Emerging adults
PI: Sylvie Naar (FSU)**, Co-I: Ruogu Fang**

U24AA029959 (NIH-NIAAA) $2,491,414 (Fang: $70,185) 09/22/2021-08/31/2022
Southern HIV and Alcohol Research Consortium Biomedical Data Repository
PI: Samuel Wu, Robert Cook, **Co-I: Ruogu Fang, Ron Cohen**

R01MH125615 (NIH-NIMH) $2,279,906 (Fang: $115,817) 08/01/2021-05/31/2026.
Acquisition, extinction, and recall of attention biases to threat: Computational modeling and multimodal brain imaging
PI: Mingzhou Ding, Keil Andreas, **Co-I: Ruogu Fang**

U01NS119562 (NIH-NIND) $5,264,645 (Fang: $69,973) 04/21/2021-03/31/2026
Web-based Automated Imaging Differentiation of Parkinsonism
PI: David Vaillancourt, **Co-I: Ruogu Fang**

1R21AG068205-01(NIH-NIA) $419,375 08/01/2020-07/31/2022
Age-associated impaired executive function: Rescue by NMDA receptor upregulation
PI: Ashok Kumar

R01AG076438 (NIH-Veteran's Affairs Research Award $88,694

NEA Effects of art therapy on symptoms of PTSD after TBI and indicators of neurophysiological response: A mixed methods feasibility study
Co-I: Damon Lamb

1P01AA029543-01 (NIH-NIAAA) $402,970 09/10/2021-8/21/2022
Cognitive and Inflammation Targeted Gut-Brain Interventions in People Living with HIV who are High-Risk Alcohol Users
PI: Eric Porges

R01EB023963-05 (NIH-NIBIB) $3,157,326 9/31/2021-6/30/2025
Simultaneous Hadamard editing of GABA and Glutathione.
PI: Richard Anthony Edward Edden, **co-I: Eric Porges (site PI)**

International Obsessive Compulsive Disease Foundation 09/01/2021-09/01/2024
Paired tVNS and exposure and response prevention to improve symptoms of OCD
PI: John WIliamson (co-I Damon Lamb)

Department of Defense 07/2021 - 07/2025
Modular design-accelerated development of minimally invasive dried plasma and saliva tests for detecting TBI sequalae for AD dementia
Site PI: John Williamson

National Endowment for the Arts 09/2120-09/2023
Effects of art therapy on symptoms of PTSD after TBI and indicators of neurophysiological response: A mixed methods feasibility study
PI: John Williamson

Technology Transfer

1. Williamson, John Bonar; Lamb, Damon Geoffrey; and Porges, Eric S. Carter. "System and method for monitoring and controlling nervous system behavior using autonomic features." U.S. Patent No. 10,426,956. 1 Oct. 2019. In 2020, this was licensed by Evren Technologies of Newberry Florida, a UF spinoff company received an Small Business NIH grant (SBIR) in 2020 to further develop the technology.
2. Porges, Eric; Lamb, Damon; Campbell Thompson, Martha; Edden, Richard. “Non-Invasive Diagnostic Biomarker for Pancreatic Islet Population.” US Patent Application #16,756,489. Issued 9/24/2020.
3. Two additional focused disclosures related to brain modulation were made and the University of Florida is exercising their right to have patent submissions made. Both are currently in the process of being filed, and the content is currently embargoed.
4. **Ruogu Fang**, Yao Xiao. U.S. Provisional Patent Application Serial No. 62/983,660, filed February 29, 2020. Multimodal CT image super-resolution via transfer generative adversarial network. Ref no.: entity status: t17996us001 (222107-8690)
5. Peng Liu and **Ruogu Fang**. U.S. Provisional Patent Application Serial No. 63/001,771, filed March 30, 2020. Cfea: collaborative feature ensembling adaptation for domain adaptation in unsupervised optic disc and cup segmentation. Inventor(s): ref no.: t18094us001 (222107-8940)

6. Ruogu Fang and Jianqiao Tian. U.S. Provisional Patent Application Serial No. 63/032,018, filed May 29, 2020. A machine learning system and method for predicting alzheimer's disease based on retinal fundus images., T18201US001 (222107-8215).
7. **Adam J. Woods, Ph.D.** Aprinda Indahlastari, Ph.D. Alejandro Albizu**, Ruogu Fang,** Ph.D., U.S. Provisional Patent Application Serial No. 63/057,447 filed on July 28, 2020. System and Method of Precision Dosing for Electrical Stimulation of The Brain.
8. **Ruogu Fang** and Peng Liu. U.S. Provisional Patent Application Serial No. 63/058,008 filed on July 29, 2020 Systems and Methods For Reconstructing Realisitic Noisy Medical Images. (T18195US001 (222107-8185))
9. **Ruogu Fang**, Max Diaz. U.S. Provisional Patent Application. Nov. 30, 2020. Machine Learning For Predicting Parkinson's Disease Based On Retinal Fundus Images.

b. **REVENUE GENERATED FROM TECHNOLOGY**

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

University of Florida Research Foundation, Inc.

Income Distribution Transmittal

Dist Event: November 2021
Agreement: AI 9358 : System and Method for Monitoring and Controlling Nervous System Behavior Using Autonomic Features
Licensee: Evren Technologies, Inc.
Project #: MA19358

INCOME

Invoice Date	Invoice #	Description	Amount
12/23/2020	RF-53266	Royalty Revenue	$2,000.00
Total Income			$2,000.00

DEDUCTIONS AND DISTRIBUTIONS

Deductions

Legal Fee Deductions	$0.00
Held back pending expense reconciliation	$0.00
Total Deductions	$0.00

Distributions

Destination	Type	Percent X Percent	Recip. Percent	Actual Distribution	Amount
Lamb, Damon	Inventor	40.00 %	33.33 %	13.33 %	$266.67
Porges, Eric	Inventor	40.00 %	33.33 %	13.33 %	$266.67
Williamson, John	Inventor	40.00 %	33.33 %	13.33 %	$266.67
UF COLLEGE - MEDICINE	College	7.50 %	66.67 %	5.00 %	$100.00
UF COLLEGE - PUBL HLTH / HLTH PROFS	College	7.50 %	33.33 %	2.50 %	$50.00
UF MEDICINE - PSYCHIATRY	Department	7.50 %	66.67 %	5.00 %	$100.00
UF PUBL HLTH / HLTH PROFS - CLINICAL / HLTH PSYCHOLOGY	Department	7.50 %	33.33 %	2.50 %	$50.00
UF PROGRAM RETURN PORGES E. CLINICAL 1 HEALTH PSYCHOLOGY	Program	10.00 %	33.33 %	3.33 %	$66.66
UF PROGRAM RETURN WILLIAMSON, J MD PSYCHIATRY	Program	10.00 %	66.66 %	6.67 %	$133.33
UFRF	UFRF	35.00 %	100.00 %	35.00 %	$700.00
Total Distribution					$2,000.00

Gift Agreement Declarations

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

Additional Comments (items that are not covered elsewhere in the report, including any negative events, loss of full-time employees (FTEs), impending departures, space, or budget that could have an impact on carrying out the Gift Agreement.)
NO

Appendices

Appendix 1

A. Affiliate Faculty

Joe Abisambra, PhD – Associate Professor – Department of Neuroscience
Kyle D. Allen, PhD – Associate Professor – Department of Biomedical Engineering
Mingzhou Ding, PhD – Professor – Department of Biomedical Engineering
Matthew Farrer, PhD – Professor – Department of Neurology
Marcelo Febo, PhD – Associate Professor – Department of Psychiatry
Charles Frazier, PhD – Associate Professor – Department of Pharmacodynamics
Shellie-Anne Levy, PhD – Clinical Assistant Professor – Department of Clinical and Health Psychology
Jada Lewis, PhD – Professor – Department of Neuroscience
Michael Marsiske, PhD – Professor – Department of Clinical and Health Psychology
Gordon Mitchell, PhD – Professor – Department of Physical Therapy
Catherine Price, PhD – Associate Professor – Department of Clinical and Health Psychology
Malu Gamez Tansey, PhD – Professor – Department of Neuroscience
Steven M. Weisberg, PhD – Assistant Professor – Department of Psychology

B. Post-Doctoral

(Bizon/Setlow) Mojdeh Faraji, PhD
(Burke) Tara Cooper, PhD
(Burke) Carly Logan, PhD
(Woods) Stacey Alvaraez Alvarado, PhD
(Woods) Joshua Crow, PhD
(Foster) Linda Bean, PhD
(Foster) Puja Sinha, PhD
(Cruz-Almeida) Soamy Montesino Goicolea, PhD
(Cruz-Almeida) Jessica Peterson, PhD
(Cruz-Almeida) Larissa Strath, PhD
(Williamson) Erin Trifilio, PhD

C. Pre-Doctoral

(Bizon) Wonn Pyon. PhD student, Biomedical Sciences Program
(Bizon) Sabrina Zequeira, PhD student, Biomedical Sciences Program
(Cohen/Porges) Mark Britton, PhD student, Clinical Health Psychology
(Cohen/Porges) Jason DeFelice, PhD student, Clinical Health Psychology
(Cohen) Brian Ho, PhD student, Clinical Health Psychology
(Cohen/Woods) Kailey Langer, PhD student, Clinical Health Psychology
(Cohen/Williamson) Alexandria O'Neal, PhD student, Clinical Health Psychology
(Burke/Mauer) Nicholas DiCola, PhD student, Biomedical Sciences Program
(Burke) Aleyna Ross, PhD student, Biomedical Sciences Program
(Burke/Bizon) Johleen Seedansingh, PhD student, Biomedical Sciences Program
(Burke) Samantha Smith, PhD student, Biomedical Sciences Program
(Woods) Alejandro Albizu, PhD student, Biomedical Sciences Program
(Woods) Emanuel M. Boutzoukas, PhD student, Clinical Health Psychology
(Woods) Nicole Evangelista, PhD student, Clinical Health Psychology
(Woods) Cheshire Hardcastle, MS, PhD student, Clinical Health Psychology
(Woods) Jessica Kraft, PhD student, Biomedical Sciences Program

(Woods) Furuna Tewolde, MA, PhD student, Clinical Health Psychology
(Woods) Jori Waner, PhD student, Clinical Health Psychology
(Foster) Vivekananda Bedamagunta, PhD student, Genetics and Genomics Program
(Alvina) Jonah Juergensmeyer, Master's student, Neuroscience Department
(Alvina) Rodrigo Thomas, PhD student, Biomedical Sciences Program
(Bauer) Jessica Bove, PhD student, Clinical Health Psychology
(Lamb) Robert Claar, PhD Student, Clinical Health Psychology
(Lamb) Binh Nguyen, MD/PhD student, Department of Psychology
(Porges) Brittany Rohl, PhD student, Clinical Health Psychology
(Porges) Destin Shorell, PhD student, Clinical Health Psychology
(Williamson) Sarah Ann Bottari, PhD student, Clinical Health Psychology
(Williamson) Aaron Colverson, PhD student, School of Music

D. Internal Advisory Board

In 2021, we created an Internal Advisory Committee. The committee will be used to advise CAM leadership as we continue to grow and formalize some of our processes and procedures. The committee met to form and discuss goals and administrative structure in November with plans to meet again in early 2022. **Drs. Steven DeKosky, Carol Matthews, and Gordon Mitchell** all agreed to serve on the committee (NIH Biosketches included below).

BIOGRAPHICAL SKETCH

NAME: Mitchell, Gordon Stewart

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

POSITION TITLE: Professor and Director, Breathing Research and Therapeutics Center

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 California, Irvine, CA, USA	BS	1975	Biological Sciences
University of California, Irvine, CA, USA	PHD	1978	Dev. And Cell Biology
Max-Planck-Institut, Göttingen, Germany	Postdoctoral	1980	Respiratory Physiology
University of Wisconsin, Madison, WI, USA	Postdoctoral	1981	Respir. Neurobiology

A. Personal Statement

Research interests: Dr. Mitchell was among the first to recognize the importance of neuroplasticity in respiratory motor control. He has spent decades studying neuroplasticity in respiratory (and more recently, non-respiratory) motor systems. Major research interests focus on intracellular and inter-cellular mechanisms of spinal motor plasticity triggered by acute intermittent hypoxia, and efforts to harness that plasticity to treat devastating clinical disorders that compromise breathing and other movements, such as cervical spinal cord injury and ALS. His team's approach spans from cell/molecular

and integrative studies of disease/injury in animal models, through translational studies in humans with injury/disease (see Scientific Contributions).

Funding and scholarly publications: Dr. Mitchell has run an active research laboratory with continuous NIH funding since January, 1983, including a MERIT Award. He currently holds 3 R01s as PI, and is co-PI or co-investigator on several other grants from NIH (R01, R21), Department of Defense, and the Craig H. Neilsen Foundation. The 3 PI R01 grants pertain to: 1) cellular mechanisms of acute intermittent hypoxia-induced phrenic motor plasticity in rats; 2) the role of microglia (and inflammation) in regulating phrenic motor plasticity (ie. inter-cellular mechanisms); and 3) applying these principles to optimize acute intermittent hypoxia protocols to maximize plasticity and therapeutic efficacy in rodent models of cervical spinal cord injury. Each grant feeds directly into ongoing human trials of acute intermittent hypoxia to restore breathing ability (or limb function) in people living with spinal cord injury or ALS. Thus, Dr. Mitchell's research program operates as a "translational flywheel," where basic science studies inform human trials, that subsequently clarify the need for additional basic research. He has ongoing collaborations with outstanding scientists with expertise in respiratory physiology, cell/molecular neurobiology, stem-cell biology, rodent models of neural injury/disease, human physiology and clinical trials of therapeutic acute intermittent hypoxia. For example, Dr. Mitchell is Co-PI (with E. Fox, UF) of a DoD clinical trial concerning combined acute intermittent hypoxia with respiratory strength training to rehabilitate breathing ability in people with chronic spinal cord injuries. He is also active in collaborations concerning: 1) the potential of acute intermittent hypoxia to preserve breathing ability in ALS patients (B. Smith & J.Wymer, UF); as well as restoring 2) walking ability (with R. Trumbower; Spaulding/Harvard, Boston); and 3) arm/hand function (W.Z. Rymer & M. Sandhu, Ability Lab, Chicago) in people living with chronic spinal cord injury.

Dr. Mitchell has >301 publications in major, peer reviewed scientific journals, an H index of 73, a 5 year H-index of 42, and an i-10 index of 246. Of particular importance, this scientific productivity continues, with 42 publications since 2018. Many, if not most of Dr. Mitchell's publications were in collaboration with trainees working in his laboratory. Thus, in addition to their scientific contribution, his publications served as an important training vehicle, preparing graduate students and post-docs for research careers.

Mentoring record: At the University of Wisconsin, Dr. Mitchell was director of the NIH funded Respiratory Neurobiology Training Program (2002-1014), and served as chair of a multi-disciplinary biomedical department, Department of Comparative Biosciences, from 1997 to 2014. After moving to the University of Florida, he founded the NIH-funded Breathing Research and Therapeutics (BREATHE) Training Program. On an individual level, he is also an experienced and successful trainer. Thirty graduate students have completed their degrees under his supervision (MS & PhD), and served on an additional ~60 additional graduate thesis committees. Thirty postdoctoral trainees have completed their training under his mentorship. He and currently supervises or co-supervises 5 PhD students and 5 postdocs.

Dr. Mitchell's trainees have been highly successful as a group, and have: 1) won >80 awards from national or international organizations for research excellence; 2) been invited to give symposium talks at national/international conferences (>40 trainees); 3) successfully competed for NIH or medical foundation fellowships (>27 trainees); 4) 9 former graduate students and 23 former postdoctoral trainees moved on to become faculty at academic institutions, many with active, extramurally funded research programs; and 5) 11 trainees moved on to careers in administration, government or industry. Dr. Mitchell has trained >20 clinically qualified trainees, including those seeking the MD/PhD degree (4), as well as post-MD (3), post-DVM (6) and post-DPT (2) research training. He has mentored >25 junior faculty (both basic & clinical), and currently provides mentoring for more than 12 faculty from different basic science and clinical disciplines.

Dr. Mitchell has successfully mentored multiple individuals from underrepresented groups or disadvantaged backgrounds, including 11 graduate students (3 African American, 7 LatinX, 1 disadvantaged), 3 postdoctoral fellows (2 LatinX, 1 disadvantaged) and 3 junior faculty. He has also supervised a number undergraduate students from under-represented backgrounds (>6 since arriving at UF in late 2014); 2 of these undergraduate students received summer research fellowships from the

American Physiology Society (STRIDE awards). Dr. Mitchell's collective training record demonstrates he is able to successfully mentor diverse trainees.

Recognition and Service: In his career, Dr. Mitchell has won multiple research and teaching awards, served as departmental chair of a multi-disciplinary biomedical department, contributed extensively through university, national and international service (eg. NIH study sections) and, after moving to the University of Florida at the end of 2014, founded the University of Florida Breathing Research and Therapeutics (BREATHE) Center. With the onset of the Covid-19 pandemic, he organized a webinar series on respiratory rehabilitation priorities in post-COVID-19 patients, participates in an *ad hoc* international team working to define research priorities in the neural control of breathing for COVID-19 patients, and founded the International Online Seminar Series on the Control of Breathing and Airway Defense in 2020 (CoBAD). He has also spearheaded formation of the Therapeutic AIH Consortium, a group of laboratories in the US and Canada interested in advancing progress in the translation of this promising therapeutic modality. To that end, he (and the BREATHE Center) organized workshops in 2016, 2018, 2020 and 2022 to create (2017) and update a "Roadmap to Clinical Translation."

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

04/17-present	Director of Breathing Research and Therapeutics Training Program, University of Florida
11/15-present	Director of Breathing Research and Therapeutics Center, University of Florida
11/14-present	Preeminence Professor of Neuroscience, Department of Physical Therapy, University of Florida
11/14-present	Affiliate appointments in Neuroscience, Neurology, Biomedical Engineering, University of Florida
11/14-present	UF Health Neuroscience and Neuromedicine Research Executive Committee
7/02-11/14	Director of Respiratory Neurobiology Training Program, University of Wisconsin-Madison
7/97-6/14	Chair, Department of Comparative Biosciences, University of Wisconsin-Madison
7/09-11/14	Professor of Pediatrics, University of Wisconsin-Madison
7/07-11/14	Professor of Neurology, University of Wisconsin-Madison
7/05-6/09	Visiting Professor, Department of Neurobiology, UCLA, Los Angeles, CA
7/92-11/14	Professor, Department of Comparative Biosciences, University of Wisconsin-Madison
7/92-11/14	Professor of Neuroscience, University of Wisconsin-Madison
7/81-6/87	Assistant Professor, Department of Comparative Biosciences, University of Wisconsin-Madison
7/87-6/92	Associate Professor, Department of Comparative Biosciences, University of Wisconsin-Madison

2011-2014	Steenbock Professor of Behavioral and Neural Science (vacated with move to UF)
2001-2012	Recipient of NIH MERIT Award
1985-1990	Recipient of NIH Research Career Development Award
1997	Walter F. Renk Distinguished Professor Award, University of Wisconsin
1995, 2002	Pfizer Award for Research Excellence, University of Wisconsin
1995	Carl J. Norden Distinguished Teacher Award, University of Wisconsin
2007, 2014	Pfizer Award for Research Excellence, University of Wisconsin
2008-2017	Editorial Boards: *Respir. Physiology & Neurobiol.*, *J. Appl. Physiology, J. Neurophysiology, Experimental Neurology;* Section Editor: *Comprehensive Physiology*
1995-99	NIH Study Sections
2002	NIH study section boundary team
2000-2004	Scientific Advisory Board, Francis Family Foundation
2006-08	NIH Study Sections
2008-2011	Councilor, American Physiological Society

2008	Special Lecturer, Society for Neuroscience
2012-18	NIH Study Sections
2014	Julius H. Comroe, Jr. Distinguished Award Lecturer, American Physiological Society
2014	Guyton Award Lecture, Association of Chairs of Departments of Physiology
2017	Keynote Lecture, American Spinal Injury Association
2017	Keynote Lecture, National SCI Conference, Canadian SCI Rehabilitation Association
2017	Plenary Lecture, Oxford Conference for Modeling & the Control of Breathing, Oxford, UK

C. Contributions to Science

Seminal contributions have been in multiple areas, particularly intermittent hypoxia and spinal motor plasticity. Intracellular & intercellular mechanisms of intermittent hypoxia-induced phrenic motor plasticity. We were the first to demonstrate that intermittent hypoxia elicits spinal respiratory motor plasticity, and to provide a detailed understanding of cellular mechanisms giving rise to this plasticity (see Mitchell et al., 2001; Dale-Nagle et al., 2010; Devinney et al., 2013; Fields and Mitchell, 2015). We use a multidisciplinary approach, including neurophysiology, neuropharmacology, breathing measurements, immunohistochemistry and cell/molecular biology techniques including flow cytometry and RNA interference *in vivo* (one of first laboratories to successfully apply this technology *in vivo*). We demonstrated mild/moderate AIH elicits serotonin release within respiratory motor nuclei, initiating cellular cascades giving rise to phrenic, intercostal and hypoglossal long-term facilitation (LTF). Phrenic LTF requires serotonin type 2-receptor activation, ERK MAP kinases, TrkB, and PKC-θ activation, and new protein synthesis of brain derived neurotrophic factor (BDNF). With severe hypoxic episodes, AIH elicits a distinct, adenosine-dependent mechanism of phrenic LTF that requires adenosine 2A receptor activation, exchange protein activated by cAMP (EPAC), Akt and mTOR activity, and new protein synthesis of TrkB (not BDNF). These distinct, competing mechanisms interact via powerful cross-talk inhibition, an important feature regulating the expression of phrenic motor plasticity. By manipulating cross-talk inhibition, emergent properties are revealed, including LTF pattern sensitivity and meta-plasticity. Our collective work in this area has arguably led to the most comprehensive understanding of any form of respiratory motor plasticity, and directly inspired translational efforts to treat motor deficits caused by spinal injury or ALS with mild AIH. Key publications include:

1. Baker-Herman, T.L., D.D. Fuller, R.W. Bavis, A.G. Zabka, F.J. Golder, N.J. Doperalski, R.A. Johnson, J.J. Watters and G.S. Mitchell (2004). BDNF is necessary and sufficient for spinal respiratory plasticity following intermittent hypoxia*. Nature Neuroscience* 7: 48-55. Accepted for publication prior to April 7, 2008 – NIH Policy does not apply.
2. Devinney, M.J., D.P. Fields, A. Huxtable, T. Peterson, E.A. Dale and G.S. Mitchell (2015). Phrenic long-term facilitation requires PKCθ activity within phrenic motor neurons*. J. Neuroscience* 35: 8107-17. PMCID: PMC4444536.
3. Fields, D.P., S. Springborn and G.S. Mitchell (2015). Spinal 5-HT7 receptors induce phrenic motor facilitation via EPAC-mTORC1 signaling. *J Neurophysiol*. 114: 2015-22. PMCID: PMC4583563.
4. Seven, Y.B., R.R. Perim, O.R. Hobson, A.K. Simon, A. Tadjalli and G.S. Mitchell (2018). Phrenic motor neuron adenosine 2A receptors elicit phrenic motor facilitation. *J. Physiol. (London)*, 596: 1501-1512. PMCID: PMC5899988.

Systemic inflammation and spinal respiratory motor plasticity. Although inflammation is a hallmark of clinical disorders that compromise breathing, the impact of inflammation on respiratory motor plasticity had never been explored. We discovered that even mild systemic inflammation from low-dose lipopolysaccharide or more intense intermittent hypoxia (8 hours; 15/hour) abolishes serotonin-dependent phrenic long-term facilitation induced by moderate intermittent hypoxia, even after microglial pro-inflammatory activities subsided (Huxtable et al., 2013, 2015). Spinal inflammation impairs phrenic

LTF by a spinal p38-MAP kinase and protein phosphatase dependent mechanism (Huxtable et al., 2015; Tadjalli et al., 2021). Since inflammation impairs intermittent hypoxia induced respiratory motor plasticity, efforts to translate low-dose intermittent hypoxia as a therapeutic modality may be undermined (Dale et al., 2014). In contrast, adenosine-dependent phrenic long-term facilitation following severe acute intermittent hypoxia is unaffected by inflammation, leaving a "back-up system" in place. Since spinal injury patients experience persistent inflammation, we are currently investigating the impact of anti-inflammatory drugs prior to low-dose intermittent hypoxia therapy in persons with chronic incomplete spinal injury. Key publications:

1. Huxtable, A.G., S.M. Smith, S. Vinit, J.J. Watters and G.S. Mitchell (2013). Systemic LPS induces spinal inflammatory gene expression and impairs phrenic long-term facilitation following acute intermittent hypoxia. *J. Appl. Physiol*. 114:879-87. PMCID: PMC3633437
2. Huxtable, A.G., S.M.C. Smith, T. Peterson, J.J. Watters and G.S. Mitchell (2015). Intermittent hypoxia-induced spinal inflammation impairs respiratory motor plasticity by a spinal p38 MAP kinase-dependent mechanism. *J. Neuroscience* 35: 6871-80. PMCID: PMC4412901.
3. Agosto-Marlin, I.M., N.L. Nichols and G.S. Mitchell (2018). Systemic inflammation inhibits serotonin receptor 2-induced phrenic motor facilitation upstream from BDNF/TrkB signaling. J*. Neurophysiol*. 119: 2176-2185. PMCID: PMC6032128.

Harnessing acute intermittent hypoxia (AIH) to treat respiratory (and non-respiratory) motor deficits from chronic, incomplete cervical spinal injury. Our goal is to harness AIH-induced plasticity to enhance respiratory and non-respiratory motor function in rodents and persons with chronic spinal injury and ALS. Striking findings to date include: 1) repetitive AIH elicits profound functional recovery of breathing and forelimb function in rat models of spinal injury (Lovett-Barr et al., 2012; Navarrete-Opazo et al., 2015, 2017); 2) leg strength, walking ability and hand function in humans with chronic spinal injuries (Hayes et al., 2014; Trumbower et al., 2017); and breathing function in humans with chronic, incomplete spinal cord injury (Sutor et al., 2021). Low-dose AIH appears to be a safe, simple and effective means to restore lost respiratory and non-respiratory function with chronic SCI (Dale et al., 2014; Navarrete-Opazo et al., 2014; Sutor et al., 2021). Key publications:

1. Lovett-Barr, M.R.*, I. Satriotomo*, G. Muir*, J.E.R. Wilkerson, M.S. Hoffman and G.S. Mitchell (2012). Repetitive intermittent hypoxia induces respiratory and somatic motor recovery following chronic cervical spinal injury. *J. Neuroscience*. 32: 3591-3600. PMCID: PMC3349282.
2. Hayes, H.B., A. Jayaraman, A., M. Herrmann, G.S. Mitchell, W.Z. Rymer and R.D. Trumbower (2014). Daily intermittent hypoxia enhances walking after chronic spinal cord injury: a randomized trial. *Neurology* 82: 104-13. PMCID: PMC3897437.
3. Navarrete-Opazo, A., B.J. Dougherty and G.S. Mitchell (2017). Enhanced recovery of breathing capacity from combined adenosine 2A receptor inhibition and daily acute intermittent hypoxia after chronic cervical spinal injury. *Exp. Neurol.* 287: 93-101. PMCID: PMC5193117.
4. Christiansen, L. M.A. Urbin, G.S. Mitchell and M.A. Perez (2018). Acute intermittent hypoxia enhances corticospinal synaptic plasticity in humans. *Elife*, e34304. PMCID: PMC5915172.

Compensatory respiratory plasticity in motor neuron disease (ALS). Compensatory respiratory plasticity preserves ventilatory capacity during motor neuron disease despite progressive respiratory motor neuron cell death. However, phrenic motor output is decreased, an indication of imminent ventilatory failure (the major cause of death in ALS patients). Stem cells implanted in the cervical spinal cord promote motor neuron survival and acute intermittent hypoxia preserve/restore respiratory motor output (Nichols et al., 2013). We also developed a rodent model of stable respiratory motor neuron cell death via intrapleural injections of Saporotoxin conjugated to cholera toxin B fragment (Nichols et al., 2014). We have begun translational efforts in an attempt to harness acute intermittent hypoxia to preserve/restore breathing function in humans with ALS. Key publications:

1. Nichols, N.L., G. Gowing, I. Satriotomo, L.J. Nashold, E.A. Dale, M. Suzuki, P. Avalos, P. Mulcrone, J. McHugh, C.N. Svendsen and G.S. Mitchell (2013). Intermittent hypoxia and stem cell implants preserve breathing capacity in a rat model of ALS. *Am. J. Resp. Crit. Care Med.* 187(5): 535-42. PMCID: PMC3733409.

2. Nichols, N.L., I. Satriotomo, L.L. Allen, A.M. Grebe and G.S. Mitchell (2017). Mechanisms of enhanced phrenic long-term facilitation in SOD1^{G93a} rats. *J. Neuroscience*. 37: 5834-5845. PMCID: PMC5473203.
3. Seven, Y.B., N.L. Nichols, M.N. Kelly, O.R. Hobson, I. Satriotomo and G.S. Mitchell (2019). Compensatory plasticity in diaphragm and intercostal muscle utilization in a rat model of ALS. *Exp. Neurol.*, 299: 148-156. PMCID: PMC5951687.

Developmental plasticity in ventilatory control. Some years ago, we discovered that when rats are reared in enriched oxygen environments (30 to 60% oxygen) for 1 to 4 weeks post-birth, peripheral chemoreceptors fail to mature (Ling et al., 1996; Ling et al., 1997; Erickson et al., 1998). Once this occurs, rats live their entire lives with suppressed hypoxic chemoreflexes (Fuller et al., 2002). Since this form of "blunting" does not occur in adult rodents exposed to similar levels and durations of hyperoxia, this is a demonstration of maladaptive developmental plasticity in ventilatory control. Follow up studies by others demonstrate that human adults that had been born prematurely and have experienced life-long bronchopulmonary dysplasia (likely due to oxygen therapy and ventilatory support) have similarly blunted hypoxic ventilatory responses. Key publications:

1. Ling, L., E.B. Olson, Jr., E.H. Vidruk and G.S. Mitchell (1996). Attenuation of the hypoxic ventilatory response in adult rats following one month of perinatal hyperoxia. J. Physiol. 495: 561-571. Accepted for publication prior to April 7, 2008 – NIH Policy does not apply.
2. Fuller, D.D. R.W. Bavis, E.H. Vidruk, Z.Y. Wang, E.B. Olson, Jr. G.E. Bisgard and G.S. Mitchell (2002). Life-long impairment of hypoxic phrenic responses in rats following 1 month of developmental hyperoxia. J. Physiol. 538: 947-955. Accepted for publication prior to April 7, 2008 – NIH Policy does not apply.

Complete List of Published Work in MyBibliography:
HTTPS://WWW.NCBI.NLM.NIH.GOV/MYNCBI/GORDON.MITCHELL.1/BIBLIOGRAPHY/PUBLIC/

BIOGRAPHICAL SKETCH

NAME: Mathews, Carol A

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

POSITION TITLE: Professor of 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
Cornell University	BA	06/1988	Biology
Johns Hopkins University School of Medicine	MD	06/1992	Medicine
University of California, San Francisco	resident	06/1996	Psychiatry
University of California, San Francisco	fellow	06/1999	Biological psychiatry (genetics)
University of California, San Francisco	fellow	06/2000	Adv. Training in Clinical Research

A. Personal Statement

Dr. Mathews is a board-certified psychiatrist with over twenty years of clinical and research expertise in HD and related phenotypes. Her research focuses on the etiology and pathophysiology of obsessive compulsive and related disorders (OCRDs), including HD, OCD, Tourette Syndrome (TS), attention deficit hyperactivity disorder (ADHD), and anxiety disorders. She has been the PI or site PI on NIH and PCORI funded studies including those examining the pathophysiology and phenomenology of HD and other OCRDs. She will act as a consultant on this project, working closely with Dr. Ayers with whom she has a longstanding working relationship.

a. Mackin RS, Arean PA, Delucchi KL, Mathews CA. (2011). Cognitive functioning in individuals with severe compulsive hoarding behaviors and late life depression. *Int J Geriatr Psychiatry.* Mar;26(3): 314–21. PMID:21319334. PMCID: PMC4431997.

b. Mackin RS, Vigil O, Insel P, Kivowitz A, Kupferman E, Hough C, Fekri S, Delucchi KL, Mathews CA. (2016) Patterns of clinically significant cognitive impairment in hoarding disorder. *Depression and Anxiety*. 2016; 33(3):211-8. PMID:26474146

c. Hough CM, Luks TL, Lai K, Vigil O, Guillory S, Nongpiur A, Fekri SM, Kupferman E, Mathalon DH, Mathews CA. (2016). Comparison of brain activation patterns during executive function tasks in hoarding disorder and non-hoarding OCD. Psychiatry Research: Neuroimaging. 255:50-59.

d. Mathews CA*, Perez VB*, Roach BJ, Fekri S, Vigil O, Kupferman E, Mathalon DH. (2016). Error-related brain activity dissociates Hoarding Disorder from obsessive compulsive disorder. *Psychol Med.*Jan;46(2):367–79. PMID: 26415671. PMCID:PMC5079649

B. Positions and Honors

Positions and Employment

1996-1999 Attending, Triage and Evaluation Clinic, HIV Psychiatry Medication Clinic, Continuing Care Medication Clinic, SF VAMC, University of California, San Francisco (UCSF)
1999-2001 Private practice, psychopharmacology and psychotherapy
1999-2000 Attending, Consultation and Brief Intervention Services Evaluation Clinic, Department of Psychiatry, UCSF
2000-2001 Assistant Adjunct Professor, Department of Psychiatry, UCSF
2000 Acting Associate Residency Training Director, Department of Psychiatry, UCSF
2001-2006 Assistant Professor in Residence, Department of Psychiatry, University of California, San Diego (UCSD)
2001-2006 Attending, Primary Care Psychiatry Clinic, VAMC, UCSD
2002-2006 Director, Obsessive Compulsive Disorders Program, Dept. of Psychiatry, UCSD
2006-2014 Associate Professor in Residence, Department of Psychiatry, UCSF
2014-2015 Professor in Residence, Department of Psychiatry, UCSF
2006-2015 Director, Obsessive Compulsive Disorders Clinic, Department of Psychiatry, UCSF
2009-2015 Co-Director, Anxiety Disorders Clinic, Department of Psychiatry, UCSF
2010-2015 Faculty Chief for Research, Department of Psychiatry, UCSF
2015-present Professor, Department of Psychiatry, University of Florida
2015-present Pre-Eminent Professor, College of Medicine, University of Florida
2015-present Brooke Professor, Department of Psychiatry, College of Medicine, University of Florida
2015-present Adjunct Faculty, Department of Psychiatry, UCSF
2017-present Vice Chair for Strategic Development, Department of Psychiatry, University of Florida

Academic Honors and Awards

1988 Phi Beta Kappa Honor Society
1988 Phi Beta Phi Honor Society
1988 cum laude, Cornell University
1991 CIBA-Geigy Community Service Award, Johns Hopkins School of Medicine
1996 Creative Achievement Award, UCSF
1996 Laughlin Fellowship, American College of Psychiatry
1997 APA Research Colloquium for Young Investigators
1998-present Member, Tourette Association of America International Consortium for Genetics
2000 Future Leaders in Psychiatry Colloquium
2000-present Member, Obsessive Compulsive Foundation International Genetics Collaborative
2001-2004 NARSAD Young Investigator
2002 Resident Teaching Award, Department of Psychiatry, UCSD
2003-present Medical Advisory Board, Little People of America
2004-2006 Medical Advisory Board, National Alliance for the Mentally Ill, San Diego Chapter
2005-2015 Medical Advisory Board, Tourette Association of America
2007-present Taskforce for Compulsive Hoarding and Cluttering, San Francisco Mental Health Association
2009 Distinguished Teaching Award, PGY2 and PGY3 Psychiatry Residents, UCSF
2009-present Steering Committee, International Obsessive Compulsive Disorders Foundation International Genetics Collaborative
2011-present Co-chair, Steering Committee, Tourette Association of America International Consortium for Genetics
2013-present TS/OCD Working Group Representative, Coordinating Committee, Psychiatric Genomics Consortium
2016-present Chair, Scientific Advisory Board, Tourette Association of America

C. Contribution to Science

1. Much of my work has focused on elaborating the etiology of Tourette Syndrome (TS) and related tic disorders. These publications help to elucidate the strong genetic component to TS and begin to identify TS-associated risk genes, as well as documenting a clear environmental component, particularly in the pre- and perinatal period. These publications include the first genome-wide association studies for TS, as well as studies examining their complex phenotypic and genetic underpinnings. My work has also added to the as yet very small literature on environmental contributions to these complex and related disorders.

a. Yu D, Sul J, Tsetsos F et al….. Mathews CA, Scharf J on behalf of the Tourette Association of America
International Consortium for Genetics (TAAICG), the Gilles de la Tourette GWAS Replication Initiative
(GGRI), the Tourette International Collaborative Genetics (TIC Genetics), and the Psychiatric Genomics Consortium Tourette Syndrome Working Group (PGC-TS); Interrogating the genetic determinants of Tourette syndrome and other TIC disorders through genome-wide association studies. The American Journal of Psychiatry; Volume 176; 26 February 2019; page 217-227 doi: doi.org/10.1179/appi.ajp.2018.18070857
b. Hirschtritt ME, Lee PC, Pauls DL, Dion Y, Grados MA, Illmann C, King RA, Sandor P, McMahon WM Lyon GJ, Cath DC, Kurlan R, Robertson MM, Osiecki L, Scharf JM, Mathews CA for the Tourette Syndrome Association International Consortium for Genetics. (2015). Lifetime prevalence, age of risk, and etiology of comorbid psychiatric disorders in Tourette Syndrome. *JAMA Psychiatry*. Apr;72(4):325–33. PMID: 25671412. PMCID: PMC4446055.
c. Darrow SM, Hirschtritt ME, Davis LK, Illmann C, Osiecki L, Grados M, Sandor P, Dion Y, King R, Pauls D, Budman CL, Cath DC, Greenberg E, Lyon GJ, Yu D, McGrath LM, McMahon WM, Lee PC, Delucchi KL, Scharf JM, Mathews CA; Tourette Syndrome Association International Consortium for Genetics.
Identification of Two Heritable Cross-Disorder Endophenotypes for Tourette Syndrome. *Am J Psychiatry*.
017; 174(4):387-396. PMID:27809572. PMCID:PMC5378637
d. Mufford M, Cheung J, Jahanshad N, van der Merwe C, Ding L, Groenewold N, Koen N, Chimusa ER,
Dalvie S, Ramesar R; Psychiatric Genomics Consortium - Tourette Syndrome working group, Knowles JA, Lochner C, Hibar DP, Paschou P, van den Heuvel OA, Medland SE, Scharf JM, Mathews CA, Thompson PM, Stein DJ. Concordance of genetic variation that increases risk for Tourette syndrome and that influences its underlying neurocircuitry. Transl Psychiatry. 2019 Mar 22;9(1):120. doi: 10.1038/s41398-0190452-3 PMID: 30902966

2. I have also been very active in research aimed at understanding the causes and pathophysiology of obsessive compulsive disorder (OCD) and related phenotypes. This work includes early work elaborating the genetic underpinnings of OCD, as well as the use of multimodal approaches to understand the underlying neurobiology of this complex disorder.

a. Stewart SE*, Yu D*, Scharf JM*, Neale BM*, Fagerness JA*, Mathews CA* et al. (2013). Genome-wide association study of obsessive-compulsive disorder. *Mol Psychiatry.* Jun;18(7):788–98. PMID:22889921.
PMCID: PMC3605224. (*co-first authors)
b. Yu D*, Mathews CA*, Scharf JM*, Neale BM, Davis LK, Gamazon ER, Derks EM, Evans P, Edlund CK,

Crane J, Fagerness JA, Osiecki L, Gallagher P, Gerber G, Haddad S, Illmann C, McGrath LM, Mayerfeld C,
Arepalli S, Barlassina C, Barr CL, Bellodi L, Benarroch F, Berrió GB, Bienvenu OJ, Black DW, ….Posthuma
D, Oostra BA, Nestadt G, Rouleau GA, Purcell S, Jenike MA, Heutink P, Hanna GL, Conti DV, Arnold PD, Freimer NB, Stewart SE, Knowles JA, Cox NJ, Pauls DL. (2015). Cross-Disorder Genome-Wide Analyses Suggest a Complex Genetic Relationship Between Tourette's Syndrome and OCD. *Am J Psychiatry*. Jan;172(1):82–93. PMID: 25158072. PMCID: PMC4282594 (*co-first authors).

c. Bralten J, Widomska J, Witte W, Yu D, Mathews CA, Scharf JM, Buitelaar J, Crosbie J, Schachar R, Arnold P, Lemire M, Burton CL, Franke B, Poelmans G. Shared genetic etiology between obsessive-compulsive disorder, obsessive-compulsive symptoms in the population, and insulin signaling. Transl Psychiatry, 2020
Apr 27; 10(10:121. doi: 10.1038/s41398-020-0793-y
d. Norman L, Taylor S, Liu Y, Radua J, Chye Y, DeWit S, Huyser C, Karahanoglu F, Luks T, Manoach D, Mathews CA, Rubia K, Sua C, Van Den Heuvel O, Yucel M, Fitzgerald K; Error-processing and inhibitory control in obsessive-compulsive disorder: a meta-analysis using statistical parametric maps. Biological Psychiatry; 2018 November 29 doi: doi.org/10.1016/j.biopsych.2018.11.010

3. I have also been very active in work aimed at elucidating the pathophysiology of Hoarding Disorder (HD) and in improving outcomes for individuals with HD. In this area, my collaborators and I use multimodal approaches to identify the neurobiological underpinnings of HD, as well as the functional outcomes, including treatment response, that may be associated with this under-recognized and disabiling disorder.

a. Archer C, Moran K, Garza K, Zakrzewski J, Martin A, Chou C, Uhm S, Chan J, Gause M, Salazar M,
Plumadore J, Smith L, Komaiko K, Howell G, Vigil O, Bain D, Stark S, Mackin R, Eckfield M, Vega E, Tsoh
J, Delucchi K, Mathews CA; Relationship between symptom severity, psychiatric comorbidity, social/occupational impairment, and suicidality in hoarding disorder. Journal of Obsessive-Compulsive and
Related Disorders; 2018 November 12 doi: doi.org/10.1016/j.jocrd.2018.11.001
b. Zakrzewski J, Datta S, Scherling C, Nizar K, Vigil O, Rosen H, Mathews CA; Deficits in physiological and self-conscious emotional response to errors in hoarding disorder. Psychiatry Research; Volume 268, 2018
October, Pages 157-164 doi: doi.org/10.1016/j.psychres.2018.07.012
c. Aranovich GJ, Cavagnaro DR, Pitt MA, Myung JI, Mathews CA. (2017). A model-based analysis of decision making under risk in obsessive-compulsive and hoarding disorders. J Psych Res. 90:126-132. PMID:
28279877
d. Mathews CA, Mackin RS, Chou CY, Uhm SY, Bain LD, Stark SJ, Gause M, Vigil OR, Franklin J, Salazar M, Plumadore J, Smith LC, Komaiko K, Howell G, Vega E, Chan J, Eckfield MB, Tsoh JY, Delucchi K. Randomised clinical trial of community-based peer-led and psychologist-led group treatment for hoarding disorder. BJPsych Open. 2018 Jul 20;4(4):285-293 PMID:30083381

Complete List of Published Work in My Bibliography:

http://www.ncbi.nlm.nih.gov/sites/myncbi/carol a..mathews,
md.1/bibliography/41099242/public/?sort=date&direction=descending

BIOGRAPHICAL SKETCH

NAME: DeKosky, Steven T.

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

POSITION TITLE: Professor of Neurology

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Bucknell University, Lewisburg, PA	A.B.	1968	Psychology
University of Florida, Gainesville, FL	Graduate School	1968-1970	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 behavioral, neurochemical, neuroanatomical, genetic, and pathological changes (amyloid, neurofibrillary tangles) in AD, MCI, and normal elderly. I have also been involved with epidemiological studies of dementia in several populations, including in western Pennsylvania and rural India. My neurochemistry and molecular neuroscience lab was funded extramurally for over 30 years; to translate my bench research studies, I began clinical studies in cognitive, behavioral, neuroimaging and therapeutic interventions correlating imaging and cognition, trials of new medications including First in Man studies in the Pitt Alzheimer's Disease Research Center (ADRC), and NIH-funded large scale (>3,000 Ss), long term (>6 years), multicenter dementia prevention trials using Gingko biloba; I was PI of the GEM trial. I was founding co-director of the University of Kentucky ADRC (1985-1990;) then director of the Pittsburgh ADRC, (1994-2008) and serve as chair of several Drug Safety Monitoring Boards. I have served as consultant/advisor for multiple pharma and biotech companies, ADRCs, and chaired the Alzheimer's Association Med-Sci Advisory Council, and the Med-Sci Advisory Panel of Alzheimer's Disease International. I chaired the American Academy of Neurology's Practice Parameter Workgroup on Early Detection, Diagnosis, and Treatment of Dementia, and served on or chaired multiple committees or review committees for the NIA regarding aging and dementia. I also served on the NCCAM (now NCCIH) Council and was a member of the NIH Council of Councils (overseeing the Common Fund). I chaired the University of Pittsburgh department of neurology for 8 years. In these capacities I have supervised undergraduates, PhDs, post docs, and both basic and clinical research faculty. Then, as Vice President and Dean of the University of Virginia School of Medicine (2008-2013) I developed further skills in management of large research and academic projects, My return to research via a sabbatical year at Penn (bioethics) and Pitt (in the PET labs) facilitated my re-entry into research and research administration. I now am Deputy Director of the McKnight Brain Institute, the center of neuroscience research and teaching at UF, Associate Director of the NIA-funded 1Florida ADRC, and involved in several research grants focused on human and animal models of age-related memory loss

and therapeutic interventions. I believe my teaching, research, and clinical experience qualifies me for the advisory roles on this proposal.

B. Positions, Scientific Appointments, and Honors

2020 Henry Wisniewski Lifetime Achievement Award, (Alzheimer's Association International Conference)
2019 Albert Nelson Marquis Lifetime Achievement Award
2017-present Who's Who in the World
2015-present Professor, Neurology and Neuroscience, Univ. of Florida College of Medicine, Gainesville, FL
2015-present Professor of Neurology Emeritus, University of Virginia
2015-present Deputy Director, McKnight Brain Institute, University of Florida
2015-present Associate Director, 1Florida Alzheimer's Disease Center
2015-present Aerts-Cosper Professor of Alzheimer's Research, University of Florida
2015-2016 Interim Executive Director, McKnight Brain Institute, University of Florida
2015 Who's Who in America (Platinum edition)
2014--present Thompson Reuters Top 1% of Cited Papers
2014-2015 Visiting Scholar, Department of Radiology (PET Center) and Neurology, University of Pittsburgh School of Medicine/UPMC, Pittsburgh, PA [Sabbatical]
2013-2015 Council of Councils (National Advisory Council to the NIH Director for the Common Fund)
2013-2014 Visiting Professor, Department of Medical Ethics and Health Policy, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA [Sabbatical]
2009-present Elected Fellow, American College of Physicians
2009-2012 National Advisory Council, National Center on Complementary and Alternative Medicine (NCCAM; now National Center on Complementary and Integrative Health, NCCIH)
2008-present Adjunct Professor of Neurology, University of Pittsburgh School of Medicine
2008-2104 Founding Chair, ISTAART (International Society to Advance Alzheimer Research & Treatment)
2008-2014 Professor of Neurology and Psychiatry and Behavioral Sciences, UVA 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
2008-2013 James Carroll Flippin Professor of Medical Science, University of Virginia
2008-2013 Council of Deans, American Association of Medical Colleges (AAMC)
2008 Alzheimer's Association Zaven Khachaturian Award
2006 NIH Clinical Center Great Teachers Award
2005-2015 Member, Board of Directors, American Society for Experimental NeuroTherapeutics (ASENT)
2005 Ronald and Nancy Reagan Research Institute Award for research/care/advocacy in AD.
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
2003-present Elected American College of Neuropsychopharmacology (ACNP)
2003-2015 *America's Top Doctors*
2003 Rita Hayworth Award, Alzheimer's Association
2002-2005 Chair, Medical and Scientific Advisory Panel, Alzheimer's Disease International
2000-2008 Chair, Department of Neurology, University of Pittsburgh, Pittsburgh, PA
2000 Distinguished Alumnus, University of Florida College of Medicine ("Wall of Fame")

1997-2008 Professor, Dept. of Human Genetics, Graduate School of Public Health, University of Pittsburgh
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
1994-2015 *The Best Doctors in America*
1994-2010 National Board of Directors, Alzheimer's Association, Chicago, IL; Vice-Chairman, 1998-2001
1994-2008 Director, ADRC, University of Pittsburgh Medical Center, Pittsburgh, PA
1992-2001 Director, Div. of Geriatrics & Neuropsychiatry, Dept. of Psychiatry/WPIC, Univ. of Pittsburgh
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
1988 Presidential Award, American Neurological Association
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
1980-1985 Teacher-Investigator Development Award, NINCDS
1979-1990 Asst.to Assoc. Prof, Depts. Neurology & Anatomy/Neurobiology, Univ. Kentucky, Lexington, KY
and Staff Neurologist, Lexington VA Medical Center
1978-1979 National Research Service Award in Developmental Neurology (Neurochemistry) NINCDS
1974 Roger Schnell Award for Excellence in Clinical Neurology (University of Florida)
1972 Alpha Omega Alpha Research Award, University of Florida College of Medicine

C. Contributions to Science

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

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

DeKosky, ST and Scheff, SW Synapse loss in frontal cortex biopsies in Alzheimer's disease: Correlation with cognitive severity. Annals of Neurology 27:457-464, 1990.
DeKosky, ST, Harbaugh, RE, Schmitt, FA, Bakay, RAE, Chui, HC…Senter, HJ, Markesbery, WR, and the Intraventicular Bethanecol Study Group. Cortical biopsy in Alzheimer's disease: Diagnostic accuracy and neurochemical, neuropathological and cognitive correlations. Annals Neurology 32:625-632, 1992.
DeKosky, ST, Ikonomovic, MD, Styren, SD, Beckett, L, Wisniewski, S, Bennett, D, Kordower, JH, and Muston, EJ. Up-regulation of choline acetyltransferase activity in hippocampus and frontal cortex of elderly subjects with mild cognitive impairment. Annals of Neurology 51:145-155, 2002.
Ikonomovic, MD, Klunk, WE, Abrahamson, EE, Wuu, J, Mathis, CA, Scheff, SW, Mufson, EJ and Cohen,

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

2) Amyloid imaging in Alzheimer's Disease

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

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

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

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

Zhao Y, Tudorascu DL, Lopez OL, Cohen AD, Mathis CA, Aizenstein HJ, Price JC, Kuller LH, Kamboh MI,
DeKosky ST, Klunk WE, Snitz BE. Amyloid β Deposition and Suspected Non-Alzheimer Pathophysiology
and Cognitive Decline Patterns for 12 Years in Oldest Old Participants Without Dementia. JAMA Neurol. 2017 Nov 6. PMID: 29114732

3) Experimental Brain Trauma:

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

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

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

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

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

4) Human Brain Trauma:

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

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

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

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

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

5) Mild Cognitive Impairment and Prevention of Dementia

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

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

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

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

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

Appendix 2

Top 20 Publications from 2021

1. Altidor, L. K-P., Bruner, M. M., Deslauriers, J. F., Garman, T. S., Ramirez, S., Dirr, E. W., Olczak, K. P., Maurer, AP., Lamb, D. G., Otto, K. J., Burke, S. N., Bumanglag, A. V., Setlow, B., & Bizon, J. L. (2021). Acute vagus nerve stimulation enhances reversal learning in rats. *Neurobiology of Learning and Memory.* 184, 107498.
2. Yegla B, Boles J, Kumar A, Foster TC (2021). Partial microglial depletion is associated with impaired hippocampal synaptic and cognitive function in young and aged rats, *Glia*, 2021, 69, 1494-1514.
3. Cruz-Almeida Y, Forbes M, Cohen RC, Woods AJ, Fillingim RB, Riley JL 3rd, Porges ES (2021). Brain gamma-aminobutyric acid, but not glutamine and glutamate levels are lower in older adults with chronic musculoskeletal pain: considerations by sex and brain location. *Pain Reports*. 2021 Sep 3;6(3):e952.
4. Gullett, J.M., Albizu, A., Fang, R., Loewenstein, D.A., Duara, R., Rosselli, M., Armstrong, M.J., Rundek, T., Hausman, H.K., DeKosky, S.T., Woods, A.J. & Cohen, R.A (2021). Baseline neuroimaging predicts decline to dementia from amnestic mild cognitive impairment. *Frontiers in Aging Neuroscience*, 828.
5. Hardcastle C, Hausman, H.K., Kraft, J., Albizu, A., Evangelista, N.D., Boutzoukas, E.M., O'Shea, A., Langer, K., Van Etten, E.J., Bharadwaj, P.K., Song, H., Smith, S.G., Porges, E., DeKosky, S.T., Hishaw, G.A., Wu, S.S, Marsiske, M., Cohen, R., Alexander, G.E., Woods, A.J. (2021). Higher-Order Resting State Network Association with the Useful Field of View Task in Older Adults. *GeroScience*.
6. Hernandez CM, Hernandez AR, Hoffman JM, King PH, McMahon LL, Buford TW, Carter C, Bizon JL, Burke SN (2021). A Neuroscience Primer for Integrating Geroscience with the Neurobiology of Aging. *Journal of Gerontology A Bioloigical Sciences/Medical Sciences*. doi: 10.1093/gerona/glab301. Online ahead of print.
7. Hupfeld KE, Hyatt HW, Alvarez Jerez P, Mikkelsen M, Hass CJ, Edden RAE, Seidler RD, Porges EC (2021). In Vivo Brain Glutathione is Higher in Older Age and Correlates with Mobility. *Cerebral Cortex*, Aug 26;31(10):4576-4594.
8. Indahlastari A, Albizu A, O'Shea A, Forbes MA, Nissim NR, Kraft JN, Evangelista ND, Hausman HK, Woods AJ (2020) Alzheimer's Disease Neuroimaging Initiative. Modeling transcranial electrical stimulation in the aging brain. *Brain Stimulation*. May-Jun;13(3):664-674.
9. Jianqiao Tian∗, Glenn Smith, Han Guo, Boya Liu, Zehua Pan, Zijie Wang, Shuangyu Xiong, Ruogu Fang (2021). Modular machine learning for Alzheimer's disease classification from retinal vasculature, in *Nature Scientific Reports*, vol. 11, no. 1, Article ID 238, 11 pages. https://doi.org/10.1038/s41598-020-80312-2. Highlighted in The Washington Post, UF Engineering News.
10. Jodeiri Farshbaf M, Alviña K (2021). Multiple Roles in Neuroprotection for the Exercise Derived Myokine Irisin. *Frontiers in Aging Neuroscience*, 16;13:649929.
11. Kraft, J., Albizu, A., O'Shea, A., Hausman, H.K., Evangelista, N.D., Boutzoukas, E., Hardcastle, C., Van Etten, E.J., Bharadwaj, P.K., Song, H., Smith, S.G., DeKosky, S., Hishaw, G.A., Wu, S., Marsiske, M., Cohen, R., Alexander, G.E., Porges, E., Woods, A.J. 2021. Functional Neural Correlates of a Useful Field of View (UFOV) Based fMRI Task in Older Adults. *Cerebral Cortex*. https://doi.org/10.1093/cercor/bhab332
12. Monnig, MA, Gullett, JM, Porges, EC, Woods, AJ, Monti, PM, Tashima, K., Jahanshad, N., Thompson, P., Nir, T., Cohen, RA. (2021). Associations of Alcohol Use, HIV Infection, and Age with Brain White Matter Microstructure. *Journal of Neurovirology,* 1-15. doi: 10.1007/s13365-021-01021-8

13. Orsini, C. A., Blaes, S. L., Hernandez, C. M., Betzhold, S. M., Perera, H., Wheeler, A-R., Ten Eyck, T. W.,Garman, T. S., Bizon, J. L., & Setlow, B. (2021). Regulation of risky decision making by gonadal hormones in males and females. *Neuropsychopharmacology.* 46, 603-613.
14. Porges EC, Jensen G, Foster B, Edden RA, Puts NA (2021). The trajectory of cortical GABA across the lifespan, an individual participant data meta-analysis of edited MRS studies. *Elife*, Jun 1;10:e62575.
15. Seider TR, Porges EC, Woods AJ, Cohen RA (2021). Dedifferentiation of Functional Brain Activation Associated With Greater Visual Discrimination Accuracy in Middle-Aged and Older Adults. *Frontiers in Aging Neuroscience*. 2021;13:651284. doi: 10.3389/fnagi.2021.651284.
16. Simpkins AN, Neeland IJ, Chip L. (2021). Tipping the Scales for Older Adults: Time to Consider Body Fat Assessment and Management for Optimal Atherosclerotic Cardiovascular Disease and Stroke Prevention? *Journal of the American Heart Association*, 10(9):e021307.
17. Smith SM*, Zequeira S*, Ravi M, Johnson SA, Hampton HA, Ross AM, Pyon W. Maurer AP, Bizon JL, Burke SN (2021). Age-related Impairments on the Touchscreen Paired Associates Learning (PAL) Task in Rats. *Neurobiology of Aging*, 109:176-191.
18. Snyder, AR, Greif, S, Clugston, J, FitzGerald, D, Yarrow, J, Babikian, T, Giza, C, Thompson, F, & Bauer, RM (2021). The effect of aerobic exercise on concussion recovery: A pilot clinical trial. *Journal of the International Neuropsychological Society*, 27(8), 790-804.
19. Williamson JB, Lamb DG, Porges EC, Bottari S, Woods AJ, Datta S, Langer K, Cohen R. Cerebral metabolite concentrations are associated with cortical and subcortical volumes and cognition in older adults, *Frontiers in Aging Neuroscience*, 12, 479.
20. Zhou Y, Sheremet A, Kennedy JP, DiCola NM, Maciel CB, Burke SN, Maurer AP (2021). Spectrum Degradation of Hippocampal LFP During Euthanasia. *Frontiers in Systems Neuroscience*, 15:647011.

Appendix 3

Top 10 Presentations at Scientific or Public Meetings

Cohen R *Symposium.* NIA: HIV, Aging and Neurodegenerative Disease Workshop: Bethesda, MD

Burke SN *Seminar.* Edinburgh Neuroscience Webinar, “A Network-based Approach for Understanding and Treating Cognitive Aging.” Edinburgh Neuroscience Webinar, May 17th, 2021.

Woods AJ. *Symposium*. High-Throughput MRI-Based Personalization of Transcranial Direct Current Stimulation for Older Adults. North American Neuromodulation Society Annual Meeting, Orlando, FL USA, January 15th, 2021.

Foster TC *Symposium*. Molecular Markers to Operationally Define Cognitive Reserve. Workshop on Research Definitions for Reserve and Resilience in Cognitive Aging and Dementia, October 31 - November 1, 2021, Bethesda, Maryland.

Bauer R *Poster presentation.* Gaynor, L.S., Olshan, S., Raffalski, A., Tillotson, S., **Gullett, J**., Duara, R., Loewenstein, D.A., & Bauer, R.M. (2021). Brain biomarkers of early disease progression predict performance on a translational cognitive marker of Alzheimer’s disease. Poster presented at the Annual Meeting of the International Neuropsychological Society, February 2-5, 2021, San Diego, CA (virtual).

Fang R *Poster presentation.* Other authors: Peng Liu*, Ke Bo, Lihan Cui, Yujun Chen, Charlie Tran*, Ruogu Fang†, Mingzhou Ding†: A deep neural network model for emotion perception, in Annual Meeting of Society of Neuroscience, November 8-16, 2021. († co-corresponding authors)

Indahlastari A *Poster presentation.* High fidelity finite element models to predict changes in functional connectivity of the working memory networks in older adults. *The 4th International Brain stimulation Conference*. Selected as the recipient of the Best Poster Award out of 300+ posters.

Mauer AP *Symposium.* Decomposing the local field potential to understand brain aging and mental health disorders. Keynote speaker at the Florida Consortium of the Neurobiology of Cognition Conference August 5th-6th, 2021

Porges E *Symposium*. Other authors: Rohl, B.; Boissoneault, J.; DeKosky, S.; Williamson, J.; Effects of nonpharmacological sleep interventions on cognitive performance in older adults: A systematic PRISMA review. International Neuropsychological Society. September 2020.

Williamson JB *Poster presentation.* Other authors Bottari, S.A., **Lamb, D.G., Porges, E.,** Murphy, A.J., Tran, A., Ferri, R., Jaffee, M., (2021) Preliminary evidence of transcutaneous vagal nerve stimulation improving effects on sleep microstructure in veterans with PTSD. Poster presented at the annual meeting of the International Neuropsychological Association (virtual, due to COVID 19).

Appendix 4

Communications

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

The number of visits to the CAM website for 2021 was 1,646. Our most trafficked month was November with 552 visits. Hosting Neuromatch brought a lot of outside traffic to our site.

Social Media: The CAM Center's Twitter account (@UF_CAMcenter) started the year off with 81 followers. By December of 2021, we had 305 followers. We saw a big spike in followers, Tweet impressions, and profile visits in November. This coincided with both hosting the Neuromatch meet-up to the greater neuro/AI community and the hiring of our administrator to focus on communication. In addition to this UF account we have numerous graduate students, postdoctoral fellows, and the following faculty have personal accounts used to share their research and achievements. There CAM investigators and their twitter handles are as follows:

Jennifer Bizon, PhD
@JenBizon (1,055 followers)

Sara Burke, PhD
@saranburke (1,227 followers)

Adam Woods, PhD
@adamjwoods (644 followers)

Karina Alvina, PhD

@kalvina0308 (816 followers)

Yenisel Cruz-Almeida, PhD
@yenisel_CruzA (195 followers)

Natalie Ebner, PhD
@natalie_ebner (292 followers)

Ruogu Fang, PhD
@ruogufang (373 followers)

Aprinda Indahlastari, PhD
@aprindaindah (93 followers)

Carolina Maciel, MD
@neurologyrules (1,257 followers)

Drew Mauer, PhD
@theta_monkey (256 followers)

Barry Setlow, PhD
@b_setlow (727 followers)

News Coverage

1/29/21- (Bizon) MBI and local media coverage on Dr. Bizon being named department Chair of the Department of Neuroscience. Dr. Jennifer Bizon named chair of UF department of neuroscience » McKnight Brain Institute » University of Florida (ufl.edu)

3/18/21 – (Burke) MBI coverage on the difference between normal and cognitive decline and pathological disease and how diet can increase resilience to memory loss: https://twitter.com/UFMBI/status/1372538276641312771
https://www.youtube.com/watch?v=NxA5Rvn-eN8&t=10s

2021 -- (Team CAM; Bizon, Burke, Cruz-Almeida)- Highlighted in the MBI "Women in Neuro" series featuring women leaders across the UF research community. Women Leaders of UF Neuro Research Archive » McKnight Brain Institute » University of Florida (ufl.edu)

6/3/21 – (Woods) MBI and University coverage on PACT trial https://mbi.ufl.edu/2021/06/03/uf-joins-preventing-alzheimers-with-cognitive-training-study/

7/19/21 – (Woods, Fang) Alligator (award-winning student newspaper) coverage on the potential treatment for dementia using AI technology https://www.alligator.org/article/2021/07/ai-dementia

9/2/21 – (Woods) BrainFacts.org coverage on tDCS research to slow cognitive decline https://www.brainfacts.org/diseases-and-disorders/therapies/2021/creating-personalized-prescriptions-for-transcranial-brain-stimulation-090221

9/21/21 – (Woods) University coverage on research about Alzheimer's disease https://news.ufl.edu/2021/09/from-florida-episode-1/

10/20/21 – (Fang) College of Engineering coverage on AI research grant https://www.eng.ufl.edu/newengineer/research-innovation/ai-university/researchers-seek-to-build-confidence-into-ai-for-healthcare-under-nsf-grant/

10/31/21 – (Bizon, Foster) among featured speaker from across the world who presented at the 3rd Workshop on Research Definitions for Reserve and Resilience In Cognitive Aging and Dementia https://reserveandresilience.com/program/

11/4/21 – (Team CAM) 18 members of CAM labs were the top fundraising team for American Foundation for Suicide Prevention (AFSB). The Center for Cognitive Aging and Memory's name was printed on the back of the event t-shirts for raising over $3,000 https://cam.mbi.ufl.edu/2021/11/04/cam-team-raises-3800-for-suicide-prevention/

11/5/21 (CAM graduate students) Podcast – CAM and Neuroscience graduate students started a Podcast addressing topics and issues around neuroscience and graduate school. The inaugural podcast discussed tips for applying to graduate schools https://cam.mbi.ufl.edu/2021/11/05/interested-in-applying-to-the-bms-phd-progra-these-current-students-break-down-the-process/

11/17/21 (Woods) Society for Neuroscience Annual Report, feature of Dr. Woods and his work on personalized brain stimulation (pgs 24-27)
https://www.sfn.org/about/what-we-do/annual-report/fy2021
https://mbi.ufl.edu/2021/11/17/uf-neuroscientist-featured-in-society-for-neuroscience-annual-report/

12/7/21 (Woods, Fang, Gullett) MBI and University coverage of research into AI's potential to predict dementia https://ufhealth.org/news/2021/uf-study-shows-artificial-intelligence-s-potential-predict-dementia

12/8/21 (Woods, Fang) Coverage on the potential treatment for dementia using AI technology
Ivanhoe Broadcasting: https://youtu.be/iaHaYP0h_rY
Also covered by TV20 News (Miami, August 2021), Fox16 WNDU (Indiana, December 2021), etc.