

2023

McKnight Brain Research



University of Florida

1/15/2024

January 8, 2023

RE: McKnight Brain Research Foundation Annual Report

Dear Trustees of the McKnight Brain Research Foundation,

It has been another year of incredible accomplishments and milestones for the UF Center for Cognitive Aging and Memory: Clinical Translational Research (CAM Center). The year has brought several important transitions, including a new leadership structure to the Center. In February, I stepped away from the CAM Center leadership to assume the Directorship of the UF Evelyn F. and William L. McKnight Brain Institute. Moreover, Dr. Ron Cohen stepped back from his Co-Director role in May. As a founding Director of the CAM Center, Dr. Cohen brought significant distinction to this position and was critical for establishing the necessary infrastructure for the Center and for attracting a cadre of exceptional faculty to UF who will continue to make novel discoveries and advance the field of cognitive aging for years to come. We look forward to Dr. Cohen's future scientific contributions in his continuing role as the Evelyn F. McKnight Chair for Clinical Translation in Cognitive Aging. With these transitions, I'm thrilled that Drs. Sara Burke and Adam Woods have now assumed the roles of Co-Directors of the CAM center. As long-standing Associate Directors of the Center who were recently promoted to Professor in recognition of their accomplishments and international reputations in the field, Drs. Burke and Woods are the perfect choice to lead UF programs on brain aging and cognition. In fact, as both were originally recruited to UF through MBRF-sponsored programs, this leadership team is a powerful illustration of the impact of the UF-MBRF alliance.

October 2023 marked the 25th anniversary of the opening of the Evelyn F. and William L. McKnight Brain Institute, and it is truly remarkable to reflect on the dynamic and collaborative programs in cognitive aging that have been built at UF in partnership with the MBRF. Consistent with the gift agreement, the CAM Center is a thriving community of world-class fundamental and translational scientists. In just this past year, this group has contributed over 140 new scientific studies, made countless scientific presentations, and received numerous new grant awards. Through a new pilot granting program, the CAM Center has further recruited additional talent from across our campus to the field of cognitive aging, expanding the interdisciplinary focus of these research programs. The growth of the education and training programs is similarly impressive. An NIH R25 (Neuron-Aging) led by Dr. Sara Burke and colleagues is providing new opportunities for training next generation talent in brain aging and cognition through a Summer Neuroscience Internship Program for undergraduates and a recently established post-baccalaureate program. A second R25 led by CAM Center members Drs. Andrew Maurer and Karina Alvina recently received an outstanding score and will further bolster undergraduate training efforts in the next year. Finally, a new jointly sponsored NIH PhD training program (T32) I led with several colleagues received a fundable score. This training program will be the first of its kind in the state of Florida and will raise the national visibility of our PhD programs, in addition to providing core early career support for our students. This program will add to our existing repertoire of NIH funded T32s including one led by Dr. Woods and colleagues for advanced graduate training related to interventions in cognitive aging. The success surrounding these educational programs is simply spectacular and is creating a training environment and pipeline of scientists in the cognitive aging and memory field that will be unparalleled nationally.

We look forward to celebrating the 25th anniversary of the MBI in February in conjunction with hosting the annual Luttge Lectureship sponsored by MBRF. Our program *"From Foundations to Frontiers: Celebrating 25 years of Collaboration and Discovery"* will include reflections from MBI scientists on 25 years of scientific advances as well as a look forward to the future landscape of scientific progress in neuroscience and neuromedicine. We are delighted that Dr. Adam Gazzaley, M.D. Ph.D., David Dolby Distinguished Professor of Neurology, Physiology, and Psychiatry at the University of California, San Francisco will deliver the Luttge lecture. Dr. Gazzaley's participation will elevate our celebration as will his insights and reflections from his many years of scientific investigations focused on interventions in cognitive aging. We are truly excited to celebrate the MBI's many accomplishments with our scientists, UF leadership and the MBRF trustees.

The University of Florida is also the host site this year for the 15th MBRF-sponsored Interinstitutional meeting, and our team has been busy making plans for what we hope will be a spectacular event. Drs. Peter Rapp and Sue Resnick from the National Institute on Aging have agreed to serve as keynote speakers which will complement the many sessions organized to highlight the research across the four McKnight Institutes. We further have organized a pre-meeting to bring back discussions regarding emerging concepts in the field and how inter-institutional efforts can position our scientists to address the most pressing and relevant barriers to successful cognitive aging. In conjunction with the pre-meeting, Dr. Burke is leading efforts to reconstitute the CAMI-core and reinvigorate the interinstitutional pilot program. We hope the pre-meeting discussions will stimulate interest in applying to this program and spur new collaborations across sites. The MBI and University leadership looks forward to hosting the inter-institutional meeting and to participating in emergent scientific discussions.

As is reflected throughout the report, the MBI and University leadership recognizes the existing strength and future promise of the CAM Center and the critical scientific research being conducted therein. This recognition is reflected throughout many of the leadership changes across the University of Florida, including the selection of Dr. Woods as Associate Dean for Research by Dr. Beth Virnig, Dean of Public Health and Health Professions. Notably, Dr. Jennifer Hunt was recently named Interim Dean of the College of Medicine following the departure of Dr. Colleen Koch. Dr. Hunt is an ardent supporter of the research mission, and we look forward to partnering with both her and Dean Virnig as we continue to support the CAM Center and build our cognitive aging and memory programs at the University of Florida. Indeed, Dr. Woods has taken a lead role in the expansion of a CAM Center Research site at the UF College of Medicine Jacksonville campus. The UF Jacksonville site has increased access to populations of older adults from diverse backgrounds that can be challenging to recruit from the Gainesville area and has provided the infrastructure to secure funding for several large multisite trials led by Dr. Woods. With strong support from our university leadership, these efforts led by the CAM team to deploy cognitive aging trials and build partnerships across the Gainesville and Jacksonville campuses will further enhance interest, awareness, and therapeutic capabilities in the domains of cognitive and brain aging research.

I would like to extend my heartfelt gratitude for our dedicated team and for the continued partnership of the McKnight Brain Research Foundation. I hope that you will be as impressed as I am with the annual accomplishments of the CAM Center membership. I am confident that with MBRF's continued support, our researchers will continue to make significant discoveries that will positively advance brain and cognitive health in older adults. Please do not hesitate to contact me if I can answer questions or provide any clarifications from the report.

Sincerely,



Jennifer L. Bizon, Ph.D.

Chair, Department of Neuroscience

Director, Evelyn F. and William L. McKnight Brain Institute

January 13, 2023

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 (the “CAM Center”) for the year ending December 31, 2023. The mission of the CAM Center is to conduct multidisciplinary research focused on brain aging and cognition as well as translate leading-edge discoveries about brain aging into interventions that will preserve cognitive function and improve the quality of lives for older adults. Additionally, the CAM Center continues to serve as a world-class training ground for undergraduate and graduate students, postdoctoral scholars, as well as early career faculty interested in preclinical or clinical translational research careers focused on preventing, alleviating, or reversing age-related cognitive decline and memory loss. This past year was marked by exciting leadership transitions as Dr. Jennifer Bizon became the first female director of the McKnight Brain Institute and resigned her role as Co-Director of the CAM Center. Additionally, Dr. Ron Cohen also resigned his role as Co-Director of the CAM Center. Drs. Bizon and Cohen continue to actively participate as faculty members in the CAM Center. These transitions afforded Drs. Sara Burke and Adam Woods the honor of moving from Associate to Co-Director roles. Drs. Woods and Burke also both received promotion to the rank of Full Professor in July 2023. The leadership of the CAM Center continues to meet bi-weekly and has been dedicated to laying a solid foundation to support a successful world-class program on cognitive aging that spans preclinical to clinical translational research.

As detailed in the full report, CAM faculty and trainees continued to be very productive this past year with significant accomplishments pursuant to the center’s research and academic missions. Listed below are the primary objectives of the CAM Center as outlined in the MOU with the McKnight Brain Research Foundation. We have highlighted under each objective the activities in the past year that collectively have advanced our mission to uncover the fundamental mechanisms of brain aging that underlie cognitive decline as well as develop interventions and preventative strategies that promote positive functional outcomes for older adults.

OBJECTIVE 1: Maintain and grow the research infrastructure for conducting preclinical and clinical translational cutting-edge cognitive aging research.

Space: Over the past several years, the marked growth of CAM Center and our larger neuroscience research community has strained our physical infrastructure. In recognition of their growing programs and to facilitate even stronger collaborative efforts, the Bizon and Setlow laboratories moved into larger, contiguous, and shared research space on the fourth floor of the MBI. The Burke and Maurer laboratories also completed their move into a larger shared space on the third floor of the MBI.

In addition to space on the main UF campus, this past year our mission benefitted from continued expansion and development of our CAM Center Research site at the UF College of Medicine Jacksonville campus. The UF Jacksonville initiative is essential to increasing the populations of older adults available for research studies by the CAM Center, particularly those that are from diverse backgrounds that can be challenging to recruit from the Gainesville area. Over the past year, we have significantly increased our presence in Jacksonville, with 1 primary faculty member and 6 full-time

clinical trial staff funded by 2 large multisite R01s where Dr. Woods serves as the UF PI. We recently finalized negotiations to expand our presence further by taking over a 1200 participant population from the University of North Florida in the context of one of these trials. This will involve hiring 6 additional staff and obtaining multiple clinical trial testing locations across UF Health locations in the city of Jacksonville.

Facilities: The CAM Center has been an essential partner to the Department of Neuroscience and McKnight Brain Institute in establishing a core resource for microscopy to facilitate state-of-the-art research. Dr. Burke is the co-director of the microscopy co-op which was created to better serve CAM Center faculty across the UF Health Science Center. The CAM Center's financial support helps to defer annual service contracts, software licensing, operating costs, and to provide increased technical expertise for microscopes that are used by affiliated faculty and their laboratories. A major advantage of this arrangement is that laboratories of primary CAM Center faculty now have free access to numerous state-of-the-art instruments (not only those in their own laboratories), which can be leveraged for new discoveries in cognitive aging. During this past year, the co-op acquired a new Nikon multi-photon microscope, adding a fifth state-of-the-art instrument to our resources.

Our CAM Center space within the Communicore Building, which houses 5 faculty and 30+ staff and students, recently underwent renovations to add two new faculty offices. While this reduced our personnel space for students and staff, it provided much needed expansion of faculty offices to accommodate our new members that joined the UF CAM Center over the past couple years. In addition, our MBI housed CAM Center biospecimen facility recently underwent much needed upgrades to the freezers and equipment that facilitate these operations. This allows us to continue providing state-of-the-art resources to our faculty and will offer the opportunity to store samples for later analyses and pave the way for new collaborations with other institutes.

Research Initiatives and Discoveries: CAM Center researchers have been exceptionally productive in 2023, publishing over 140 peer-reviewed manuscripts, advancing their research programs, and securing approximately \$11.3 million in new awards, a \$1.3 million increase over 2022. Details regarding the impressive accomplishments of individual CAM Center investigators are summarized in the body of this report.

Additionally, during this past year the CAM Center sponsored two new research initiatives. First, we launched a pilot program to seed new projects at UF focused on understanding and treating cognitive aging. UF investigators submitted short proposals, met with CAM Center leadership and then 4 investigators were selected to receive funding (Drs. Russel Hepple, Eleonora Rossi, Shinichi Someya, and Steve Weisberg) with the understanding that they will apply for extramural funding related to cognitive aging within the next year and that they would become active members of the CAM Center. Details of the individual pilot awards are summarized in the body of this report along with NIH biosketches of our new CAM Center Members.

The second CAM Center-sponsored research initiative was to establish a transgenic rat colony for animals that have the humanized apolipoprotein (APOE) gene (either the E3 or E4 allele) knocked-in to replace the endogenous rat APOE gene. Humans that are positive for the APOE4 allele are at higher risk for experiencing poorer cognitive outcomes in advanced age. Additionally, it is believed that diet-based interventions may not be as effective at improving cognition in individuals with an APOE4 allele. Several CAM Center laboratories at UF are planning to conduct research with these animals, including Drs. Hepple, Someya, Setlow, Maurer, Bizon and Burke. By sponsoring the breeding core, these animals will be broadly accessible to our researchers.

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

The CAM Center continues to develop as a premiere training destination for those interested in building a research career

in the cognitive aging field. 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. The faculty currently serve as mentors for 62 graduate students and 16 postdoctoral scholars who are conducting research related to cognitive aging in human and animal models. In the past year, several students successfully defended their qualifying exams, Master's theses, and doctoral dissertations. Additionally, Ms. Zequeira won the "3-minute Thesis Competition" for the Southeast Region and went to compete nationally for her talk on the effects of cannabis on cognition in aging. The CAM Center further supported two CAM Graduate scholars (Samm Smith and Johleen Seedansingh). Ms. Smith just received a Notice of Award for her F31 graduate fellowship that will examine the role of hippocampal-striatal interactions in behavioral strategy use across the lifespan. Ms. Seedansingh made exceptional progress in her two years of graduate study and was honored with the First Place Prize for the MBRF Poster Competition at this year's Society for Neuroscience meeting. She is researching the physiological and cognitive effects of vagus nerve stimulation and testing whether this intervention increases cognitive resilience in advanced age. We continue to have multiple students funded by T32s across the CAM faculty labs. The list of awards given to our trainees far exceeds the space allotted in this letter but can be found in the main body of the report. To further support the training of our rising stars, this past year the CAM Center sponsored travel awards as well as dissertation awards.

Currently, CAM Center faculty play a major role on three NIH-funded T32 grants that support training relevant to cognitive aging. These include T32 programs focusing on aging and neuromodulation (Marsiske, Woods, MPis), aging and Alzheimer's disease and delated dementias (Lewis and Chakrabarty, PIs) and NeuroHIV (Cook, PI, Cohen, Porges). Furthermore, Drs. Burke and Alviña recently recruited the second cohort of undergraduate students for their R25 grant from the NIH/NIA entitled, "**Networking and Expanding Undergraduate Research On the Neurobiology of Aging to Advance Diversity (NEURON-Aging).**" The major goal of this award is to expand the pool of underrepresented researchers interested in biomedical, behavioral, and clinical aspects of brain aging, Alzheimer's disease and related dementias (ADRDs) through undergraduate research activities that enhance diversity. Additionally, Drs. Alviña and Maurer recently received a fundable score (impact of 25) on another R25 that will support a postbaccalaureate program for students that will serve as a bridge to PhD training in cognitive aging. Finally, Dr. Bizon received a fundable score (impact of 20) on a T32 that would support the first two-years of graduate training that is likely to further bolster our ability to recruit trainees with exceptional potential to the UF CAM Center.

The CAM Center has continued to support 4 undergraduate summer scholars that participate in the UF Summer Neuroscience Internship Program (SNIP). Every summer the Department of Neuroscience, in conjunction with the Evelyn F. and William L. McKnight Brain Institute, hosts a 10-week internship for undergraduate students interested in pursuing a Ph.D. in neuroscience. SNIP places paid interns in active neuroscience research labs to obtain hands-on laboratory and research experience, personalized guidance on graduate school admissions and professional development and career planning. This past summer students worked in the laboratories of Drs. Alviña, Burke, Porges, and Burns.

The CAM Center also continues to support junior faculty to facilitate their research career and building of independent research programs relevant to cognitive aging. As detailed in the full report, Dr. Joe Gullet received a K23 award. CAM Center funds also supported the following faculty in the past year: Drs. Stacey Alvarez-Alvarado, Breton Asken, Matthew Burns, Aprinda Indahlstari, and Dr. Shellie-Anne Levy. Notably, Dr. Levy is also a co-I on the NEURON-Aging R25 and she coordinates a summer series on minority health disparities in cognitive aging. Dr. Alvarez-Alvarado is working with Dr. Woods to lead our expansion in UF-Jacksonville. In addition, we also supported the retention of some of our strongest faculty over the past year. Finally, we recruited a new faculty member to the CAM Center: Dr. Jennifer Applebaum. Dr. Applebaum brings to the CAM Center a novel approach for understanding the impact of aging on underserved communities by investigating human-animal interactions.

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

We have continued to make progress in expanding our community at UF. Beyond those faculty and trainees mentioned within this report (who received funding from the CAM Center), we have many more UF faculty who affiliate with the CAM Center and conduct research on related topics. A full list of these affiliate faculty can be found on our website: <https://cam.mbi.ufl.edu/faculty/>. This past year we hosted our annual CAM Center Research Day on May 17, 2023, which targeted the full UF community of researchers and included paired talks in which pre-clinical and clinical translational researchers presented on the same research topics to nurture the core value of collaboration among our scientific community. We also had a poster session for trainees and ended the day with a reception at Cypress & Grove Brewery. Next year, in place of our annual research day, we will be hosting the 15th Annual MBRF Inter-Institutional meeting from May 15-17, 2024. To further support community engagement, we also hosted 2 CAM Center Socials on January 12, 2023 and October 20, 2023. Both events were well attended by CAM Center Faculty and trainees.

One key activity that locally raises visibility for the mission of the CAM Center is the annual William G. Luttge Lectureship that was established and is supported by a generous endowment provided by the McKnight Brain Research Foundation ten years ago. On February 23, 2023, we were fortunate to host the 8th Annual William G. Luttge Lectureship in Neuroscience, with **Dr. Joshua A. Gordon, MD, PhD** as our invited speaker. Dr. Gordon is the Director of the National Institute of Mental Health (NIMH), the lead federal agency for research on mental disorders. He oversees an extensive research portfolio of basic and clinical research that seeks to transform the understanding and treatment of mental illnesses, paving the way for prevention, recovery, and cure. This upcoming year, we are delighted that the Luttge Lecture will coincide with the 25th Anniversary Celebration of the UF McKnight Brain Institute. On February 2, 2024, we will host **Dr. Adam Gazzaley, MD/PhD** from the University of California, San Francisco to give the annual Luttge Lecture. Dr. Gazzaley is the David Dolby Distinguished Professor in Neurology, Physiology and Psychiatry at University of California, San Francisco. He is also the Founder/Executive Director of Neuroscape, a translational neuroscience center engaged in technology creation and scientific research aimed at improving cognition in older adults and individuals with mental health disorders. Dr. Gazzaley has authored over 180 scientific articles and delivered over 700 invited presentations around the world. His research and perspectives have been consistently profiled in high-impact media, such as The New York Times, New York Times Magazine, New Yorker, Wall Street Journal, TIME, Discover, Wired, PBS, NPR, CNN, and NBC Nightly News. He wrote and hosted the nationally televised PBS special “The Distracted Mind with Dr. Adam Gazzaley” and co-authored with Dr. Larry Rosen the MIT Press book: “The Distracted Mind: Ancient Brains in a High-Tech World”, winner of the 2017 PROSE Award in the category of Biomedicine and Neuroscience. Dr. Gazzaley has received many awards and honors, including the Society for Neuroscience – Science Educator Award, a 2020 Global Gaming Citizen Honor and was included in Newsweek's 2021 Inaugural list of America’s Greatest Disruptors. He is a Board of Trustee and Science Council Member and Fellow of the California Academy of Sciences.

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

Increasing visibility of the CAM Center’s research and affiliated faculty is an important goal and we have continued to grow in this area. We actively update our website (<https://cam.mbi.ufl.edu/>) and have a communications plan that involves engagement with social media and the press. We have improved the tracking of our current and former trainees through LinkedIn, and several CAM Center faculty maintain accounts on this platform. We also have an active Twitter account (@UF_CAMcenter), which has grown to 565 followers over the past year. Posts related to the research accomplishments of CAM Center faculty and trainees are made regularly and this is an important platform for amplifying our visibility. We continue to work with other McKnight Institutes and the MBRF Communications Working Group to coordinate our efforts and ensure we use our account to also amplify research accomplishments from our McKnight partners. Other Communication efforts supported by the UF CAM Center on included in the main text of this report.

This past year, Cristina Besosa continued to produce her podcast, “In Your Brain”, which can be found on Spotify and Apple ([https://twitter.com/ in_your_brain](https://twitter.com/in_your_brain)). The podcast takes various topics of neuroscience and presents them in digestible 20-min episodes that both scientists and the lay audience can engage with when convenient. Last year, episodes featured the Luttge Speaker, Dr. Joshua Gordon, discussing mental health and the CAM Center Co-Director, Dr. Burke, talking about learning and memory.

CAM Center faculty have also received enhanced visibility and media coverage this past year. Some highlights include:

Dr. Sara Burke wrote an article for the *Conversation* on a potential relationship between ultraprocessed foods and cognitive decline (<https://theconversation.com/ultraprocessed-foods-like-cookies-chips-frozen-meals-and-fast-food-may-contribute-to-cognitive-decline-196560>), which was re-published by multiple media outlets across the world and read over 230,000 times.

Dr. Ron Cohen and Brian Ho wrote an article for the *Conversation* on combined aerobic and strength training exercise promoting brain health in adults over 80 years (<https://theconversation.com/aerobic-and-strength-training-exercise-combined-can-be-an-elixir-for-better-brain-health-in-your-80s-and-90s-new-study-finds-212433>), which was re-published by multiple media outlets and has already been read almost 50,000 times over the past 3 months.

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

A major goal of the CAM Center is to increase cohesion between our discovery and translational research programs. In addition to our current community building efforts, such as the Research Day, CAM Center Socials, and the annual Luttge Seminar, we are working with the MBI, COM, and PHHP leadership to ensure that our Center is fully integrated with larger initiatives in the broad neuroscience community and takes full advantage of new opportunities provided by the UF AI initiative and the expansions to UF Jacksonville. With Dr. Bizon now serving as the new director of the MBI, we have a revived partnership with the MBI and are currently working with their leadership on new strategic initiatives for supporting research infrastructure, training grants, and large program project grants. Finally, we are excited about a new CAM Center partnership with the Center for Advanced Spatial Biomolecule Research (CASBR; <https://casbr.biochem.med.ufl.edu/>). The CASBR Co-Directors, Drs. Sun and Gentry, will both be presenting at the MBRF Inter-Institutional meeting and are collaborating with CAM faculty to use spatial metabolomics, lipidomics, and proteomics to identify new therapeutics targets for improving cognition in older adults.

OBJECTIVE 6: Increase interactions with the other McKnight Brain Institutes and increase visibility of CAM Center Core Programs.

In addition to long-standing projects that extend across McKnight Institutes, we also describe in this year’s report a number of new inter-institutional collaborations. This year, Dr. Burke agreed to chair the Cognitive Aging and Memory Intervention (CAMI) Core pilot program committee. This program was initiated and successfully developed by Drs. Woods and Rundek in 2016 to provide seed funding for new inter-institute collaborations aimed at developing novel interventions for improving cognitive function in older adults. We are excited to lead new efforts at revitalizing this important initiative and Dr. Burke has already recruited faculty from the University of Arizona, University of Miami, and University of Alabama, Birmingham to support these efforts. Working with the MBRF Trustees, we hope to launch a new funding announcement at the next Inter-Institutional meeting.

The ongoing NIA-funded REVITALIZE trial, led by Drs. Bowers (UF), Woods (UF) and Alexander (UA), recently completed enrollment of participants and will complete its final assessment in the coming month at the University of Florida and University of Arizona as part of a Phase II non-invasive near infrared photobiomodulation trial seeking to remediate

cognitive aging. As you might recall, this collaboration was seeded by one of the Cognitive Aging and Memory Intervention Core projects and leveraged the ACT trials infrastructure.

Towards increased visibility of our core programs, Dr. Woods and his lab are playing a central role in two seminal trials currently underway and funded by NIA. The Preventing Alzheimer's through Cognitive Training (PACT) trial is currently enrolling 7600 older adults into a trial that serves as a definitive evaluation of whether cognitive training versus a matched placebo condition results in decreased Mild Cognitive Impairment and Dementia conversion rates at a 3-year timepoint. As noted earlier in the letter, in addition to our original 838 participants across Gainesville and Jacksonville, we have now agreed to take over 1200 participants initially recruited by UNF: resulting in UF being responsible for 2038 of the 7600 participants in this landmark trial. All enrollment activities will be completed as of April 2024. This trial is the largest of its type and will have a far-reaching impact on the cognitive aging field upon completion, not to mention the high potential for long-term follow-up of this unique cohort. The study involves sites at University of South Florida, Duke University, Clemson University, and University of Florida. The recently funded trial, ACTIVE MIND, will leverage the infrastructure from the aforementioned trial to enroll a cohort of 1300 older adults with Mild Cognitive Impairment (300 at UF GNV and JAX) to query which of four cognitive training types vs. a matched placebo control produce significant preservation of functional abilities in patients with MCI – best reducing the incidence of dementia conversion. Each of these trials serves as seminal studies of cognitive training and its potential for remediating cognitive aging and reduction of dementia prevalence. Our role in these trials is a key example of our expanding footprint in the cognitive aging intervention community. In addition, new pilot trials within the CAM Center for person-specific/brain-specific dosed transcranial direct current stimulation, transcranial shockwave treatment, novel advanced cognitive decline prediction models, new artificial intelligence driven analytic tools, and wide variety of other novel approaches will serve as the next generation of funded trials and studies to advance our understanding and ability to intervention on age-related declines in thinking and memory.

We are proud of our many accomplishments during this past year and 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,



Sara N Burke, PhD

Co-Director, CAM Center

Professor and Vice Chair for Faculty Development, Department of Neuroscience



Adam J. Woods, PhD

Co-Director, CAM Center

Professor, Clinical and Health Psychology

Associate Dean for Research in the College of Public Health and Health Professions

December 13, 2023

Dear Trustees of the McKnight Brain Research Foundation:

In this final letter from me in my capacity as Evelyn F. McKnight Chair for Clinical Translational Research in Cognitive Aging, I would like to report on the state of the center and my activities over the course of my tenure and over the past year ending December 31, 2023. Before doing so, I want to thank you for the opportunity that you provided to me to help in the development of the Center for Cognitive Aging and Memory over the past 11 years. Your support enabled the growth and success of the center and facilitated our research on successful cognitive and brain aging and that of its many faculty and trainees. I and the other members of the center are very grateful for this support. I am happy to report continued success and scientific productivity by all of the faculty. As this is described in detail in the full report, I will only summarize these accomplishments here. However, I want to convey my pride in the work they have done and my happiness in contributing to these efforts. We continue to be highly productive, meeting our planned research objectives with multiple achievements consistent with the Center's mission. A major thrust of my own activity over the past year has been to facilitate the transition of leadership. In July, Dr. Adam Woods assumed my prior role as co-director of the center. I have worked closely with him to ensure a smooth transition and the continued success of the center. I believe that we have been successful in this regard.

With respect to my own research, multiple funded R01 projects continue with significant progress on all fronts. Perhaps the most significant accomplishment with respect to new funding this past year is the renewal of my NIDDK-supported R01 WISE study of the effects of bariatric surgery on brain function. This study examines these effects in the context of age-dependent obesity impact. We obtained a perfect score of 10 on this renewal application and have been notified that the institute intends to fund the renewal. Now we are waiting for the resolution of the congressional budget reconciliation for the funding to be released. This renewal application was submitted as a project with multiple PIs. I am happy to have Drs. Porges and Williamson as MPIs who will facilitate the success of the study, contributing important expertise related to vagus nerve function of direct relevance to the study aims. We continue to publish manuscripts based on data from the parent WISE study with a number of noteworthy findings, including evidence that microstructural white matter changes occur with obesity and exhibit changes post-surgery, cerebral metabolite alterations occur in relationship to BMI and A1C, and resting fMRI alterations occur post-surgery that associated with cognitive changes.

Other R01 projects focusing on the interactions of HIV, substance use and aging continue, most notably the NIA funded ROGUE study 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 (PLWH). Findings to date demonstrate that gut microbiome impacts cognitive function among PLWH with effects varying as function of age. The P01 and U24 studies supported by NIAAA are underway with Dr. Eric Porges (CAM faculty) leading the research component examining the effects of vagus nerve stimulation and supplementation with probiotics among PLWH who consume large quantities of alcohol. Findings from the NIDA-funded MAPLE study of HIV and cannabis use and from the 30-Day Challenge an NIAAA-funded study of cognitive and neuroimaging benefits from alcohol abstinence have been published, with manuscripts submitted or in preparation. In analyses of aging in the MAPLE cohort, we have found that the prevalence of cognitive deficits was greater than expected, as over 40% of participants over the age of 65 met criteria for MCI based on criteria used in Alzheimer's research. These findings have been submitted for publication recently.

With respect to our studies of successful aging in healthy older adults, the McKnight Brain Aging Registry (MBAR) has yielded several submitted manuscripts and recently published study (Ho et al., 2023) showing high rates of aerobic and strength exercise in the cohort, associated with stronger cognitive function. This study has already received a large number

of readings. Blood samples from the MBAR have been analyzed with findings related to cytokines in relationship to cognitive function and neuroimaging findings being prepared in manuscripts. NIA supported R01 studies were funded at Tufts University and Brown University, on which I am a co-investigator, are now in the data collection phase. The Tufts study (Roberts, PI) examines the cognitive benefits of nutritional supplementation with flavanol in older adults. The Brown study (Salmoirago-Blotcher, PI) examines the effects of mindfulness training on cognitive functioning in older adults. Preliminary findings were published in a manuscript "Exploring Effects of Aerobic Exercise and Mindfulness Training on Cognitive Function in Older Adults at Risk of Dementia: A Feasibility, Proof-of-Concept Study." These lines of research are important as they examine the potential benefit of these nutritional/behavioral approaches for enhancing functioning in older adults. As part of my preparation for transition to Professor Emeritus status later this coming year, I reviewed my productivity to date via Google Scholar. My research papers have been cited approximately 30,000 times with an H index of 96. The H index reflects impact, and my index is currently the highest of members of my academic department and among the highest for faculty in Neurology and Psychiatry as well. My major emphasis at this point though is the training and mentoring of the next generation of researchers who will continue lines of investigation currently underway and move the science into new cutting-edge areas. The CAM has flourished since my arrival at UF in 2012 at which time the clinical translational focus within MBI was nascent, evidenced by the success of our faculty and the graduate students who have played key roles and made major contributions. I have summarized their achievements in prior reports to the MBRF. At this point, all core faculty are funded from NIH supported grants, with younger faculty receiving career development awards over the past year (e.g. Dr. Joseph Gullett, K23). Dr. Woods is carrying this role forward serving as a mentor on such grants. I was asked to serve as a mentor on six career development awards this past year, and I continue to serve as a mentor on doctoral committees for a number of graduate students. In conjunction with Dr. Williamson, we were also successful in getting the Brain Rehabilitation Research Center of the VAMC refunded with aging and associated comorbidities and risk factors being an emphasis of the renewal. Overall, I feel that my tenure as chair is ending on a very positive note with a high level of continued research productivity for the CAM. I am confident that our faculty and trainees will continue to make important scientific contributions in the study of cognitive and brain aging.

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

Center for Cognitive Aging and Memory - Clinical Translational Research Program (CAM-CTRP)

Evelyn McKnight Chair for Clinical Translation in Cognitive Aging

December 19, 2023

I am pleased to present the 2023 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.

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 age-related 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

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. Over the course of aging, the methylation state of some DNA sites is altered in a relatively reliable manner across individuals and across species. This has resulted in the creation of DNA methylation (DNAm) clocks. DNAm age acceleration is calculated as the difference between the age predicted by the DNAm clock and chronological age. Thus, an individual may be biologically older or younger than their actual chronological age. The DNAm clock is used as a biomarker of aging and the rate of DNAm age acceleration is predictive of lifespan and the trajectory of decline in cognition and motor function, and increased pain sensitivity. An important aspect of epigenetic modifications is that many of the marks are influenced by environment factors (e.g. lifestyle) and therapeutic interventions. Several papers published this past year have focused on the environment (i.e. economic status) in relation to DNAm and aging phenotypes in humans (Jackson, Spector et al. 2023, Peterson, Crow et al. 2023, Strath, Peterson et al. 2023). Moreover, we found that the specific genes that are differentially methylated may reflect processes of biological aging such as increased inflammation or decreased vitamin D levels (Strath, Meng et al. 2023).

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. We are currently using technologically advanced spatial transcriptomics with single cell resolution, to examine age and sex differences in response and recovery from sepsis. In addition, several grant proposals examining age and sex differences in the response and recovery of sepsis have been submitted and one has been funded on Sepsis and the Systemic Cytokine Storm in Aging and Alzheimer Disease Models (Moldawer PI).

Collaborative Projects Outside of the University of Florida:

I have been collaborating with Dr. Daohong Zhou to examine a potential therapeutic treatment. Dr. Zhou recently moved from the University of Florida to the University of Texas Health Science Center at San Antonio. Due to the stressors of

aging (e.g. DNA damage or oxidative stress) some cells will become senescent, altering their function by initiating survival programs, including the release of stress signals (e.g. cytokines) that promote inflammation. Senolytic drugs selectively remove senescent cells. We have been examining the role of senescent cells in brain aging; chemotherapy induced cognitive impairment, and the influence of senescence on sex differences in the trajectory of cognitive decline. In a recent paper we describe how age-related cognitive decline is linked to senescence of peripheral cells (Budamagunta, Kumar et al. 2023). The results indicate that senolytic treatment preserved cognition, which was associated with the removal of peripheral senescent cells, decreasing systemic inflammation that normally drives neuroinflammation, blood-brain barrier (BBB) breakdown, and impaired synaptic function. Specifically, we examine similar and differential effects of two senolytic treatments, ABT-263 and dasatinib + quercetin (D+Q), in preserving cognition, markers of peripheral senescence, and markers of brain aging thought to underlie cognitive decline. Male rats were treated from 12 to 18 months of age with D+Q, ABT-263, or vehicle, and were compared to young (6 months). Both senolytic treatments rescued memory, preserved the BBB integrity, and prevented the age-related decline in hippocampal N-methyl-D-aspartate receptor (NMDAR) function associated with impaired cognition. Senolytic treatments decreased senescence-associated secretory phenotype (SASP) and inflammatory cytokines/chemokines in the plasma (IL-1 β , IP-10, and RANTES), with some markers more responsive to D+Q (TNF α) or ABT-263 (IFN γ , leptin, EGF). Both senolytic treatments decreased the expression of immune response and oxidative stress genes and increased the expression of synaptic genes in the brain (dentate gyrus, DG). However, D+Q influenced twice as many genes as ABT-263. Relative to D+Q, the ABT-263 group exhibited increased expression of DG genes linked to cell death and negative regulation of apoptosis and microglial cell activation. Furthermore, D+Q was more effective at decreasing morphological markers of microglial activation. The results indicate that preserved cognition was associated with the removal of peripheral senescent cells, decreasing systemic inflammation that normally drives neuroinflammation, BBB breakdown, and impaired synaptic function. Dissimilarities associated with brain transcription indicate divergence in central mechanisms, possibly due to differential access to the brain.

Current studies are examining chemotherapy induced DNA damage and increase in the number of senescent cells, associated with impaired memory and sex differences in responsiveness to senolytic treatment.

We had collaboration with Dr. Dan Nicholson, an Associate Professor in the Department of Neurological Sciences at Rush University Medical Center, Chicago, IL to examine the role of the GluN2B subunit of NMDA receptors in age-related cognitive decline and possible cell death signaling in Alzheimer's disease. Unfortunately, Dr. Nicholson passed away this past June. We have submitted a grant based on preliminary data from this collaboration and I will be reporting on the results from this collaboration at the Winter Conference on Neural Plasticity in 2024.

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. In particular, 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.

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 will serve on a discussion panel and act as a mentor for early career post-doctoral and graduate student investigators (Jayakody, Nolin, Peixoto, Velázquez Delgado).

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. In particular, 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 Esser (Department of Physiology and Functional Genomics), we have previously documented altered circadian rhythms in predicting the trajectory of cognitive decline.

I am on the scientific committee for the Winter Conference on Neural Plasticity, where I promote scientific sessions related to cognitive aging. I am overseeing a session on “What is new in brain aging?”. In addition, I will present recent data obtained in collaboration with Dr. Nicholson.

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 Dr. Katherine Keyes (Columbia University) and Dr. Vijay Ramchandani (NIAAA) and Dr. Doug Matthews (University of Wisconsin), I have participated in a special issue for the journal *Alcohol*. I published a review article on alcohol’s effects on the aging brain. Much of the review focused what researchers need to consider when studying the aging brain and cognition and is designed to serve as a resource for alcohol researchers laboring to learn how aging impacts the brain (Foster 2023).

Finally, I am planning on teaching a course entitled “Aging and the Brain” for Spring of 2024. This class will address questions of the primary causes of aging, biomarkers of aging, and the history of research on aging. Theories of aging will be applied to the brain and cognitive decline. Whenever possible, examples are drawn from recent research in humans involving large populations and cellular molecular mechanisms examined using animal models. Differences in the rate of aging due to sex, resilience, compensation, and cognitive reserve and the role of aging in disease will be discussed. Finally, therapeutic implications will be explored.

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,

A handwritten signature in black ink, appearing to read "Tom Foster". The signature is fluid and cursive, with the first name "Tom" and last name "Foster" clearly distinguishable.

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

2023 at a Glance

Summary of Major Scientific, Programmatic, outreach and Training Accomplishments



Sara Burke, PhD
Professor, Department of Neuroscience
Co-Director, CAM center

2023 was marked by several scientific achievements for the Burke laboratory. First, I was honored to receive promotion to Full Professor in the College of Medicine Department of Neuroscience and become Co-Director of the CAM Center. To prepare for these new roles, I completed the Three Rivers Serving Leadership Course. This course involved approximately 72 hours of interactive leadership instruction and personal leadership coaching over 6 months. 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. My NIH/NIA R01/RF1, entitled “The Contribution of Declines in Functional Connectivity to Cognitive Aging,” entered the third year of funding. With the support of this award, we have continued to develop novel analytical tools to bridge levels of analysis from single cells to global brain dynamics. In collaboration with engineers at MIT’s Lincoln Laboratory, we are implementing machine learning approaches to co-register 3-dimensional light sheet microscopy images that contain single-cell resolution with MRI datasets. It is our goal to use this method of bridging levels of analysis to enhance the translational potential of discovery science for understanding that treating human cognitive aging. Integral to the research mission of both my lab and the CAM is the training of graduate and undergraduate students. My graduate student, Samm Smith, was awarded an F31 from the NIA and my other student Alyena Ross successfully advanced to candidacy. I am also delighted that through the efforts of myself and my colleagues to support undergraduate research opportunities, we recently recruited our second cohort of undergraduate students are being supported by the CAM-sponsored R25 training grant from the NIH/NIA, entitled “Networking and Expanding Undergraduate Research on the Neurobiology of Aging to Advance Diversity (NEURON-Aging).” Along with Drs. Karina Alviña (CAM Center Faculty) and José Abisambra (CAM Center Affiliate), we are providing enhanced research opportunities for underrepresented students both from UF and other colleges/universities. We just recruited another 7 talented first- and second-year undergraduate students that will be starting research in labs that investigate cognitive aging at the beginning of 2024, along with the 6 students that joined our program last year. 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 related to the topic of cognitive aging. Additionally, Dr. Abbi Hernandez and I recently had a paper accepted to *Frontiers in Aging Neuroscience* that documents the impact of a long-term ketogenic diet on immediate-early gene expression in the prelimbic cortex and CA3 subregion of the hippocampus. This highlights the ongoing and productive collaboration between the Evelyn F. McKnight Brain Institutes at UF and UAB. I also gave 3 invited talks at international meetings, including receiving the honor of being a plenary speaker the International Conference on the Neurobiology of Learning and Memory, Invited Speaker at the 8th Global Ketogenic Symposium, and an Invited Speaker at the International Behavioral Neuroscience Society Conference. Furthermore, my trainees presented at the annual meeting of the Florida Consortium on the Neurobiology of Cognition, the CAM Center Annual Research Day, and McKnight Brain Research Foundation Poster Reception at the Society for Neuroscience meeting.



Adam J. Woods, PhD
Associate Dean of Research, College of Public Health and Health Professors
Professor, Department of Clinical Health Psychology
Co-Director, CAM center

Cognitive function declines as we age. As our thinking and memory skills decline, the rate of functional dependence, mortality, and acute illness requiring hospitalization increases. Increased rates of cognitive and functional decline associated with dementia represent a growing concern considering our rapidly aging population. There is currently a paucity of effective treatments for recovering age-related declines in cognitive function. A variety of methods have been proposed to counteract cognitive aging and/or slow onset of dementia (e.g., cognitive training). Unfortunately, these techniques have limited degrees of success and transfer to everyday life. My work demonstrates that combining treatments like cognitive training with non-invasive brain stimulation (tDCS, TMS, tACS) facilitates neural plastic response, improves cognitive abilities (specifically working memory, attention, and speed of processing), and leads to long-term improvement. In combination with modern multimodal neuroimaging, artificial intelligence, and electrophysiology recording, this work not only identifies mechanisms underlying improvement, but also provides information important for further optimizing treatment effectiveness. At present, my lab maintains over 17 million dollars in active NIH funding (4 concurrent R01/RF1s) to investigate non-invasive brain stimulation and other neuromodulation-based interventions. Collectively, my work aims to slow the effects of cognitive aging and delay the onset of dementia using non-invasive and minimally invasive approaches. At present, a major focus in my lab uses machine learning and other artificial intelligence approaches paired with multimodal imaging, behavior and clinical variables/outcomes to identify novel pathways to precision dosing/medicine applications of non-invasive brain stimulation methods in patient populations.



Jen Bizon, PhD
Professor and Chair
Department of Neuroscience
Director, McKnight Brain Institute

My NIH-funded research program broadly focuses on determining the neural processes that support cognitive and behavioral changes in aging. Using rodent models, my laboratory employs an integrative approach that combines sensitive behavioral assessments with cellular, molecular, optogenetic, and pharmacological methodologies. Our long-term goal is to identify the circuit and cellular alterations associated with brain aging and disease that are most relevant to cognitive dysfunction and to design strategies that target these mechanisms to improve cognitive health and life quality in older adults. We are currently pursuing vagus nerve stimulation (VNS) and cannabis/cannabinoids as interventional strategies for cognitive remediation in aging. Data from our lab thus far suggest that both strategies hold potential for reversing age-related deficits in some forms of cognition (particularly prefrontal cortex-mediated executive functions), and ongoing work is investigating the mechanisms underlying these pro-cognitive effects. In addition, we are continuing to pursue research on the neural mechanisms by which aging causes shifts in decision-making strategies in aging, and we have recently added the capacity to conduct fiber photometry, which allows us to record the activity of genetically defined neuron populations in behaving rats. During this year, we published five manuscripts with a sixth currently in revision. My laboratory also made over fifteen conference presentations and three of my trainees received

recognitions at the MBRF-sponsored poster session at the Society for Neuroscience meeting in Washington DC. In addition, members of the lab have completed several large studies across multiple funded projects and currently preparing 4 additional manuscripts.



Ron Cohen, PhD
Evelyn McKnight Chair of Clinical Translation in Cognitive Aging and Memory
Professor, Clinical and Health Psychology

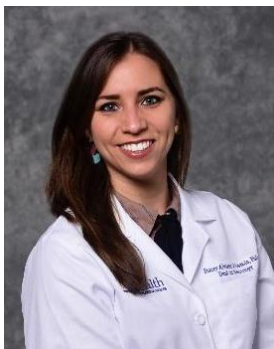
A major thrust of my own activity over the past year has been to facilitate the transition of leadership. In July, Dr. Adam Woods assumed my prior role as co-director of the CAM Center. I have worked closely with him to ensure a smooth transition and the continued success of the center. I believe that we have been successful in this regard. With respect to my own research, multiple funded R01 projects continue with significant progress on all fronts. Perhaps the most significant accomplishment with respect to new funding this past year is the renewal of my NIDDK-supported R01 WISE study of the effects of bariatric surgery on brain function. This study examines these effects in the context of age-dependent obesity impact. Other R01 projects focusing on the interactions of HIV, substance use and aging continue, most notably the NIA funded ROGUE study 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 (PLWH). Findings to date demonstrate that gut microbiome impacts cognitive function among PLWH with effects varying as function of age. With respect to our studies of successful aging in healthy older adults, the McKnight Brain Aging Registry (MBAR) has yielded several submitted manuscripts and recently published study (Ho et al., 2023) showing high rates of aerobic and strength exercise in the cohort, associated with stronger cognitive function. This study has already received a large number of readings. Blood samples from the MBAR have been analyzed with findings related to cytokines in relationship to cognitive function and neuroimaging findings being prepared in manuscripts. As part of my preparation for transition to Professor Emeritus status later this coming year, I reviewed my productivity to date via Google Scholar. My research papers have been cited approximately 30,000 times with an H index of 96.



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

Epigenetic techniques from my lab are employed to develop biomarkers to be used as diagnostic and prognostic indicators. Over the course of aging, the methylation state of some DNA sites is altered in a relatively reliable manner across individuals and across species. This has resulted in the creation of DNA methylation (DNAm) clocks. DNAm age acceleration is calculated as the difference between the age predicted by the DNAm clock and chronological age. Thus, an individual may be biologically older or younger than their actual chronological age. An important aspect of epigenetic modifications is that many of the marks are influenced by environment factors (e.g. lifestyle) and therapeutic interventions. Several papers published this past year have focused on the environment (i.e. economic status) in relation to DNAm and aging phenotypes in humans (Jackson, Spector et al. 2023, Peterson, Crow et al. 2023, Strath, Peterson et al. 2023). Moreover, we found that the specific genes that are differentially methylated might reflect processes of biological aging such as increased inflammation or decreased vitamin D levels (Strath, Meng et al. 2023). Due to the stressors of aging (e.g. DNA damage or oxidative stress) some cells will become

senescent, altering their function by initiating survival programs, including the release of stress signals that promote inflammation. Senolytic drugs selectively remove senescent cells. In a recent paper, we describe how age-related cognitive decline is linked to senescence of peripheral cells (Budamagunta, Kumar et al. 2023). The results indicate that senolytic treatments preserved cognition, which was associated with decreasing systemic inflammation that normally drives neuroinflammation, blood-brain barrier (BBB) breakdown, and impaired synaptic function. Specifically, we examine similar and differential effects of two senolytic treatments, ABT-263 and dasatinib + quercetin (D+Q). Male rats were treated from 12 to 18 months of age with D+Q, ABT-263, or vehicle, and were compared to young (6 months). Both senolytic treatments rescued memory, preserved the BBB integrity, and prevented the age-related decline in hippocampal N-methyl-D-aspartate receptor (NMDAR) function that underlies impaired memory. Senolytic treatments decreased the senescence-associated secretory phenotype (SASP) and inflammatory cytokines/chemokines in the plasma (IL-1 β , IP-10, and RANTES), with some markers more responsive to D+Q (TNF α) or ABT-263 (IFN γ , leptin, EGF). Both senolytic treatments decreased the expression of immune response and oxidative stress genes and increased the expression of synaptic genes in the brain (dentate gyrus, DG). However, D+Q influenced twice as many genes as ABT-263. Relative to D+Q, the ABT-263 group exhibited increased expression of DG genes linked to cell death and negative regulation of apoptosis and microglial cell activation. Furthermore, D+Q was more effective at decreasing morphological markers of microglial activation. The results indicate that preserved cognition was associated with the removal of peripheral senescent cells, decreasing systemic inflammation that normally drives neuroinflammation, BBB breakdown, and impaired synaptic function. Dissimilarities associated with brain transcription indicate divergence in central mechanisms, possibly due to differential access to the brain.



Stacey Alvarez-Alvarado, PhD
Assistant Professor
Department of Neurology - Jacksonville

Over the past year, my role as an Assistant Professor in the Department of Neurology at the College of Medicine-Jacksonville has been marked by important achievements in cognitive aging related research. This feat has been possible due to a great local and cross-campus collaboration (Jacksonville and Gainesville). Our primary focus has been to understand and mitigate the risks associated with cognitive decline/Alzheimer's disease, and our efforts have encompassed a wide range of approaches, from research initiatives to community engagement and outreach programs. One of our major accomplishments has been the successful recruitment of over 150 participants for the PACT study at the UF College of Medicine-Jacksonville site. This study, along with the recently launched ACTIVE MIND trial, holds immense potential for advancing our knowledge of cognitive aging and developing interventions to counteract Alzheimer's disease. Our commitment to community ties and outreach programs has been a cornerstone of our work, ensuring that we have a diverse and representative participant pool. In addition to recruitment efforts, I've actively participated in various outreach initiatives to promote clinical research education within the community. A notable example was participating in the Victory AM 1360 WCGL Radio Morning show with Dr. Jackson. During this interview, conducted alongside UNF, we discussed the significance of community health and engagement in the context of clinical research. Building trust between the community and local medical institutions is crucial, and initiatives like these contribute to fostering that trust and encouraging individuals to participate in clinical research. Additionally, participating as a panelist at the Jacksonville Urban League was a particularly rewarding experience. This nonprofit organization, dedicated to empowerment, provided a platform for us to address topics on aging, clinical research, and community

partnerships. The presentation, "Aging Perspectives & Clinical Research Participation: Building the Toolbox for the Future," allowed us to share insights and build awareness, further strengthening our ties with the community. Lastly, the Celebration of Resident and Fellow Education and Research Day at the University of Florida-Jacksonville was another meaningful endeavor, where I had the opportunity to support young researchers by serving as a poster judge and moderator. Looking ahead, my efforts are directed towards securing support for future projects building-off from my CTSI K12 application submitted in December 2023. This project will target older adults and build an initial cohort following cognitive and physical aging trajectories, with a special emphasis on minority recruitment and retention within our clinical research infrastructure. Recognizing the importance of diversity in research, I am dedicated to understanding the nuances of cognitive aging across different populations. In review, my first year as an assistant professor has been marked by a fruitful blend of research accomplishments and community engagement. These endeavors lay a robust foundation for impactful contributions to the field of cognitive aging. I am extremely excited about the potential for future advancements in our understanding of Alzheimer's disease and related dementias.



Karina Alvina, PhD
Assistant Research Professor
Department of Neuroscience

I am a member of the CAM Center and Co-Director of the NEURON-Aging Program with Dr. Burke. This program provides research training for talented undergraduate students from diverse backgrounds, many of which are conducting experiments in the laboratories of CAM Center Faculty. My own research examines the intersection of aging, stress, exercise and cognitive. Alzheimer's Disease (AD) is a neurodegenerative aging disorder that is associated with impairment in both short- and long-term memory and anxiety-like behaviors. AD damages the hippocampus first, one of the regions of the brain that is involved in learning, memory encoding, memory consolidation and spatial navigation. On the contrary, exercise has been shown to improve cognitive decline in AD models and to a certain extent in humans. Amongst many mechanisms that are modulated by exercise, stimulation of the production of myokines such as Irisin has been linked to neuroprotection. Recent findings postulate that Irisin could rescue cognitive decline and potentially halt neurodegeneration. Therefore, one of the goals of our research is to determine how exercise, and in particular Irisin, could improve cognitive outcomes in aging and AD mouse models.



Breton Asken, PhD, ATC
Assistant Professor
Department of Clinical and Health Psychology

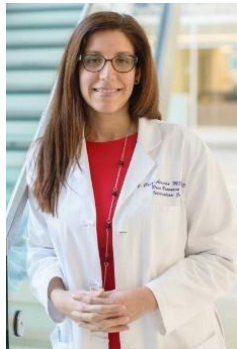
Funded research through the 1Florida ADRC Development Grant mechanism and the Mangurian-Fixel-McKnight Foundation. Through the ADRC Development Grant, I successfully oversaw measurement of the plasma proteome in a unique sample of older adults with traumatic encephalopathy syndrome, Alzheimer's disease, and healthy controls to identify novel physiological pathways and specific proteins especially relevant to the long-term brain health of individuals with prior repetitive head trauma. Related abstracts have been submitted to national and international conferences, and a manuscript is in preparation. Through the Mangurian-Fixel-McKnight Foundation, I have support to collect skin biopsies and test for presence of alpha-synucleinopathy pathology in the 1Florida Alzheimer's Disease Research Center as well as initiate collection and banking of corresponding cerebrospinal fluid (CSF) sample for future analyses. Recruitment is now ongoing. I have authored several

publications advancing our understanding of multimodal biomarkers in the assessment of Alzheimer's disease and related causes of dementia.



Matt Burns, MD, PhD
Assistant Professor
Department of Neurology

I am a board-certified in neurology by the American Board of Psychiatry and Neurology and my research interests broadly include aging, deep brain stimulation, neurodegenerative disorders, and bodily coordination. My lab is interested in the interaction between aging and neurodegenerative disease. We use aged rat models to induce synucleinopathy (the pathologic protein associated with Parkinson's disease, Dementia with Lewy Body, and Multiple System Atrophy), and employ cognitive assessments, high field MRI imaging, and immunohistochemistry to understand how aging contributes to cognitive and affective symptoms in these diseases.



Yenisel Cruz-Almeida, PhD
Associate Professor
Department of Dentistry

I am currently a tenured Associate Professor in the Department of Community Dentistry and Behavioral Sciences, as well as affiliate faculty in the Departments of Neuroscience and Epidemiology. I serve as Associate Director of the UF Pain Research & Intervention Center of Excellence and a core leader on the UF Pepper Center. This past year has been a remarkably productive one for my laboratory. In total we published 25 peer-reviewed papers. Highlights include our reproducibility of accelerated brain aging in persons with osteoarthritis pain with over 600 participants from institutions around the US, and the feasibility of applying brain aging algorithms to MRIs collected at various clinical scanners in UFHealth facilities. Our findings suggest that brain age can be derived from different types of clinical images in different facilities.



Natalie Ebner, PhD
Professor
Department of Psychology
Member, CAM center

I am a Distinguished Professor in the Department of Psychology, in the College of Liberal Arts and Sciences, at the University of Florida. I also hold an adjunct faculty position in the Department of Aging & Geriatric Research in the College of Medicine at the University of Florida and am affiliated with the Institute on Aging, the McKnight Brain Institute, and the Florida Institute for Cybersecurity Research on campus. My expertise is in experimental behavioral aging research. Coupled with my background in affective, social, and cognitive neuroscience, this affords a comprehensive view of brain-behavior relationships in the study of healthy aging. To do this research my lab uses a multi-methods approach in that combines convergent measures, including self-report, cognitive-behavioral measures, eye tracking, structural and functional neuroimaging (fMRI, ERP), and as of recently, highly innovative pharmacological (oxytocin administration), neurofeedback training (real-time fMRI), and applied (cybersecurity related) interventional approaches, with the aim to integrate introspective, behavioral, and neurobiological data. This past year, my laboratory continued to publish our research on

social cognitive and affective aging in top-tier peer reviewed scientific journals and obtained additional grant funding (including an R21 and an NIH diversity supplement for one of our trainees).



Ruogu Fang, PhD
Associate Professor
J. Crayton Pruitt Family Department of Biomedical Engineering
College of Engineering

An AI researcher in medicine and healthcare, Dr. Ruogu Fang is a tenured Associate Professor and Pruitt Family Endowed Faculty Fellow in the J. Crayton Pruitt Family Department of Biomedical Engineering at the University of Florida. Her research revolves around the integration of artificial intelligence (AI) and deep learning with the intricacies of the human brain. Her research encompasses two principal themes: AI-empowered precision brain health and brain/bio-inspired AI. Her work involves addressing compelling questions, such as using machine learning techniques to quantify brain dynamics, facilitating early Alzheimer's disease diagnosis through novel imagery, predicting personalized treatment outcomes, designing precision interventions, and leveraging principles from neuroscience to develop the next generation of AI. Fang's current research is also rooted in the confluence of AI and multimodal medical image analysis. She is the PI of NIH NIA RF1 (R01-equivalent), NSF Research Initiation Initiative (CRII) Award, NSF CISE IIS Award, Ralph Lowe Junior Faculty Enhancement Award from Oak Ridge Associated Universities (ORAU). She has also received numerous recognitions. She was selected as the Inaugural recipient of the Robin Sidhu Memorial Young Scientist Award from the Society of Brain Mapping and Therapeutics, Best Paper Award from the IEEE International Conference on Image Processing, University of Florida Herbert Wertheim College of Engineering Faculty Award for Excellence in Innovation, UF BME Faculty Research Excellence Award, among others. Fang's research has been featured by Forbes Magazine, The Washington Post, ABC, RSNA, and published in Lancet Digital Health. Her research has been supported by NSF, NIH, Oak Ridge Laboratory, DHS, DoD, NVIDIA, and the University of Florida. At the heart of her work is the Smart Medical Informatics Learning and Evaluation (SMILE) lab, where she is tirelessly dedicated to the creation of groundbreaking brain and neuroscience-inspired medical AI and deep learning models. The primary objective of these models is to comprehend, diagnose, and treat brain disorders, all while navigating the complexities of extensive and intricate datasets.



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

I am recruiting study participants for my K23 project which includes older adults with amnesic MCI. We are teamed up with a parent project R01, the Active Mind Trial, and will be collecting MRI as well as cognitive test data prior to randomizing participants to either an active control condition or one of several cognitive training paradigms. My specific study will look at the sub-group of participants with amnesic MCI who also obtained MRI and I will use AI approaches to examine the ability of their baseline MRI to predict their response to the cognitive training intervention. I am also preparing to start recruiting for a small clinical trial using a first-ever FDA IDE device to stimulate the brain of mild dementia patients with mild shockwave pulses. In this study, we will randomize to either active or sham stimulation, and will also include a comparison group of healthy older adults as part of our efforts to examine cognitive aging effects.



Aprinda Indahlastari, PhD
Assistant Professor
Department of Clinical and Health Psychology

This past year, I published two first author papers (one of which in high impact journal of 8.9), two co-author papers, and one under review related to cognitive aging and tDCS. I submitted KL2 grant (December 2022) and K25 NIH grant (June 2023). I was not selected for KL2, but advanced to the top 4 finalists and received an average score of 2. My K25 was discussed at the NIA study section and received a score just seven points away from the funding cutoff. I am in the process of resubmitting the K25 for March 2024 deadline. These grants are focusing on investigating mechanistic effects of tDCS on cognition in older adults. I taught the new AI course I developed last year, which has seen a slight increase in enrollment to 36 students (GatorEvals average > 4.0). I won a scientific image contest for the CASC 2024 brochure, with my image chosen from hundreds of submissions to be featured. These images were a representation of tDCS computational models that I mainly do. I also presented at the International Brain Stimulation Conference in Portugal (Feb'23), AI4Health (April'23), NVAITC (May'23). All conferences were in the topic of cognitive aging intervention and AI. I co-chair a new working group within the college, the PHHP AI Committee. We successfully hosted two seminars with an attendance of around 40-50 people each. We'll host our first external seminar, featuring a speaker from Stanford, in January 2024. My pilot study investigating in-scanner tDCS effects on working memory in older adults is making steady progress, with IRB-approved protocols, a new hire research coordinator (fully trained), and a pilot MRI scan scheduled for December 2023. This pilot study will be pivotal in providing the pilot data to support my K25 submission and other planned NIH NIA grants, such as R03 and R21.



Ashok Kumar, PhD
Research Associate Professor
Department of Neuroscience

My research has centered on delineating the mechanisms contributing to age-related cognitive impairment. Specifically, I focus on interventions such as environmental enrichment, exercise, anti-inflammatory compounds, senolytics, and viral vector gene delivery to reverse age-related cognitive impairment and synaptic plasticity deficits.



Damon Lamb PhD
Assistant Professor
Department of Psychiatry

My research is interested in the complex interaction of autonomic, 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 using advanced computational methods. Our research project investigating a putative treatment for age-related memory loss, evaluated in an amnesic mild cognitive impairment cohort, was published this year. In outreach and training, I taught Neuroscience Artificial Intelligence/Machine Learning and developed a new graduate data science/statistics course for the neuroscience department, presented

new magnetic resonance imaging results at the SfN Annual Meeting, and continued work on research projects funded by the VA, DOD, and JDRF.



Andrew Maurer, PhD
Associate Professor
Department of Neuroscience

Our research endeavors to decipher the neurophysiological basis of cognitive decline in aging, with a focus on rats as our model organisms. We concentrate on examining brain network dynamics, utilizing advanced electrophysiological methods to track neural activity with high precision in these animals. Alongside, we employ behavioral assessments specifically designed for rats to evaluate cognitive functions, thereby establishing a correlation between neural changes and observable behaviors. Additionally, we are expanding our investigation to explore the impact of lifestyle factors, such as dietary regimes and sleep patterns, on the aging trajectory in rats. This holistic approach, encompassing both neural and behavioral aspects, coupled with lifestyle considerations, aims to provide a comprehensive understanding of cognitive aging in rats, offering valuable insights that might be extrapolatable to broader aging research. This past year, we continued to publish and present data related to alterations in synaptic activity that are related to advanced age and cognitive decline. Additionally, I submitted and received a fundable score (impact of 25) on an R25 grant that will create a research postbaccalaureate for students in cognitive aging that will facilitate their transition to PhD training.



Eric Porges, PhD
Associate Professor
Department of Clinical Health Psychology

Over the past year, we have continued our work in cognitive aging and accelerated aging. Participant enrollment and data collection are ongoing in our NIH-funded exploration of the cognitive, neurophysiological, and systemic inflammatory impact of both non-invasive transcutaneous vagus nerve stimulation (taVNS) and microbiome interventions in adults and older adults who are vulnerable to accelerated cognitive aging (e.g. people living with HIV and high-risk alcohol drinkers). Additionally, the McKnight Brain Research Foundation supported collection of data in a normal aging cohort to complement our NIH/NIA-funded study of older adults with mild cognitive impairment. This study explores the acute cognitive and neurophysiological impacts of taVNS in older adults and preliminary results describing whole brain functional connectivity during stimulation (seeded in the solitary nucleus) have been accepted for presentation at the International Neuropsychological Society in 2024 by lab member Abel Pichardo. Data collection continues for our NIH-funded project in collaboration with Johns Hopkins University. Our team's aim is to characterize the trajectory of the macromolecular spectrum during normal aging via Magnetic Resonance Spectroscopy (MRS). A second RO1 was funded as part of this collaboration and data collection will start on that project in the new year. An R01 with CAM MPis (Cohen, Porges, Williamson) has been awarded to continue our work in the cognitive impacts of surgically induced weight loss. With this project, we are in the midst of finalizing IRB approval and expect data collection to begin shortly after. A manuscript has been submitted for review using McKnight Brain Aging Registry data on adults 85+ has been used to extend our previous characterization of lifespan trajectory changes to frontal cortical GABA (the principal inhibitory neurotransmitter) to include this important advanced-age population (led by graduate student Mark Britton).



Barry Setlow, PhD
Professor
Department of Psychology

There has been considerable progress in the past year on a number of fronts related to our cognitive aging research program, all of which is conducted in collaboration with Dr. Bizon. The lab continued work under three R01 grants from NIA, focused on a) neural mechanisms of age-related changes in decision making, b) the application of vagus nerve stimulation to remediating cognitive decline in aging, and c) the effects of cannabis on age-related cognitive decline, as well as work under a grant from the Florida Department of Health to investigate effects

of cannabinoids on age-related cognitive decline and Alzheimer's disease-like pathology. We have publications in preparation on all of these projects, and we anticipate a half-dozen of them to be submitted in the next year. We are also initiating a new line of research in which we will be assessing whether psilocybin and similar "psychedelic" drugs hold potential for remediating age-related cognitive impairments. I authored 10 peer-reviewed papers and one book chapter in 2023. Only two of these were focused specifically on aging, but others lay the groundwork for future projects that will incorporate aging. Lab trainees presented their research at local, state, national, and international meetings. In addition, I gave four invited presentations, including one at the MBRF Interinstitutional Meeting in May.



John Williamson, PhD
Associate Professor
Department of Psychiatry

My research includes both mechanistic and treatment development work in healthy brain aging and factors that contribute to unhealthy brain aging. I am excited about a project in which we just recently began data collection designed to assess factors leading to poor recovery from mild to moderate traumatic brain injury in older adults. This Department of Defense supported longitudinal study incorporates blood, multi-modal neuroimaging and neurocognitive assessment to address hypotheses related to brain aging, injury characteristics, and trajectories of recovery in adults over the age

of 65. We are using similar methodological approaches to assess younger to middle-aged adults with both acute and chronic TBI from mild to severe. Thus, data will span ages 18-90 and allow us to examine both cross-sectionally and longitudinally with cohorts effects of inflammation, vascular factors, neurodegenerative correlates, and white matter injury correlates on neurobehavioral outcomes as a function of age. My team is also excited about a new bariatric surgery project (Eric Porges, Ron Cohen, and I are mPIs) in which we will be able to assess factors associated with obesity, changes in obesity, and vagal function on brain health over time. This project is supported by a newly awarded (just received the NOA) R01. Obesity and associated metabolic syndrome are factors which may change the trajectory of brain and cognitive aging. Thus, there are critical features to understand relative to these mechanisms in developing interventions. The MBRF has funded a pilot project on a vagal intervention with our team and the University of Arizona. This longitudinal study includes pre and post multi modal MRI to paired transcutaneous vagus nerve stimulation and cognitive training in older adults. We completed our enrollment in this project at UF (20+ participants) and UA is working on completing their enrollment. Current combined sample size is over 30. Thus, this study will provide rich mechanistic information on the potential function of this technology in modifying neurophysiological processes associated with learning in older adults.

New CAM Center Members



Jennifer W. Applebaum, PhD

Assistant Professor

Department of Environmental and Global Health

I am broadly interested in the impact of social inequalities on relationships between pets and people and their downstream health impacts. I have investigated these questions among older adults and specifically considered cognitive aging as an important outcome in this context. Trajectories of cognitive aging may be impacted by interactions with companion animals; pet ownership could potentially protect against cognitive decline if the environment and social network are supportive of the relationship and the individual isn't subject to concerns around resource access, pet-friendly housing, zoonotic disease transmission, and other pet-related issues.



Russel T. Hepple, PhD

Professor

Department of Physical Therapy and Muscle Biology

We are interested in understanding whether targeting of an event known as mitochondrial permeability transition (mPT) using pharmacological approaches to restore "youthful" mitochondrial resilience to Ca²⁺ overload can slow cognitive aging. The premise is that mPT is a well-established pathological mechanism involved in neurodegeneration and cardiac replacement-fibrosis with aging. Our data also implicates mPT in the decline in skeletal muscle mass and function seen with aging. As such, mPT represents a pathological mechanism that is likely relevant to aging in general, consistent with evidence in nematodes that modulation of mPT can in turn modulate the rate of aging. Since the amount of Ca²⁺ needed to trigger mPT is reduced in multiple tissues with aging, we hypothesize that restoration of a "youthful" Ca²⁺ threshold for mPT would help normalize mPT and thereby attenuate age-related tissue degeneration, including that which contributes to cognitive decline.



Eleanora Rossi, PhD

Assistant Professor

Department of Linguistics

My line of research in cognitive aging uses new language training paradigms as a lens to understand neural plasticity in older adults, and asks if new language learning can serve as an engaging and training tool to build neurocognitive resilience and boost cognitive reserve. In collaboration with Faculty in linguistics, we also apply computational linguistics and machine learning tools to test if we can capture markers of early cognitive decline through the analysis of language productions and outcomes.



Shinichi Someya, PhD

Associate Professor

Department of Physiology and Aging

Hearing loss is the third most prevalent chronic health condition affecting older adults and age-related hearing loss is the most common form of hearing impairment. My research focuses on the cellular and molecular mechanisms underlying sex differences in hearing, mitochondrial function, and aging. I have long-standing interests in elucidating how X chromosomes influence auditory function and why mitochondria exhibit strong sex-specificity. I am also interested in understanding how hearing loss affects cognitive function. My work employs electrophysiology, histology, biochemistry, and molecular biology to assess auditory function, mitochondrial function, and cochlear pathology. We use mice as a model system because the mouse inner ear is anatomically similar to that of human and the homologies between the mouse and human genomes are well-established.



Steven Weisberg, PhD

Assistant Professor

Department of Psychology

My research uses tools from cognitive neuroscience to examine spatial navigation and its neural and behavioral underpinnings across the adult lifespan. Our research reveals dramatic shifts in spatial behavior across age groups and in Alzheimer's disease and related dementia, which are associated with distinct patterns of cognitive decline. For example, we show that altered visual attention function correlates with poorer navigation behavior in healthy older adults, but not individuals with subjective cognitive decline. We also examine the neural correlates of these behavioral differences showing, for instance, that regions associated with vestibular function and decision-making are less active in older adults when learning a new environment.

Most Important Research Achievements 2023

Sara Burke, PhD

Over this past year, an important research achievement has been the observation that a long-term ketogenic diet led to increased neuron activation in the prelimbic cortex, and this was associated with enhanced cognitive function. Young and aged rats were given 3 months of a ketogenic diet or a calorie-match control diet and then expression of the immediate-early genes *Arc* and *Homer 1a* were measured to examine neural ensemble dynamics during cognitive testing. The ketogenic diet group had increased activation of neurons in the superficial layers of the prelimbic cortex, but there were no changes in CA3 subregion of hippocampus. This observation suggests that the availability of ketone bodies in the frontal cortices may permit the engagement of compensatory mechanisms that produce better cognitive outcomes. These findings are significant because they suggest that compensatory mechanisms for improving cognition are engaged in the presence of elevated ketone bodies. This metabolic shift away from glycolysis can meet the energetic needs of the frontal cortices when glucose utilization is compromised in advanced age.

Adam J. Woods, PhD

Our continued analyses of the recently completed ACT trial demonstrated that active tDCS paired with cognitive training produced a significant and clinically meaningful improvement in state anxiety in older adults when compared to those undergoing cognitive training and sham/placebo tDCS. In addition, these same patients showed a moderate improvement in late life depression symptoms. In a separate analysis of changes in independent activities of daily living 9 months after completion of tDCS with cognitive training, we found significant benefits for reported IADLs in the group receiving active stimulation vs. sham/placebo stimulation. As decline in IADLs is a critical marker relative to dementia diagnosis, these findings generate much excitement.

Jen Bizon, PhD

Notable scientific achievements in the past year include: 1) Demonstration that chronic daily vagus nerve stimulation can enhance working memory performance in aged rats. This same vagus nerve stimulation regimen also produces shifts in expression of several inflammatory cytokines for which expression is dysregulated in aging; 2) Demonstration that across a battery of tests of executive functions, aged female rats show remarkably preserved cognition compared to young adult female rats. These findings contrast with those shown previously in male rats, in which performance is impaired in aged subjects compared to young adults. Preliminary data from ongoing experiments suggests that the relatively preserved cognition in aged female rats may be linked to maintenance of ovarian function at advanced ages; 3) Demonstration that both acute and chronic exposure to delta-9-tetrahydrocannabinol (THC, the primary psychoactive component of cannabis) can enhance some forms of cognition (specifically prefrontal cortex-dependent working memory) in aged but not young adult rats. In contrast, the same exposure regimens have no effect on, and may even impair, other forms of cognition (specifically hippocampus-dependent episodic/spatial memory) in aged rats.

Ronald Cohen, PhD

As outlined above my scientific contributions are in several lines of research. With respect to normal cognitive and brain aging, our findings with respect to preservation of semantic neural network connectivity is particularly noteworthy (Frontiers in Aging Neuroscience). We have two other manuscripts on semantic networks and aging under review. These findings show preservation of these neural networks with advanced age. Important findings regarding the impact of obesity and diabetes on the brain and cognition and benefits of reductions in these risk factors illustrates the importance of these modifiable risk factors on brain function, of particular relevance in the context of aging. These include findings regarding neuroimaging biomarkers, including fMRI, MRS, and DTI. A number of findings related to HIV effects on the brain and cognition in the context of aging and also substance abuse has been a significant contribution to the literature, providing evidence the viral infection in older adults is a concern, with alcohol use exacerbating these effects.

Tom C. Foster, PhD

The results from our work indicate that peripheral senescence and the senescence-associated secretory phenotype (SASP) are major drivers of age-related cognitive decline. Furthermore, senolytic treatments that remove peripheral senescent cells are relatively safe and decrease systemic inflammation, sometimes referred to as inflamm-aging. In turn, this systemic inflammation drives neuroinflammation and increased oxidative stress in the brain. Oxidative stress initiates programs that are expressed as senescent neurophysiology, which underlies impaired memory. Thus, our results indicate that senolytic treatments rescued hippocampal synaptic transmission and associated memory. Ongoing research indicates that senolytic treatments can preserve cognition in the face of chemotherapies that induce brain aging and

cognitive impairment (i.e. chemo brain). However, these studies are limited by a focus on males. Therefore, ongoing research is also examining the effect of senolytic treatments in females.

Stacey Alvarez Alvarado, PhD

The most significant scientific achievement of the past year is the submission of my CTSI NIH K12 project, PASOS: Physical and Cognitive Aging Study in Older Hispanic Adults. The primary objective is to conduct a large-scale, population-based investigation aimed at advancing our understanding of the association between physical activity and the risk of Alzheimer's disease and related dementias. Of particular importance, within this proposal is the strategic focus of engaging the Hispanic American community of Florida in clinical research. This foundational step is crucial for supporting future in-depth investigations into the link between physical activity and Alzheimer's disease and related dementias risk. In parallel, I completed my first-year milestone as an Assistant Professor in the Department of Neurology during the month of September. During this period, the PACT trial has exceeded 150 participants in Jacksonville, and the ACTIVE MIND trial was successfully launched. Notably, the Gainesville-Jacksonville initiative has gone beyond research activities, leading to the creation of internal infrastructure tailored to the specific needs of multi-site clinical trials. Collaborations with local and central stakeholders facilitated resource coordination, equipment acquisition, and efficient training protocols. Active involvement in employee retention (5 clinical research coordinators) practices demonstrates a comprehensive approach to trial success.

Karina Alvina, PhD

We used Adeno-Associated Virus (AAV) technology to directly target the mouse hippocampus to induce the expression of Irisin. We then examined changes in short term working memory and anxiety-like behaviors using object recognition and spatial awareness tests following hippocampal Irisin overexpression. Our preliminary results show that in AD mouse models the overexpression of Irisin in the hippocampus is able to prevent short term memory decline observed in the novel object recognition test in AD transgenic mice. My lab also established a new collaboration with the Martinez lab in the College of Dentistry. We partnered to study fungal diseases that affect the brain and cause diverse neurological conditions. We expect to expand on our findings and study how infectious diseases can lead to neurodegeneration and/or cognitive decline as patients age.

Jennifer W. Applebaum, PhD

My manuscript on pet ownership and cognition among older adults received substantial press attention and brought a discussion of pets and cognitive aging into the mainstream and lay media.

Breton Asken, PhD

Plasma-based biomarkers of Alzheimer's neuropathological changes remain a rapidly advancing and exciting field. In the past year, we have seen continued progress towards standardization of measurement and honing on the specific markers likely to be "clinic-ready" sooner than later. There has also been increasingly novel use of AD-related plasma biomarkers for understanding the role of AD co-pathology in other neurodegenerative conditions (e.g., Lewy body disease), and better characterizing neuropathological etiologies in groups with common but nonspecific cognitive complaints (e.g., memory loss), as well as in cognitively normal individuals to better understand "healthy aging" processes. The excitement with relatively noninvasive AD biomarkers has also sparked progress in the biological measurement of other diseases like alpha-synucleinopathies via skin biopsy and novel blood-based indicators of important pathophysiological processes like inflammation and vascular disease. Increasingly comprehensive biomarker panels will significantly improve patient-centered care and precision medicine approaches in aging and dementia clinical research.

Matthew Burns, MD, PhD

My lab has worked to establish a multimodal whole brain data acquisition and analysis pipeline and core facility at the McKnight Brain Institute. We are able to combine whole brain tissue clearing, light sheet microscopy, MRI imaging, and Matrix Assisted Laser Deposition/Ionization techniques to answer questions about the molecular and neural circuit basis of aging and cognitive impairment.

Yenisel Cruz-Almeida, PhD

This past year, my laboratory published 25 papers. Among these we showed that we can calculate brain aging biomarkers from clinically-obtained imaging, not only T1-weighted, but other types of neuroimaging acquisition modalities. Thus, brain aging biomarkers could be implemented clinically for identifying individuals at the highest risk of accelerated brain aging and cognitive decline.

Natalie Ebner, PhD

We have received NIH funding for an R21 on oxytocin's role in reducing pain and abuse liability from opioid treatment in aging. As part of our NIH R01 on the characterization and modulation of the neurocognitive mechanisms of learning to trust and distrust in aging as well as from the FDOH to build a consortium on research of psychological factors underlying deception detection in aging, first conceptual and empirical peer-reviewed papers have been published significantly advancing current understanding of deception in aging, including in most vulnerable populations (including those from underrepresented backgrounds; with cognitive impairment; with chronic pain).

Ruogu Fang, PhD

We have several important works published on Fair AI & Ethnic Disparity of AI/ML (Nature Digital Medicine), precision brain stimulation (Brain Stimulation), generalizable trustworthy AI in medical image segmentation (MICCAI 2023). I have also got a new nearly ~\$1M NSF grant as PI on brain-inspired AI. I received the Rising Star Recognition from Academic of Science, Engineering & Medicine of Florida (ASEMFL).

Joseph Gullett, PhD

Attainment of K23 Funding is my primary scientific achievement in this past calendar year. Second, being the first site in the US to obtain FDA Investigational Device Exemption for the Transcranial Pulse Stimulation shockwave device. This clinical trial will be the first step toward providing a potential alternative treatment for early dementia in the US, as is being done all over Germany currently with this device.

Russell T. Hepple, PhD

We are currently in the process of validating the dose-response of a novel mPT-targeting compound known as MC066. This work is ongoing.

Aprinda Indahlastari, PhD

My most important scientific achievements would be my academic growth through the organization of multiple AI related activities, such as leading a classroom, giving multiple guest lectures related to AI, organizing seminar committee and working groups (both in department and college lever), which are aligned with the AI initiative at UF and increase exposure of UF in the realm of AI. I have also succeeded in earning high scores on the both KL2 and K25 NIH grant (K25 - Mentored Quantitative Career Development Award). Although the K25 was not funded, it received positive reviews and has been resubmitted. Additionally, I was also a co-Investigator on an R01 grant that was funded in May 2023.

Ashok Kumar, PhD

We demonstrated that prefrontal serine racemase upregulation in middle-aged rats can improve the learning of task contingencies for visual discrimination and increase glutamatergic synaptic transmission, including NMDA receptor activity (published in *Aging*). Additionally, we showed that preserved cognition is associated with the removal of peripheral senescent cells, decreasing systemic inflammation that normally drives neuroinflammation, blood-brain barrier breakdown, and impaired synaptic function (published in *Aging Cell*).

Damon Lamb, PhD

We found a relationship between GFAP, a putative blood-based biomarker, and cognitive function in patients with traumatic brain injury. In another study, we found that transcutaneous vagus nerve stimulation may improve sleep quality in the context of PTSD in part through increased deep sleep and increased parasympathetic nervous system activity.

Andrew Maurer, PhD

This past year has been marked by the culmination of numerous projects initiated by previous students. While these projects have not yielded significant new discoveries, they have been instrumental in laying the groundwork for future research. The highlight of our year, however, has been the acquisition of a cutting-edge fiber photometry system. This sophisticated technology represents a major leap forward for our lab, enabling us to monitor glucose utilization in the brain in real-time during various behaviors. Leveraging this technology, we are poised to embark on groundbreaking studies that will explore the intricate interplay between diet, blood glucose levels, neurophysiology, and aging. These studies will be further enriched by incorporating comprehensive behavioral assessments, allowing us to draw more nuanced connections between physiological processes and behavioral outcomes. This integrative approach promises to open new avenues in our understanding of how lifestyle factors influence cognitive health in the aging process.

Eric Porges, PhD

Our two most significant achievements were 1) The successful deployment of concurrent multiweek, self-administered taVNS and microbiome interventions to explore their utility modulate brain inflammation and cognitive function. In nearly all subjects we have achieved compliance. Data will not be unblinded in the near future, but this NIH-funded study is demonstrating that compliance with these interventions, in targeted populations (including older adults), can be achieved outside of the lab or clinic. 2) The publication of our book “Vagus Nerve Stimulation” by Springer Nature, Frasch, M. G., & Porges, E. C. (Eds). This was the book in the Springer Neuromethods series covers the latest research and development in the areas of vagus nerve stimulation (VNS) as it relates to bioelectronic medicine from neonate to adult. The chapters in this book cover topics such as invasive and non-invasive VNS including methodological considerations (study design, stimulation parameters, and use of heart rate variability metrics); mechanisms of action (automatic regulation and immune plasticity); and disorders where VNS approaches may be therapeutic (migraine and cluster headaches, mood disorders, trauma-related disorders, and language learning). Chapters were contributed by authors affiliated with the CAM including Drs. Burke, Bizon, and Williamson.

Eleanora Rossi, PhD

Since the beginning of the project, the team has prepared all the tasks (both behavioral and EEG) that will be used to the older adults starting January 6. Older adults have been identified who have already participated to previous MRI studies at UF. As such, those older adults have already some structural and functional MRI measures and behavioral screening data.

Barry Setlow, PhD

Under the R01 and Florida Department of Health grant that support our work on cannabinoids and aging, we have been using rats to assess the effects of chronic daily oral consumption of THC on multiple forms of cognitive function in young adult and aged rats of both sexes. In a test of working memory that depends on the integrity of the prefrontal cortex, daily THC has no effect on task accuracy in young adult rats, but enhances accuracy in aged rats (who are otherwise impaired relative to young adults). In contrast, in the Morris water maze test, which assesses spatial memory and depends on the integrity of the hippocampus, daily THC has no effect in either young adult or aged rats. Additional data from this project show that daily oral THC consumption tends to reduce expression of pro-inflammatory cytokines, which are elevated in aged compared to young rats. The data from the oral THC consumption model are significant for a number of reasons. First, they shown that THC (the primary psychoactive component of cannabis) can enhance at least one aspect of cognitive performance in aged rats. Second, this cognitively-enhancing effect is evident at a dose that is well-tolerated; the dose employed (1.0 mg/kg) produced minimal if any adverse effects, as the rats consumed it voluntarily across multiple weeks. Finally, as older adults are the fastest-growing group of cannabis users, it is important to understand how this drug affects cognitive performance in this age group. A manuscript describing this work should be submitted by early 2024.

Shinichi Someya, PhD

Females display better high-frequency hearing compared to males at most ages, yet the biological mechanism underlying this improved auditory function is unknown. With a team of collaborators, we characterized the CBA/CaJ mouse strain for sex differences in body composition, physical activity, balance performance, auditory function across the lifespan (Kim et al., Hearing Research 2023).

Steven Weisberg, PhD

This past year, we completed data collection for three fMRI projects, which we are analyzing and planning to present at conferences next year. We also submitted three manuscripts for publication, two of which were accepted.

John Williamson, PhD

My colleagues and I (Lexi O'Neal, Eric Porges, Damon Lamb, Steve DeKosky, Ron Cohen, Ken Heilman et al) published findings from an R21 project examining the effects of transcutaneous vagus nerve stimulation (tVNS) during fMRI on functional connectivity within semantic brain networks. We demonstrated that tVNS modified both semantic network connectivity and hippocampal network connectivity compared with sham stimulation. This was shown in older adults with amnesic mild cognitive impairment as determined by clinical consensus conference (DeKosky/Williamson) based on CDR, MOCA, HVLTR and activities of daily living assessment. These findings suggest that tVNS affects brain networks relevant to decline in patients with amnesic MCI. We will perform similar analyses in the longitudinal MBRF funded pilot in healthy older adults of the effects of daily tVNS over a two-week period on semantic and hippocampal network function. A few years ago, I started a new direction of research incorporating blood biomarkers in my work on mechanisms of traumatic brain injury effects on long term neurobehavioral outcomes. This Department of Defense funded work was affected by COVID (subject enrollment). We received extensions to finish the work, which we did. This year, we published our first findings from the project (with two manuscripts published and a third in press, likely to come out early in 2024) demonstrating roles of GFAP, pNF-H and NF-L, and tau and pTau in neurobehavioral outcomes of traumatic brain injury. These findings include acute to chronic tracking of trajectory of biomarker change in people with moderate to severe TBI to long term cognitive outcomes. Similarly, another project affects

by COVID was my work on the effects of tVNS on sleep quality in Veterans with PTSD. We recently published our first paper from this project, demonstrating tVNS affects slow wave sleep stability and increases high frequency heart rate variability (an indicator of increased influence of the parasympathetic nervous system on HRV). We also finished a nine-parameter dosing study on these metrics.



CAM Research Day poster session.

Financial Summary

Evelyn F. McKnight Cognitive Aging and Memory Research Fund University of Florida Foundation Endowment Account

Financial Summary
January 1 to December 31, 2023

*04/28/2000 - Initial Donation	\$ 12,856,687
05/05/2000 - Additional Donation	\$ 110,995
11/07/2002 - 03/23/2004 UF Match Portion	\$ 12,999,999
Additional contributions to the fund from various benefactors	\$ 100
As of 09/30/2023	
Book Value	\$ 25,967,781
**12/31/2023 - Market Value projected	\$ 34,539,586
**12/31/2023 - Return on Investment Projected	\$ 1,868,578
**12/31/2023 - Endowment Income Transferred to UF Side Spendable Projected	\$ 1,307,884

There are no outstanding matching funds.

*Back on April 28, 2000 there was a stock gift of \$12,889,003.60. There was a loss on the sale of the stock of \$32,316.65

Includes **projected amounts for the Fiscal Year 2024 second quarter (October 2023- December 2023).
Fiscal Year 2024, Quarter 2 Financials have not been closed.

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 a volunteer Board of Directors and President of the University of Florida

Evelyn F. McKnight Cognitive Aging and Memory Research Fund
University of Florida Spendable Accounts

Financial Summary
January 1 to December 31, 2023

<u>The Age Related Memory Loss Program</u>		
Beginning balance, January 1, 2023		\$ 312,970
Cumulative Carryforward		\$ 600,592
Endowment income transferred to the UF Side for Age Related Memory Loss Program_Revenue Calendar Year 2023		
	January 2023	\$ 161,962
	April 2023	\$ 161,962
	July 2023	\$ 165,009
	October 2023	\$ 165,009
Total endowment income transferred into Spendable for the Age Related Memory Loss Program		\$ 653,942
Expenditures		
Faculty, Research Staff, Staff Earnings, Graduate Assistant & Post Doctoral	\$ 331,412	
Research equipment, supplies, pilot support, and services	\$ 70,447	
Tuition Waivers/Assistance/Continuing Education	\$ 12,555	
Publications	\$ 267,250	
Office Infrastructure	\$ 14,409	
Travel		
Total Expenditures		\$ 696,073
Ending balance December 31, 2023		\$ 871,431
<u>The Cognitive Aging and Memory Clinical Translational Research Program</u>		
Beginning balance, January 1, 2023		\$ 141,762
Cumulative Carryforward		\$ 2,033,464
Endowment income transferred to the UF Side for the Clinical Translational Research Program_Revenue Calendar Year 2023		
	January 2023	\$ 161,962
	April 2023	\$ 161,962
	July 2023	\$ 165,009
	October 2023	\$ 165,009
Total endowment income transferred into Spendable for the Clinical Translational Research Program		\$ 653,942
Expenditures		
Faculty, Research Staff, Staff Earnings, Graduate Assistant & Post Doctoral	\$ 391,582	
Research equipment, supplies, pilot support, and services	\$ 162,221	
Tuition Waivers/Assistance/Continuing Education	\$ 30,933	
Publications	\$ 8,501	
Office Infrastructure	\$ 141,825	
Travel		
Total Expenditures		\$ 735,062
Ending Balance December 31, 2023		\$ 2,094,106
NET ENDING BALANCE ON THE UF SIDE for the Cognitive Aging and Memory Research Fund		\$ 2,965,537

McKnight Endowed Chair for Brain Research in Memory Loss

Tom Foster, PhD

Financial Summary

January 1 to December 31, 2023

UNIVERSITY OF FLORIDA FOUNDATION ENDOWMENT ACCOUNT	
12/15/1999 & 12/31/1999 - Donations made prior to the Gift Agreement and subsequently included.	\$ 275,000
04/28/2000 - Initial Donation	\$ 1,725,001
05/31/2020 - UF Match	\$ 2,000,001
As of 09/30/2023	
Book Value	\$ 3,995,677
**12/31/2023 - Market Value projected	\$ 4,637,630
**12/31/2023 - Return on Investment Projected	\$ 250,894
**12/31/2023 - Endowment Income Transferred to UF Side Spendable Projected	\$ 175,609
There are no outstanding matching funds.	
**Includes <i>projected</i> amounts for the Fiscal Year 2024 second quarter (October 2023 - December 2023). Fiscal Year 2024, Quarter 2 Financials have not been closed.	
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 a volunteer Board of Directors and President of the University of Florida	

UNIVERSITY OF FLORIDA FOUNDATION SPENDABLE ACCOUNT	
<u>McKnight Endowed Chair for Brain Research in Memory Loss</u>	
Beginning balance, January 1, 2023	\$ 311,594
Endowment income transferred to the UF Side for the McKnight Endowed Chair for Brain Research in Memory Loss	
January 2023	\$ 43,493
April 2023	\$ 43,493
July 2023	\$ 44,311
October 2023	\$ 44,311
Total endowment income transferred into the Spendable for the McKnight Endowed Chair for Brain Research in Memory Loss	\$ 175,609
Expenditures	
Faculty Compensation	\$ 181,192
Lab Supplies	\$ 16,786
Lab Services	\$ 149
Publishing	\$ 3,190
Travel	\$ 487
Total Expenditures	\$ 201,804
Ending balance December 31, 2023	\$ 285,399

McKnight Endowed Chair for Clinical Translational Research in Cognitive Aging

Ron Cohen, PhD

Financial Summary

January 1 to December 31, 2023

UNIVERSITY OF FLORIDA FOUNDATION ENDOWMENT ACCOUNT	
11/01/2015 - Initial Transfer of Funds	\$ 4,000,000
3 Million earnings from the McKnight Brain Research Foundation Endowment	
1 Million earnings from the McKnight Endowed Chair for Brain Research In Memory Loss	
As of 09/30/2023	
Book Value	\$ 4,000,000
**12/31/2023 - Market Value projected	\$ 4,635,624
**12/31/2023 - Return on Investment Projected	\$ 250,785
**12/31/2023 - Endowment Income Transferred to UF Side Spendable Projected	\$ 175,534
There are no outstanding matching funds.	
**Includes <i>projected</i> amounts for the Fiscal Year 2024 second quarter (October 2023 - December 2023). Fiscal Year 2024, Quarter 2 Financials have not been closed.	
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 a volunteer Board of Directors and President of the University of Florida	

UNIVERSITY OF FLORIDA FOUNDATION SPENDABLE ACCOUNT	
<u>McKnight Endowed Chair for Brain Research in Memory Loss</u>	
Beginning balance, January 1, 2023	\$ 87,169
Endowment income transferred to the UF Side for the McKnight Endowed Chair for Clinical Translational Research in Cognitive Aging	
January 2023	\$ 43,475
April 2023	\$ 43,475
July 2023	\$ 44,292
October 2023	\$ 44,292
Total endowment income transferred into the Spendable for the McKnight Endowed Chair for Clinical Translational Research in Cognitive Aging	\$ 175,534
Expenditures	
Faculty Compensation	\$306,277
Total Expenditures	\$306,277
Ending balance December 31, 2023	\$ (43,574)

Dr. William G. Luttge Lectureship in Neuroscience

Financial Summary

January 1 to December 31, 2023

UNIVERSITY OF FLORIDA FOUNDATION ENDOWMENT ACCOUNT		
06/01/2012 - Initial Donation	\$	250,000
Additional contributions to the fund from various benefactors	\$	360
Book Value as of 09/30/2023	\$	250,360
**12/31/2023 Market Value projected	\$	319,453
**12/31/2023 Return on Investment projected	\$	17,282
**12/31/2023 Endowment Income to UF Side Spendable Projected	\$	12,096
There are no outstanding matching funds.		
**Includes <i>projected</i> amounts for the Fiscal Year 2024 second quarter (October 2023 - December 2023). Fiscal Year 2024, Quarter 2 Financials have not been closed.		
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 a volunteer Board of Directors and President of the University of Florida		

UNIVERSITY OF FLORIDA SPENDABLE ACCOUNT		
<u>Dr. William G. Luttge Lectureship in Neuroscience</u>		
Beginning balance, January 1, 2023		\$22,115
Endowment income transferred to the UF Side for Age Related Memory Loss Program		
	January 2023 \$2,996	
	April 2023 \$2,996	
	July 2023 \$3,052	
	October 2023 \$3,052	
Total endowment income transferred in to Spendable for the Age Related Memory Loss Program		\$12,096
Expenditures		
Lecture Series Expenditures	\$5,254	
Total Expenditures		\$5,254
Ending balance December 31, 2023		\$28,957

**McKnight Brain Research Foundation
Age Related Memory Loss Program
Budget - Fiscal Year 2023**

Faculty, Research Staff, Staff Earnings, Graduate Assistant & Post Doctoral	\$	335,000
Research equipment, supplies, and services	\$	9,000
Tuition Waivers/Assistance	\$	20,000
Pilot Projects/Development Funds	\$	289,942
Total Budget	\$	653,942

**McKnight Brain Research Foundation
Clinical Translational Research Program
Budget - Fiscal Year 2023**

Faculty, Research Staff, Staff Earnings, Graduate Assistant & Post Doctoral	\$	365,000
Research equipment, supplies, and services	\$	75,000
Tuition Waivers/Assistance	\$	25,000
Publications	\$	10,000
Office Infrastructure	\$	120,000
Travel	\$	1,000
Pilot Projects/Development Funds	\$	57,942
Total Budget	\$	653,942

Grand Total Budgeted for McKnight Brain Research Foundation Funds **\$ 1,307,884**

The budget amount for the fiscal year is based on the actual funds transfers from the UF Foundation to the McKnight Brain Research Foundation Fund in the McKnight Brain Institute at the University of Florida from the previous fiscal year. The total amount of funds transferred in Fiscal Year 2023 was \$1,307,884. Those funds are equally divided between the Age Related Memory Loss Program and the Clinical Translational Research Program.



FUND IMPACT REPORT

McKnight Brain Research Foundation
Evelyn F. McKnight Cognitive Aging and Memory Research Fund
Spendable Fund Transfers since endowment inception

FY 2023/2024 To Date	\$ 330,018
FY 2022/2023	\$ 1,295,695
FY 2021/2022	\$ 1,295,695
FY 2020/2021	\$ 1,145,191
FY 2019/2020	\$ 1,067,240
FY 2018/2019	\$ 1,046,557
FY 2017/2018	\$ 1,041,290
FY 2016/2017	\$ 1,041,290
FY 2015/2016	\$ 1,071,895
FY 2014/2015	\$ 1,117,603
FY 2013/2014	\$ 1,063,533
FY 2012/2013	\$ 1,028,384
FY 2011/2012	\$ 1,026,301
FY 2010/2011	\$ 971,846
FY 2009/2010	\$ 941,689
FY 2008/2009	\$ 1,086,475
FY 2007/2008	\$ 1,172,824
FY 2006/2007	\$ 1,056,031
FY 2005/2006	\$ 881,347
FY 2004/2005	\$ 843,131
FY 2003/2004	\$ 729,335
FY 2002/2003	\$ 651,801
FY 2001/2002	\$ 657,852
FY 2000/2001	\$ 648,384
	\$23,211,407



FUND IMPACT REPORT

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

FY 2023/2024 To Date	\$ 44,312
FY 2022/2023	\$ 173,973
FY 2021/2022	\$ 173,973
FY 2020/2021	\$ 153,765
FY 2019/2020	\$ 143,298
FY 2018/2019	\$ 140,521
FY 2017/2018	\$ 139,814
FY 2016/2017	\$ 139,814
FY 2015/2016	\$ 143,923
FY 2014/2015	\$ 170,407
FY 2013/2014	\$ 162,162
FY 2012/2013	\$ 156,803
FY 2011/2012	\$ 156,485
FY 2010/2011	\$ 148,182
FY 2009/2010	\$ 143,584
FY 2008/2009	\$ 165,660
FY 2007/2008	\$ 178,827
FY 2006/2007	\$ 161,019
FY 2005/2006	\$ 134,384
FY 2004/2005	\$ 127,813
FY 2003/2004	\$ 124,127
FY 2002/2003	\$ 125,768
FY 2001/2002	\$ 100,869
FY 2000/2001	\$ 99,417
FY 1999/2000	\$ 3,438
	\$3,412,338



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 2023/2024 To Date	\$ 44,292
FY 2022/2023	\$ 173,898
FY 2021/2022	\$ 173,898
FY 2020/2021	\$ 153,698
FY 2019/2020	\$ 143,236
FY 2018/2019	\$ 140,460
FY 2017/2018	\$ 139,854
FY 2016/2017	\$ 139,754
FY 2015/2016	\$ 143,861
	\$ 1,252,951



FUND IMPACT REPORT

McKnight Brain Research Foundation
William G. Luttge Lectureship in Neuroscience
Spensible Fund Transfers since endowment inception

FY 2023/2024	\$ 3,052
FY 2022/2023	\$ 11,983
FY 2021/2022	\$ 11,983
FY 2020/2021	\$ 10,591
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
	\$ 111,534

Collaborative Programs

Inter-Institutional McKnight Collaborations

UF-UAB Collaborations:

Throughout 2023, Dr. Burke has been working with Dr. Hernandez (UAB) on a collaborative project to examine the impact of the ketogenic diet on cognitive and peripheral health. Recently, they published a paper together that documents how long-term ketosis affects the expression of the immediate-early genes in the hippocampus and prefrontal cortex.

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 R01 to the National Institute on Aging on this topic.

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:

This year, Dr. Burke agreed to chair the Cognitive Aging and Memory Intervention (CAMI) Core pilot program committee and is joined by Ihtsham ul Haq (UMiami), Matthew Grilli (UA), and Keith McGregor (UAB) who have all agreed to complete 2- or 3-year terms. This program was initiated and successfully developed by Drs. Woods (UF) and Rundek (UMiami) in 2016 to provide seed funding for new inter-institute collaborations aimed at developing novel interventions for improving cognitive function in older adults. In the past several years, submissions to the pilot program have been limited. The MBRF Leadership Council's opinion is that this is in part because it is extremely challenging to conduct a high-quality intervention pilot across multiple sites within the scope of the award mechanism as designed. In addition, it has become clear after administering several rounds of these grants that coordinating a robust pilot mechanism across all four institutes requires a not-yet-established centralized administrative infrastructure that (1) retains core historical knowledge about the program year-to-year, (2) efficiently facilitates inter-institutional communications and (3) offers administrative support for the rotating Pilot Program Leaders. The new CAMI Core Committee has already begun drafting a revised proposal for revitalizing this important Inter-Institutional initiative.

Collaborations Beyond McKnight Institutes

Dr. Woods has ongoing collaborations in his areas of expertise in non-invasive brain stimulation and neuromodulation methods (e.g., cognitive training, NIR photobiomodulation, etc.) as well as 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. Drs. Burke, Lamb and Bizon continue to 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 Drs. Sun and Gentry in the Department of Biochemistry to examine how aging impacts the spatial distribution of the metabolome, glycome and lipidome in the brain. Finally, Dr. Burke is also collaborating with researchers in the Institute of Aging (Anton) and UF ADC (Smith) to develop dietary interventions to improve cognition in older adults with metabolic dysfunction.

Faculty Awards and Recognitions

Sara Burke, PhD

- Promotion to Full Professor
- Completed serving leadership course
- Appointed Co-Director of the CAM Center
- Exemplary teaching award 2023, College of Medicine

Adam J. Woods, PhD

- Promotion to Full Professor
- Appointed Co-Director of the CAM Center

Jen Bizon, PhD

- Appointed Director of the UF McKnight Brain Institute

Tom Foster, PhD

- Editorial board for Aging Brain
- Discussion Panel for Reserve and Resilience Workshop
- Neurodevelopment, Synaptic Plasticity and Neurodegeneration study section member
- Reviewer for the Pennsylvania DOH Review, 22-23 Cycle A

Jennifer W. Applebaum, PhD

- People's Choice Best Poster Award, Florida CPR Conference

Yenisel Cruz-Almeida, PhD

- Chair of Neurobiology of Pain & Itch (NPI) NIH study section
- Elected to Executive Committee, Pain in Older Adults from International Association for the Study of Pain
- Inducted Honorary member, Omicron Kappa Dental Honor Society
- Journal of Pain Associate Editor

Natalie Ebner, PhD

- Fellow of the Association for Psychological Science
- Trish Calvert Ring Endowed Professor in Psychology
- Honorary appointment as Visiting Professor at the University of Technology Sydney, Australia

Ruogu Fang, PhD

- Received distinguished recognition as 'Rising Stars (Engineering)' from the Academy of Science, Engineering, and Medicine of Florida.

Joseph Gullett, PhD

- Research Mentor Award from UF's College of Public Health and Health Professions, 2023

Eric Porges, PhD

- Promotion to Associate Professor with Tenure

Barry Setlow, PhD

- Received the Dr. Maveis Agbandje-McKenna Distinguished Mentoring Award from the UF College of Medicine

Shinichi Someya, PhD

- Excellence in Teaching Award from UF's College of Public Health and Health Professions, 2023

John Williamson, PhD

- Exemplary Teacher Award from UF's College of Medicine, 2023

Trainee Awards and Recognitions (A representative sample)

Alejandro Albizu (Graduate Student, Woods Lab)

- 2nd place winner in Award for Aging Research Program sponsored by the Leighton E. Cluff Endowment and the Institute of Learning in Retirement at Oak Hammock

Fapianey Alexandre (Undergraduate Student, Burke Lab)

- 1st place at the poster competition at the Annual Biomedical Research Conference for Minoritized Students
- Exemplary Undergraduate Research winner at CAM Research Day's poster presentation

Mark Britton (Graduate Student, Cohen/Porges Lab)

- Received an F32 grant from the NIH
- Receive a UF Graduate Student Council travel award to present at the Research Society on Alcohol annual meeting.

Katherine Gonzalez (Graduate Student, Bizon/Setlow Lab)

- 1st place winner in Award for Aging Research Program sponsored by the Leighton E. Cluff Endowment and the Institute of Learning in Retirement at Oak Hammock
- 3rd place winner at the MBRF poster competition at SfN

Jessica Kraft (Graduate Student, Woods Lab)

- Named an MBI Rising Star

Daniel Rodriguez (Graduate Student, Fang Lab)

- Received a T32 training grant from the NIH

Johleen Seedansingh (Graduate Student, Bizon/Burke Lab)

- 1st place at the MBRF SfN poster competition at SfN

Destin Shortell (Graduate Student, Porges Lab)

- 3rd place winner at CAM Research Day's poster presentation

Samm Smith (Graduate Student, Burke Lab)

- 1st place winner at CAM Research Day's poster presentation
- Honorable Mention at the MBRF poster competition at SfN
- Received an F31 grant from the NIH for her project entitled "Examining the contributions of cognitive load and anterior cingulate cortex activity"

Skylar R. Stolte (Graduate Student, Fang Lab)

- 2nd place winner, WiM Inspirational Leadership Legacy at the International Conference on Medical Image Computing and Computer Assisted Intervention

Jori Waner (Graduate Student, Woods Lab)

- 2nd place winner at CAM Research Day's poster presentation
- 1st place winner at PPHP Research Day's poster presentation

Sabrina Zequiera (Graduate Student, Bizon/Setlow Lab)

- 1st place for the Southeast Division of the Three Minute Thesis competition
- 2nd place at the MBRF poster competition at SfN

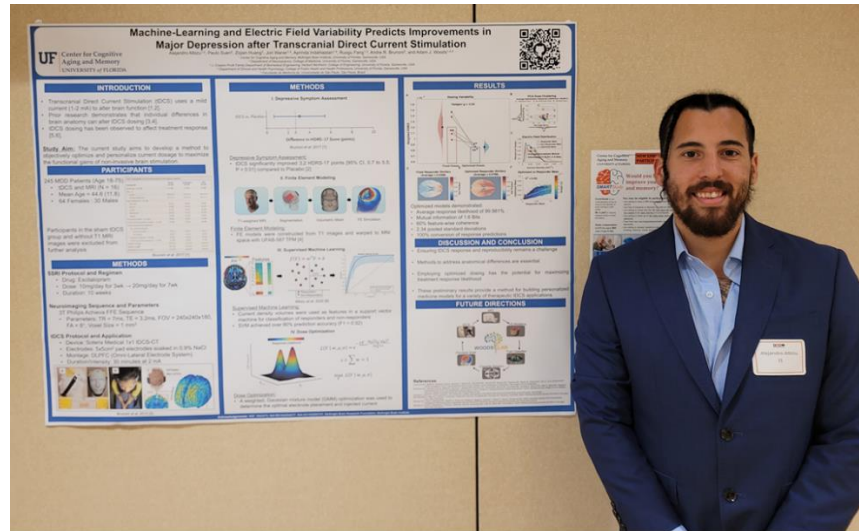
New Grants

NSF NCS-FO-2318984	\$920,000	09/2023-8/2027
NCS-FO: Brain-Inspired Goal-Oriented and Bidirectional Deep Emotion Inference. PI: Fang		
NIA R01AG081477	\$4,801,618	05/2023-04/2027
Upregulating frontal cerebral circuits to enhance executive and mobility function: UPfront-2 Declines in cognitive function and walking function are highly related in older adults. PI: Clark, Co-I: Woods, Williamson		
NIDDK R01AG083039	\$1,361,614	09/2023-08/2026
An end-to-end informatics framework to study Multiple Chronic Conditions (MCC)'s impact on Alzheimer's disease using harmonized electronic health records. PI: Bian, Co-I: Woods		
Mangurian-Fixel-McKnight Foundation	\$40,000	07/2023 - 06/2024
Integrating Alpha-Synuclein Biomarker Testing into the 1Florida ADRC PI: Asken		
NIA K01-AG070333-01	\$70,000	01/2023 – 01/2024
Critical Life Event Supplement to K01-AG070333- PI: Ebner (contact), Weisberg , Co-I: DeKosky , Ding		
NINDS R01NS128626	\$2,218,350	07/2023 - 06/2027
Sepsis and the Systemic Cytokine Storm in Aging and Alzheimer Disease Models PI: Moldawer, Co-I: Foster		
DOD/CDMRP: W81XWH-22-1-1089Gap	\$7,999,917	10/2022-8/2026
Based Milieu Biomarkers for Traumatic Brain Injury (GAMBIT-TBI) PI: Rubenstein, Site PI: Lamb		
NIMH R01 MH130778	\$1,851,638	03/2023-02/2028
Role of cortical catecholamines in regulating motivated behavior and striatal dopamine. PI: Urs, Co-I: Setlow		
NINDS R01 NS132293	\$2,506,458	04/2023-03/2028
Cholinergic mechanisms in Lewy body dementia. PI: Moehle, Co-I: Setlow		
NIDA R61/33 DA056922	\$881,552	06/2023-05/2028
Patterns and neurocognitive consequences of opioid-alcohol polysubstance use. MPIs: Knackstedt, Cottler, Co-I: Setlow		
Consortium for Medical Marijuana Clinical Outcomes Research	\$75,000.00	07/2023-06/2024
The Influence of Cannabis Smoke Condensate on Drug Metabolizing Enzymes in the Human Lung. PI: Markowitz, Co-I: Setlow		

NIMH R01 MH134141	\$50,875	07/2023-05/2028
(Doucette) Evaluating the potential of neural oscillation biomarkers in a rodent model of intervention outcome variation: Toward personalized mental health care PI: Doucette, Co-I: Setlow		
Pilot Cure Sanfilippo Foundation Grant	\$99,934	04/2023 – 03/2025
Effects of TLR4 antagonism on brain and bone function in MPS IIIB PI: Heldermon, Co-I: Someya		
NIDDK R01	\$3,787,062	02/2024-01/2029
WISE II - Obesity and Type-2 Diabetes: Bariatric Surgery Effects on Brain PI: Williamson, Co-I: Cohen, Porges		
Department of Veterans Affairs	\$5,000,000	02/2024-01/2029
Brain Rehabilitation Research Center (Center renewed)		
NIBIB R01EB016089-09 (Edden; PI)	\$2,692,148	04/2023-03/2027
Universal Edited MRS at 3T This project will address the issue of out-of-voxel (OOV) echos in edited MRS collected in challenging anatomy. The acquisition protocol will be deployed in a whole-lifespan cohort in order to reveal neurochemical changes in development and aging. PI: Edden, Site-PI: Porges		
NIDA R61DA056922	\$3,126,314	06/2023-04/2028
Patterns and Neurocognitive Consequences of Opioid-Alcohol Polysubstance Use Co-I: Ebner PI: Knackstedt, Co-I: Ebner		
McKnight Brain Research Foundation	\$120,000	05/2023-04/2025
Cued High-Speed Multidirectional Yoga: Impact on Retinal Microvascular and Cognitive Measures Co-PI: Signorile, Co-I: Ebner		
NIDA R21DA056813	\$419,375	05/2023-04/2025
The Potential of Oxytocin to Reduce Opioid Abuse Liability and Pain Among Older Adults PI: Ebner , Co-I: Berry, Cruz-Almeida		
Swedish Research Council	\$495,047	01/2023-12/2026
Using Precision Neuroimaging and AI to Understand How the Human Brain Processes Socioemotional Cues from Others: A Multimodal Proof-of-Concept Project PI: Fischer, Co-I: Ebner		

Technology Transfer

Patent. 2023. Inventors: Adam J. Woods, Alejandro Albizu, Ruogu Fang, Aprinda Indahlastari. Title: System and method for precision dosing for electrical stimulation of the brain. U.S. Patent No. 2023/0293899, Publication date: September 21, 2023.



Dr. Albizu poster presentation

Were any funds used for Prohibited Purpose during the report period?

NO

Do we 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

Submitted by:

**Kathleen McIntyre
Administrative Specialist
Center for Cognitive Aging and Memory
University of Florida**

Appendix 1

CAM Center Affiliate Members and Trainees

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
Malú Gamez Tansey, PhD – Professor – Department of Neuroscience

B. Post-Doctoral

(Bizon/Setlow) Mojdeh Faraji, PhD
(Bizon/Setlow) Zak Krumm, PhD
(Woods) Serkan Aksu, PhD
(Foster) Puja Sinha, PhD
(Alvina) Marcela Cuestas Torres, PhD
(Cruz-Almeida) Javier Tamargo, PhD
(Cruz-Almeida) Soamy Montesino, PhD
(Cruz-Almeida) Larissa Strath, PhD*
(Ebner) Didem Pehlivanoglu, PhD
(Fang) Peng Liu, PhD
(Fang) Diandra Prioleau Ojo, PhD
(Lamb) Clayton Swanson, PhD
(Lamb) Abigail Waters, PhD
(Weisberg) Adam Barnas, PhD
(Williamson) Erin Trifilio, PhD
(Williamson) Abigail Waters, PhD

C. Pre-Doctoral

(Bizon/Setlow) Wonn Pyon. PhD student, Biomedical Sciences Program, *T32 ARDC funded*
(Bizon/Setlow) Sabrina Zequeira, PhD student, Biomedical Sciences Program, *T32 ARDC funded*

(Bizon/Setlow) Katherine Gonzalez, PhD student, Biomedical Sciences Program
(Burke) Aleyna Ross, PhD student, Biomedical Sciences Program
(Burke) Samantha Smith, PhD student, Biomedical Sciences Program, *CAM scholar*
(Burke) Tara Cooper, PhD student, Biomedical Sciences Program
(Woods) Alejandro Albizu, PhD student, Biomedical Sciences Program, *NSF GRFP funded*
(Woods) Emanuel M. Boutzoukas, PhD student, Clinical Health Psychology, *T32 PT funded*
(Woods) Nicole Evangelista, PhD student, Clinical Health Psychology, *T32 CHP funded*
(Woods) Hanna Hausman, PhD student, Clinical Health Psychology
(Woods) Kailey Langer, PhD student, Clinical Health Psychology
(Bizon/Setlow) Emely Gazarov, PhD student, Neuroscience
(Bizon/Burke) Johleen Seedansingh, PhD student, Biomedical Sciences Program, *CAM scholar*
(Cohen/Porges) Mark Britton, PhD student, Clinical Health Psychology, *CTRP Funded*
(Cohen/Porges) Jason DeFelice, PhD student, Clinical Health Psychology, *T32 EPI funded*
(Cohen/Gullett) Brian Ho, PhD student, Clinical Health Psychology, *T32 ARDC funded*
(Cohen/Woods) Kailey Langer, PhD student, Clinical Health Psychology, *T32 CHP funded*
(Cohen/Williamson) Alexandria O'Neal, PhD student, Clinical Health Psychology
(Foster) Vivekananda Bedamagunta, PhD student, Genetics and Genomics Program
(Alvina) Melissa Rosas-Rossi, Masters student, Neuroscience
(Applebaum) Joi Saulsberry, Masters Student, Environmental and Global Health
(Asken) Jessica Bove, PhD student, Clinical Health Psychology
(Asken) Emily Matusz, PhD student, Clinical Health Psychology
(Asken) Shannon Lee, PhD student, Clinical Health Psychology
(Asken) Olivia Emanuel, PhD student, Clinical Health Psychology
(Burns) Hannah Phelps, Master's student, Neuroscience
(Cruz-Almeida) Ania Lipat, PhD student, Dentistry
(Cruz-Almeida) Kristina Bell, PhD student, Dentistry
(Ebner) Kylie Wright, PhD student, Psychology
(Ebner) Alayna Shoenfelt, PhD student, Psychology
(Ebner) Rebecca Polk, PhD student, Psychology
(Ebner) Peiwei Liu, PhD student, Psychology
(Fang) Kyle See, PhD student, Biomedical Engineering
(Fang) Skylar Stolte, PhD student, Biomedical Engineering
(Fang) Seowung Leem, PhD student, Biomedical Engineering
(Fang) Chaoyue Sun, PhD student, Electrical & Computer Engineering
(Fang) Joseph Cox, PhD student, Biomedical Engineering
(Fang) Tianqi Liu, PhD student, Electrical & Computer Engineering
(Fang) Zhuobiao Qiao, PhD student, Electrical Engineering

(Fang) Pankaj Chand, PhD student, Computer Science
(Fang) Daniel Rodriguez, PhD student, Electrical and Computer Engineering
(Hepple) Cole Lukasiewicz, PhD student, Rehabilitation Science
(Gullett) Cameron Perrin, PhD student, Clinical Health Psychology
(Lamb) Robert Claar, PhD student, Clinical Health Psychology
(Maurer) Cristina Besosa, PhD student, Biomedical Sciences Program
(Porges) Brittany Rohl, PhD student, Clinical Health Psychology
(Porges) Destin Shorell, PhD student, Clinical Health Psychology
(Rossi) Megan Nakamura, PhD student, Linguistics
(Rossi) Cesar Rosales, PhD student, Linguistics
(Rossi) Yihan Chen, PhD. Student, Linguistics
(Someya) Laura Infante, PhD student, Audiology
(Someya) Mason Palaga, PhD student, Audiology
(Someya) Lianna Becker, PhD student, Audiology
(Someya) Jaclyn Colopietro, PhD student, Audiology
(Weisberg) Eliany Perez, PhD student, Psychology, *T32 funded*
(Weisberg) Ece Yuksel, PhD student, Psychology
(Weisberg) Ashish Sahoo, PhD student, Psychology
(Weisberg) Chengsi Yi, PhD student, Psychology
(Williamson) Sarah Ann Bottari, PhD student, Clinical Health Psychology
(Williamson) Alexandria O’Neal, PhD student, Clinical Health Psychology, *T32 ARDC funded*
(Williamson) Laura Jones, PhD student, Clinical Health Psychology
(Williamson) Samantha Penhale, PhD student, Clinical Health Psychology

D. Undergraduate Training Programs in the CAM Center

NEURON-Aging

Drs. Sara Burke, Karina Alviña and José Abisambra (CAM Center Affiliate) secured NIH funding to support a program designed to expand the pool of researchers interested in biomedical, behavioral, and clinical aspects of brain aging and ADRDs through undergraduate research activities that enhance diversity. The grant funds selected undergraduate students at the University of Florida to work in a research lab for two years, provides them with a research mentor and a personalized mentorship committee, and supports them in presenting their research at scientific meetings and conferences.

The inaugural class of the grant (entitled NEURON-Aging program) began in January of 2023. Six students were initially accepted with a 7th student being added from our Summer Neuroscience Internship Program (SNIP) in the fall. The second cohort of students will begin January 12, 2024.



(Burke) Fapianey Alexandre, Sophomore
(Candelario) Valerie Cabrera, Senior
(Casadesus) Ana Ojeda, Freshman
(Cruz-Almeida) Ariana Robinson, Freshman
(Rossi) Faith Broersma, Freshman
(Setlow) Jose Rodriguez, Sophomore
(Tansey/Joers) Ann Titus, Freshman

SNIP

Every summer CAM sponsors students in the Summer Neuroscience Internship Program (SNIP). SNIP places paid summer interns in active neuroscience research labs to obtain hands-on laboratory and research experience, personalized guidance on graduate school admissions and professional development and career planning. Additional students are also funded through our NEURON-Aging grant.



(Burke) Jerrica Francisco, Lamar University (NEURON-Aging)
(Abisambra) Kenedy Cox, Western Illinois University (NEURON-Aging)
(Alvina) Lorena Mesquita Ragonesi, Nova Southeastern University (NEURON-Aging)
(Burns/Wong) Vedant Garg, University of Florida (CAM)
(Maurer) Niang Thang, Palm Beach Atlantic University (NEURON-Aging)
(McIntyre) Caleb Reichbaum, Troy University (NEURON-Aging)
(Moehle) Julia Langman, Nova Southeastern University (NEURON-Aging)
(Porges) Abel Pichardo, San Diego State University (CAM)
(Setlow) Drew Smith, Nova Southeastern University (NEURON-Aging)
(Tansey) Jazmyn Coronado, University of Florida

UF's University Scholars Program

The University of Scholars Program introduces undergraduate students at the University of Florida to the exciting world of academic research. In the program, students work one-on-one with UF faculty on selected research projects.

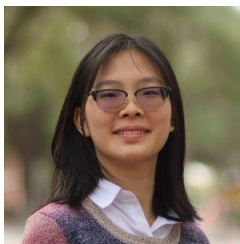
(Bizon/Setlow) Natalie Barber, College of Medicine
(Bizon/Setlow) Isabella Mark, College of Medicine
(Bizon/Setlow) Bailey McCracken, College of Medicine
(Weisberg) Merrill Garlington, College of Liberal Arts and Sciences

As a part of UF's AI initiative, two Biomedical Engineering students received scholarships from UF's University AI Scholars Program to study aging-related topics under the mentorship of Dr. Ruogu Fang.



Akahay Ashok

Title: Diffusion Model Synthesis: Evaluating Older Aging vs. Parkinson's Disease Specific Biomarkers in UK Biobank Fundus Imaging



Grace Cheng

Title: Aging in Caenorhabditis Elegans

E. New Faculty

In 2023, CAM grew to welcome five new faculty members to the center. **Drs. Eleanora Rossi, Steven Weisberg, and Russell Hepple**, were all awarded Pilot grants from CAM. **Dr. Rossi's** project is entitled "New language training and machine learning as tools to measure and promote neurocognitive resilience in healthy aging". **Dr. Weisberg's** project is entitled "Detection of impairment and preservation of navigation function in Alzheimer's Disease and related dementias." **Dr. Hepple's** project is entitled

“Investigating mitochondrial dysfunction’s role in cognitive decline.” **Dr. Shinichi Someya** also received funding to investigate sex differences in age-related hearing loss and how this impacts cognitive function. **Dr. Jennifer Applebaum** is a new faculty recruit to the University of Florida. She is examining pet-human interactions across the lifespan and how this impacts cognitive aging. We are excited to welcome them and look forward to their continued contributions to aging research. (NIH Biosketches included below).

BIOGRAPHICAL SKETCH

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

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

NAME: Applebaum, Jennifer W

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

POSITION TITLE: Assistant Professor

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Emerson College, Boston, MA	BA	12/2005	Interdisciplinary Studies
University of Florida, Gainesville, FL	MS	05/2017	Veterinary Medical Sciences
University of Florida, Gainesville, FL	PHD	05/2023	Sociology
University of Florida, Gainesville, FL	NIH training grant	08/2022	Clinical and Translational Science

A. Personal Statement

I am a medical sociologist whose research takes an interdisciplinary approach to explore the impact of human-animal interactions and social inequalities on human health outcomes. My formal training to date has enabled me to apply qualitative and quantitative social research methods to the translational study of the health consequences of social stressors at the intersection of the One Health framework (i.e., the interdependency of human, animal, and ecological health) and Social Determinants of Health framework. In my current role as an Assistant Professor, I have applied these frameworks to the study of HIV and substance & alcohol use by conducting survey research among people with HIV (PWH) who own pets.

I have engaged in several successful collaborations with mentors and colleagues, many of which I initiated and led. The collaborative work that I initiated and co-led during the COVID-19 pandemic has been cited as a foundational research contribution to understanding relationships with pets during public health emergencies. As a result of this work, I was invited to give several talks, including the Keynote for the 2021 Purdue University Center for Animal Welfare Science symposium. Furthermore, my collaborative work with colleagues at American Pets Alive on disparities in access to pet-friendly housing was cited in several state congressional sessions regarding housing policy change. In addition to the aforementioned empirical work, I also published a first-author conceptual paper on relationships between HAI, health disparities, and interpersonal adversity. In this paper, we delineate the differential health impacts of HAI on various populations who face chronic stress via marginalization and adversity (Applebaum et al., *Comprehensive Psychoneuroendocrinology*, 2021). This paper has been cited over 40 times to date and has been used as a theoretical background for many empirical studies about HAI and human health.

I have also successfully acquired funding to support my research. In 2020, I was awarded a prestigious NIH/NCATS predoctoral TL1 fellowship in Clinical and Translational Science to conduct team science-based

research regarding older adults and pet ownership. In 2021, I obtained a Southern HIV and Alcohol Research Consortium (SHARC) pilot award to develop a module on pet ownership and human-animal interaction that was administered in SHARC's survey of PWH (Florida Cohort Study) in 2021-2023.

Ongoing and relevant projects I would like to highlight:

1. **Applebaum JW**, McDonald SE, Widmeyer M, Fabelo HE, Cook RL. The impact of pet ownership in healthcare access and utilization among people with HIV. *PLOS One*. 2023. 18(11): e0292658. PubMed Central PMCID: PMC10619778.
2. **Applebaum JW**, McDonald SE, Porges EC, Widmeyer M, Fabelo HE, Kertes DA, Cook RL. Pet ownership is associated with harmful alcohol use among a cohort of people with HIV: A brief research report. *Front Psychiatry*. 2023 Oct 16; 14:1258850. PubMed Central PMCID: PMC10613728.
3. **Applebaum JW**, McDonald SE, Zsembik BA. Longitudinal associations between allostatic load, pet ownership, and socioeconomic position among U.S. adults aged 50. *SSM Popul Health*. 2023 Mar;21:101344. PubMed Central PMCID: PMC9853381.
4. **Applebaum JW**, MacLean EL, McDonald SE. Love, fear, and the human-animal bond: On adversity and multispecies relationships. *Compr Psychoneuroendocrinol*. 2021 Aug;7 PubMed Central PMCID: PMC8415490.

B. Positions, Scientific Appointments and Honors

Selected Scientific Appointments

2023 - present	Assistant Professor, University of Florida, Department of Environmental and Global Health, College of Public Health and Health Professions, Gainesville, FL
2020 - 2022	TL1 Fellow, University of Florida, Clinical and Translational Science Institute, Gainesville, FL
2019 - 2020	Research Assistant, University of Florida, Department of Sociology and Criminology & Law, College of Liberal Arts and Sciences, Gainesville, FL

Other Experiences and Professional Memberships

2023 - present	Associate Editor, Human-Animal Interactions journal
2019 - present	Member, International Society for Anthrozoology
2018 - present	Member, Animals & Society Institute
2022 - 2023	Teaching Assistant (TA): Instructor of Record, University of Florida, Department of Sociology and Criminology & Law, College of Liberal Arts and Sciences, Gainesville, FL
2018 - 2019	TA: Instructor of Record, University of Florida, Department of Sociology and Criminology & Law, College of Liberal Arts and Sciences, Gainesville, FL
2017 - 2018	TA, University of Florida, Department of Sociology and Criminology & Law, College of Liberal Arts and Sciences, Gainesville, FL
2015 - 2017	Veterinary Care Manager, University of Florida, Veterinary Community Outreach Program, College of Veterinary Medicine, Gainesville, FL
2014 - 2015	Student Services Coordinator, University of Florida, Maddie's Shelter Medicine Program, College of Veterinary Medicine, Gainesville, FL
2013 - 2014	Foster and Adoption Coordinator, Humane Society of North Central Florida, Gainesville, FL

Honors

2020 - 2021	Reading Group Seed Funds, Center for Humanities and the Public Sphere, University of Florida, Gainesville, FL
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2020 - 2021	Speaker, UK Economic and Social Research Council Festival of Social Sciences, University of York, York, UK
2017 - 2020	Grinter Fellowship, University of Florida, Gainesville, FL
2016 - 2017	Research Grant Award, American Society for Prevention of Cruelty to Animals, New York, NY
2023	People's Choice Best Poster Award, Florida HIV CPR Conference, Gainesville, FL
2022	Speaker, One Health Today Series, Food and Drug Administration, Silver Spring, MD
2022	Speaker, Shelter Medicine Grand Rounds, Gainesville, FL
2022	Speaker, Campbell Centre for the Study of Animal Welfare Seminar Series, University of Guelph, Guelph, ON, Canada
2022	Speaker, Veterinary Meeting & Expo (VMX), Orlando, FL
2021	Pilot Award, Southern HIV and Alcohol Research Consortium, Gainesville, FL
2021	Keynote Speaker, Center for Animal Welfare Science Symposium, Purdue University, West Lafayette, IN
2021	Speaker, Animal Welfare Seminar Series, University of British Columbia, Vancouver, BC
2021	Speaker, Seminar Series, Gerontological Society of America, Washington, DC
2020	Martha Bryant Student Travel Award, International Society for Anthrozoology Annual Meeting, Buffalo, NY
2020	Best Poster Award, International Society for Anthrozoology Annual Meeting, Buffalo, NY

C. Contributions to Science

- Examining relationships between pet ownership and HIV health outcomes and co-morbidities.** Previous research suggests that pet ownership can promote health among PWH. I was awarded a pilot grant to include a module about pet ownership and human-animal interaction to the Florida Cohort Study. We found that pet ownership was associated with current hazardous alcohol use and the historical use of other substances in this sample. Additionally, we identified potential healthcare access and utilization issues faced by PWH who have pets. These findings have important implications for understanding multifaceted, bi-directional, and often resource-intensive human-animal bonds and resulting health implications for PWH.

 - Applebaum JW**, McDonald SE, Widmeyer M, Fabelo HE, Cook RL. The impact of pet ownership in healthcare access and utilization among people with HIV. *PLOS One*. 2023. 18(11): e0292658. PubMed Central PMCID: PMC10619778.
 - Applebaum JW**, McDonald SE, Porges EC, Widmeyer M, Fabelo HE, Kertes DA, Cook RL. Pet ownership is associated with harmful alcohol use among a cohort of people with HIV: A brief research report. *Front Psychiatry*. 2023 October 16; 14:1258850. PubMed Central PMCID: PMC10613728.
 - Applebaum JW**, McDonald SE, Widmeyer M, Fabelo H. Healthcare access and utilization among pet-owning people with HIV in Florida: Findings from the Florida Cohort Pet Module. Poster presented at: Florida HIV Community, Providers, Researchers; 2023 Sept 23; Gainesville, FL.
 - Applebaum JW**, McDonald SE, Widmeyer M, Fabelo HE, Cook RL. Can pet ownership impede access to healthcare for people living with HIV? Preliminary findings from an ongoing cohort study. Paper presented at: International Society for Anthrozoology; 2022 Jul 7-9; Virtual.
- Elucidating the stress-related health facilitators and barriers among pet owners from marginalized backgrounds (e.g., minoritized racial and ethnic groups, low-income communities, LGBTQ+ identities).** In this line of research, we explored the human-animal bond in the context of systemic inequalities to challenge human-animal interaction researchers to look beyond individual outcomes

and biased samples in previous work. We employed quantitative and qualitative population-based approaches to identifying and understanding the relationship between health disparities and human-animal interaction. We found that pets often provide important stress relief and social support; however, pets can also cause or exacerbate stress for pet owners in adverse situations. Implications from this work suggest a need for broader social programs to support pet owners from marginalized backgrounds so they can access the protective effects of the human-animal bond.

- a. McDonald S, Murphy J, Tomlinson C, Matijczak A, **Applebaum JW**, Wike T, Kattari S. Relations Between Sexual and Gender Minority Stress, Personal Hardiness, and Psychological Stress in Emerging Adulthood: Examining Indirect Effects via Human-animal Interaction. *Youth & Society*. 2022; 54(2):240-261. DOI: 10.1177/0044118X21990044.
 - b. **Applebaum JW**, Horecka K, Loney L, Graham TM. Pet-Friendly for Whom? An Analysis of Pet Fees in Texas Rental Housing. *Front Vet Sci*. 2021;8:767149. PubMed Central PMCID: PMC8606550.
 - c. **Applebaum JW**, MacLean EL, McDonald SE. Love, fear, and the human-animal bond: On adversity and multispecies relationships. *Compr Psychoneuroendocrinol*. 2021 Aug;7 PubMed Central PMCID: PMC8415490.
 - d. McDonald S, Matijczak A, Nicotera N, **Applebaum JW**, Kremer L, Natoli G, O’Ryan R, Booth L, Murphy J, Tomlinson C. "He was like, my ride or die": Sexual and gender minority emerging adults’ perspectives on living with pets during the transition to adulthood. *Emerging Adulthood*. 2022;10(4):1008-1025. DOI: 10.1177/21676968211025340.
3. **Assessing the human health and well-being implications of pet ownership during the COVID-19 pandemic.** Pet ownership is believed to have increased during the COVID-19 pandemic, and it was hypothesized that pets would help to buffer some of the effects of social isolation by imposed COVID-19 precautions. We deployed a survey to 3,000 pet owners from April through July of 2020 to test hypotheses regarding the impact of pet ownership during this novel public health emergency. We found that many owners believed their pets were instrumental to their mental well-being, while others were facing extenuating circumstances that made caring for pets more difficult. This work is now considered foundational in the field and has been cited extensively.
- a. Adams BL, **Applebaum JW**, Eliasson MN, McDonald SE, Zsembik BA. Child and Pet Care-Planning During COVID-19: Considerations for the Evolving Family Unit. *Fam Relat*. 2021 Jul;70(3):705-716. PubMed Central PMCID: PMC8250816.
 - b. McDonald SE, O’Connor KE, Matijczak A, Tomlinson CA, **Applebaum JW**, Murphy JL, Zsembik BA. Attachment to Pets Moderates Transitions in Latent Patterns of Mental Health Following the Onset of the COVID-19 Pandemic: Results of a Survey of U.S. Adults. *Animals*. 2021 Mar 21;11(3) PubMed Central PMCID: PMC8004029.
 - c. **Applebaum JW**, Adams BL, Eliasson MN, Zsembik BA, McDonald SE. How pets factor into healthcare decisions for COVID-19: A One Health perspective. *One Health*. 2020 Dec 20;11:100176. PubMed Central PMCID: PMC7543786.
 - d. **Applebaum JW**, Tomlinson CA, Matijczak A, McDonald SE, Zsembik BA. The Concerns, Difficulties, and Stressors of Caring for Pets during COVID-19: Results from a Large Survey of U.S. Pet Owners. *Animals (Basel)*. 2020 Oct 15;10(10) PubMed Central PMCID: PMC7602525.
4. **Assessing the impact of pet ownership on the health of older adults.** Pet ownership is believed to be beneficial to older adults because pets can reduce social isolation and loneliness. In this line of

research, we used various approaches to studying pet ownership and health outcomes among older adults: secondary survey analysis, primary survey collection, and qualitative focus groups. We found that older adult pet owners tended to have better cognitive health and lower allostatic load scores than non-owners, and older adults found pets to be very important social support during the COVID-19 pandemic. However, older adults also found it difficult to maintain the health and well-being of their human and pet family members due to their declining health and limited resources. Taken together, these studies imply that pet ownership may have many benefits for older adults, but they also come with unique risks in this population.

- a. **Applebaum JW**, Ellison C. “Whoever takes the dog gets the house”: How older adults negotiate, budget, and deploy resources for multispecies family health and well-being. *Social Work in Mental Health*. 2023 October 15; 21(6):757-783. PMID: NIHMS1935075
- b. **Applebaum JW**, Shieu MM, McDonald SE, Dunietz GL, Braley TJ. The Impact of Sustained Ownership of a Pet on Cognitive Health: A Population-Based Study. *J Aging Health*. 2023 Mar;35(3-4):230-241. PubMed Central PMCID: PMC10280126.
- c. **Applebaum JW**, McDonald SE, Zsembik BA. Longitudinal associations between allostatic load, pet ownership, and socioeconomic position among U.S. adults aged 50. *SSM Popul Health*. 2023 Mar;21:101344. PubMed Central PMCID: PMC9853381.
- d. **Applebaum JW**, Ellison C, Struckmeyer L, Zsembik BA, McDonald SE. The Impact of Pets on Everyday Life for Older Adults During the COVID-19 Pandemic. *Front Public Health*. 2021;9:652610. PubMed Central PMCID: PMC8062698.

5. **Examining the impact of pet ownership on patients receiving hospital care.** Previous research suggests that the responsibilities associated with pet ownership may impact the owners’ ability to access and utilize healthcare. In this line of ongoing research, we are assessing patients’ pre-related needs while receiving care. Findings from this research suggest that patients often have a need for supportive pet services, such as walking, feeding, and temporary boarding that their social network may not be able to provide.

- a. **Applebaum JW**, Alvero A, Hogan WR. Use of natural language processing to identify patient human-animal interactions in human electronic health records. Paper presented at: International Society for Anthrozoology; 2023 Jun 15-18; Edinburgh, Scotland.
- b. Polick CS, **Applebaum JW**, Hanna C, Jackson D 2nd, Tsaras-Schumacher S, Hawkins R, Conceicao A, O'Brien LM, Chervin RD, Braley TJ. The Impact of Pet Care Needs on Medical Decision-Making among Hospitalized Patients: A Cross-Sectional Analysis of Patient Experience. *J Patient Exp*. 2021;8 PubMed Central PMCID: PMC8489745.

Complete List of Published Work in My Bibliography:

<https://www.ncbi.nlm.nih.gov/myncbi/jennifer.applebaum.1/bibliography/public/>

BIOGRAPHICAL SKETCH

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

NAME: Russell T. Hepple

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

POSITION TITLE: Professor

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Saskatchewan, CAN	BSc	05/1988	Physiology
University of Toronto, CAN	MSc	12/1991	Physiology
University of Toronto, CAN	PhD	04/1996	Physiology
University of California San Diego, USA	Postdoc	10/1999	Physiology

A. Personal Statement

I am a Professor of Muscle Biology with more than 20 years of independent research experience exploring issues related to skeletal muscle in aging and disease. This has included research addressing the muscle biology associated with extremes of physical function in elderly humans (from frail elderly to world class octogenarian masters athletes), mechanistic studies in rodents addressing the role of mitochondrial permeability transition in skeletal muscle pathophysiology, and rodent studies addressing the impact of restricted energy intake (caloric restriction) and physical activity in modulating aging muscle physiology. Key focal points of my research include identifying the features of aging skeletal muscle biology that are most relevant in precipitating impaired mobility, identifying circulating factors that predict extremes of physical and cognitive function (high vs low), and identifying therapeutic targets in skeletal muscle that have translational promise for facilitating better retention of skeletal muscle mass and contractile function in advanced age. A major focus for my lab currently is in understanding the significance of an event known as mitochondrial permeability transition (mPT) in skeletal muscle. The reasons for this are manifold and include the fact that we see mitochondria exhibit a lower threshold for inducing mPT in heart and skeletal muscle with aging. Furthermore, we have shown that mPT in skeletal muscle drives muscle atrophy through mitochondrial reactive oxygen species and increased Caspase 3 activity. We are currently pursuing two parallel areas of research concerning mPT. Firstly, in the context of aging we are interested in determining whether modulation of mPT in skeletal muscle by knocking in mutants of the mPT-

promoting protein cyclophilin D (CypD) that either resist mPT or make it easier for mPT to occur can attenuate or exacerbate, respectively, the decline in skeletal muscle mass and function with aging. In this context, we are also interested in testing whether mPT occurring in skeletal muscle also contributes to systemic “inflammaging” that may exacerbate cognitive decline through alterations in the skeletal muscle secretome. Secondly, in view of the accumulation of mitochondria in skeletal muscle exhibiting hallmark features of mPT (swollen morphology with distorted cristae) in both sepsis and cancer cachexia, we are interested in determining if strategies to increase the Ca²⁺ threshold for inducing mPT in skeletal muscle can attenuate the severity of adverse muscle impact in these conditions.

Ongoing Projects of Relevance:

NIH R01 AG076490 (CoPIs: Ryan/Hepple) Linking kynurenine accumulation and the AHR pathway to exacerbated aging. 02/01/2022-01/31/2027

NIH R56 AG066758 (PI: Hepple) Mitochondrial Permeability Transition in Aging Muscle. 08/2021-07/2024

NIH R01 AG059416 (CoPIs: Cummings/Kritchevsky/Newman/Hepple) The Study of Muscle, Mobility and Aging (SOMMA). 06/2018-05/2024

Key publications from my group include:

1. D. Neyroud, R.L. Nosacka, A.R. Judge, and R.T. Hepple. Colon 26 adenocarcinoma (C26)-induced cancer cachexia impairs skeletal muscle mitochondrial function and content. *J Muscle Res Cell Motil.* 40(1): 59-65, 2019. PMID 30945134
2. S.K. Skinner, A. Solania, D.W. Wolan, M.S. Cohen, T.E. Ryan, and **R.T. Hepple**. Mitochondrial permeability transition causes mitochondrial reactive oxygen species- and caspase 3-dependent atrophy of single adult skeletal muscle fibers. *Cells*10: 2586, 2021. PMID: 34685566. PMID: 34685566.
3. C. Ubaida-Mohien, S. Spendiff, A. Lyashkov, R. Moadell, N.J. MacMillan, M-E. Filion, J.A. Morais, T. Taivassalo, L. Ferruci, and **R.T. Hepple**. Unbiased proteomics, oxphos histochemistry, and mtDNA copy number reveal better mitochondrial health in muscle of high functioning octogenarians. *ELife* 11: e74355, 2022. PMID: 35404238
4. M. Picard, D. Ritchie, K.J. Wright, M.M. Thomas, S.L. Rowan, T. Taivassalo, and **R.T. Hepple**. Mitochondrial Functional Impairment with Aging is Exaggerated in Isolated Mitochondria compared to Permeabilized Myofibers. *Aging Cell* 9(6): 1032-1046, 2010. PMID: 20849523

B. Positions, Scientific Appointments, and Honors

- | | |
|------|--|
| 2018 | The Physiological Society member |
| 2017 | Professor, Dept of Physical Therapy and Dept of Physiology, University of Florida |
| 2015 | Society of Sarcopenia, Cachexia and Muscle Wasting Disorders member |
| 2014 | NIH Common Fund working group on the Molecular Transducers of Physical Activity (MoTrPac). Co-Chair of Mitochondria/Energetics subgroup (with B. Goodpaster) |
| 2012 | Director, McGill Research Center for Physical Activity & Health |

- 2011 Associate Professor, Dept of Kinesiology & Physical Education, Dept of Medicine, McGill University
- 2005 Associate Professor, Faculty of Kinesiology and Faculty of Medicine, University of Calgary
- 2003 Canadian Institutes of Health Research, Institute of Aging Advisory Board member
- 2002 Gerontological Society of America member
- 2000 American Physiological Society member
- 1999 Assistant Professor, Faculty of Kinesiology and Faculty of Medicine, University of Calgary

Editorial Board Memberships

- 2021- *Muscle*
- 2020- *Cells* (Associate Editor of *Mitochondria* section)
- 2020- *Faculty Opinions*
- 2018- *The Journal of Physiology* (Reviewing Editor)

Awards

- 2014&15 Nesbitt-McMaster Award for Excellence in Medicine and Surgery, Research Institute of the McGill University Health Center
- 2013-14 Fonds de Recherche Quebec Sante Chercheur Boursiers Senior
- 2007-10 Alberta Heritage Foundation for Medical Research Senior Scholar
- 2003-08 Canadian Institutes of Health Research New Investigator Award
- 2003 Canadian Institutes of Health Research Special Recognition Award (for top ranked applicant in the CIHR Open Grant Competition from the field of Aging Research)
- 2002-07 Heart & Stroke Foundation of Canada New Investigator Award (declined 2003-07 portion)

Other Experience and Professional Memberships

- 2019- Cancer Cachexia Society member
- 2018- Reviewing Editor for *The Journal of Physiology*
- 2018- The Physiological Society member
- 2015- Society on Sarcopenia, Cachexia and Muscle Wasting Disorders member
- 2014-15 NIH Common Fund working group exploring needs and opportunities on “Molecular Mechanisms Whereby Physical Activity Prevents Disease and Improves Health Outcomes”, resulting in the Common Fund Molecular Transducers of Physical Activity funding opportunities. Co-Chair of Mitochondria/Energetics Subgroup (with B. Goodpaster)
- 2007-10 Canadian Institutes of Health Research, Institute Advisory Board Member, Institute of Aging

2002-10 Gerontological Society of America member


2000- American Physiological Society member

C. Contributions to Science

1. Mitochondrial permeability transition (mPT) induces atrophy in skeletal muscle (Burke et al. *Cells* 2021), and increases in aging skeletal muscle (Gouspillou et al. *FASEB J.* 2014; Spendiff et al. 2016).
 - a. S.K. Skinner, A. Solania, D.W. Wolan, M.S. Cohen, T.E. Ryan, and **R.T. Hepple**. Mitochondrial permeability transition causes mitochondrial reactive oxygen species- and caspase 3-dependent atrophy of single adult skeletal muscle fibers. *Cells* 10: 2586, 2021. PMID: 34685566. PMCID: PMC8534155.
 - b. G. Gouspillou, N. Sgarlato, S. Kapchinsky, F.M. Purves-Smith, B. Norris, C. Pion, S. BarbatArtigas, F. Lemieux, T. Taivassalo, J.A. Morais, M. Aubertin-Leuhedre, and **R.T. Hepple**. Increased sensitivity to mitochondrial permeability transition and myonuclear translocation of endonuclease G in atrophied muscle of physically active older men. *The FASEB Journal* 28(4): 1621-33, 2014. DOI: 10.1096/fj.13-242750. PMID: 24371120
 - c. S. Spendiff, M. Vuda, S. Aare, T. Gove, G. Gouspillou, S. Kapchinsky, J. Morais, C. Pilon, M. Aubertin-Leuhedre, S. Hettwer, T. Taivassalo and **R.T. Hepple**. Denervation Drives Mitochondrial Dysfunction in Skeletal Muscle of Octogenarians. *The Journal of Physiology* 594.24: 7361-7379, 2016. PMID: 27619626. PMCID: PMC5157074.
2. Aging skeletal muscle exhibits an impairment in aerobic capacity, independent of a reduction in convective oxygen delivery, and is associated with impaired mitochondrial function (Hagen et al. *J Gerontol Biol Sci.* 2004). This decline in muscle aerobic function and mitochondrial function can be completely prevented by long-term caloric restriction (Hepple et al. *FASEB J.* 2005), but not long-term endurance exercise training (Betik et al. *Am J Physiol* 2009).
 - a. J.L. Hagen, D.J. Krause, D.J. Baker, M. Fu, M.A. Tarnopolsky, and **R.T. Hepple**. Skeletal muscle aging in F344BN F1-hybrid rats: I. Mitochondrial dysfunction contributes to the age-associated reduction in VO_{2max} . *Journals of Gerontology Biological Sciences* 59A(11): 1099-1110, 2004. DOI: 10.1093/gerona/59.11.1099. PMID: 15602055
 - b. **R.T. Hepple**, D.J. Baker, J.J. Kaczor and D.J. Krause. Long-term caloric restriction abrogates the age-related decline in skeletal muscle aerobic function. *The FASEB Journal* 19(10): 1320-1322, 2005. DOI: 10.1096/fj.04-3535fje. PMID: 15955841
 - c. D.J. Baker, A.C. Betik, D.J. Krause, and **R.T. Hepple**. No decline in skeletal muscle oxidative capacity with aging in long-term caloric restricted rats: effects are independent of mtDNA integrity. *Journals of Gerontology Biological Sciences* 61A: 675-684, 2006. DOI: 10.1093/gerona/61.7.675. PMID: 16870628
 - d. A.C. Betik, M.M. Thomas, K.J. Wright, C.D. Riel and **R.T. Hepple**. Exercise training from late middle age to senescence does not attenuate the declines in skeletal muscle aerobic function.

American Journal of Physiology Regulatory Integrative and Comparative Physiology 297(3): R744-755, 2009. DOI: 10.1152/ajpregu.90959.2008. PMID: 19571205

3. Denervation is the primary cause of muscle fiber atrophy in advanced age, and the accumulation of persistently denervated muscle fibers parallels the accelerating phase of muscle atrophy in both slow and fast twitch muscles, where denervated muscle fibers exhibit an up-regulation of the proteolytic machinery and muscles generally exhibit an up-regulation of micro-RNAs that are predicted to target neurotrophin genes involved in promoting reinnervation (Rowan et al. *PLoS One* 2012; Purves-Smith et al. *Exp Gerontol.* 2012; Aare et al. *Skeletal Muscle* 2016). Furthermore, mitochondrial dysfunction in advanced age reflects in part changes that originate in persistently denervated muscle fibers, underscoring the complexity of factors that can impact mitochondrial function in skeletal muscle with aging (Spendiff et al. *J Physiol.* 2016);
 - a. S.L. Rowan, K.A. Rygiel, F.M. Purves-Smith, N.M. Solbak, D.M. Turnbull and **R.T. Hepple**. Denervation Causes Fiber Atrophy and Myosin Heavy Chain Co-expression in Senescent Skeletal Muscle. *PLoS One* 7(1): e29082, 2012. PMID: 22235261. PMCID: PMC3250397.
 - b. F.M. Purves-Smith, N.M. Solbak, S.L. Rowan, and **R.T. Hepple**. Severe Atrophy of Slow Fibers in Aging Muscle is Concealed by MHC Co-expression. *Experimental Gerontology* 47(12): 913-918, 2012. DOI: 10.1016/j.exger.2012.07.013. PMID: 22884852
 - c. S. Aare, S. Spendiff, M. Vuda, D. Elkrif, A. Perez, Q.Wu, D. Mayaki, S.N. Hussain, S. Hettwer, and **R.T. Hepple**. Failed Reinnervation in Aging Skeletal Muscle. *Skeletal Muscle* Sept. 1; 6(1): 29, 2016. PMID: 27588166. PMCID: PMC5007704.
 - d. S. Spendiff, M. Vuda, S. Aare, T. Gove, G. Gouspillou, S. Kapchinsky, J. Morais, C. Pilon, M. Aubertin-Leuhedre, S. Hettwer, T. Taivassalo and **R.T. Hepple**. Denervation Drives Mitochondrial Dysfunction in Skeletal Muscle of Octogenarians. *The Journal of Physiology* 594.24: 7361-7379, 2016. PMID: 27619626. PMCID: PMC5157074.
- B.** The traditional approach of mechanically isolating mitochondria from skeletal muscle to study their function dramatically alters not only mitochondrial reticular structure, but also potentiates mitochondrial ROS emission and sensitivity to permeability transition relative to a preparation where mitochondrial structure is preserved (saponin-permeabilized myofibers) (Picard et al. *PLoS One* 2011). Similarly, the magnitude and nature of mitochondrial dysfunction in aging skeletal muscle is highly dependent upon the method used to interrogate the function, where an *in situ* method that preserves mitochondrial structure and permits representation of all mitochondria (saponin-permeabilized myofibers) reveals considerably smaller changes with aging than are seen with mechanically isolated mitochondria (Picard et al. *Aging Cell* 2010). Some of these changes in mitochondrial function in humans can be prevented by maintaining a high level of physical activity (Gouspillou et al. *FASEB J.* 2014) and are associated with marked differences in representation of proteins that regulate various aspects of mitochondrial biology (UbaidaMohien et al. *eLife* 2022).
 - a. M. Picard, D. Ritchie, K.J. Wright, M.M. Thomas, S.L. Rowan, T. Taivassalo, and **R.T. Hepple**. Mitochondrial Functional Impairment with Aging is Exaggerated in Isolated Mitochondria compared to Permeabilized Myofibers. *Aging Cell* 9(6): 1032-1046, 2010. PMID: 20849523
 - b. M. Picard, T. Taivassalo, D. Ritchie, K.J. Wright, M.M. Thomas, C. Romestaing, and **R.T. Hepple**. Mitochondrial Structure and Function are Disrupted by Standard Isolation Methods. *PLoS One* 6(3): e18317, 2011. PMID: 21512578

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- c. G. Gouspillou, N. Sgarioto, S. Kapchinsky, F.M. Purves-Smith, B. Norris, C. Pion, S. Barbat-Artigas, F. Lemieux, T. Taivassalo, J.A. Morais, M. Aubertin-Leuhedre, and **R.T. Hepple**. Increased sensitivity to mitochondrial permeability transition and myonuclear translocation of endonuclease G in atrophied muscle of physically active older men. *The FASEB Journal* 28(4): 1621-33, 2014.
PMID: 24371120
- d. C. Ubaida-Mohien, S. Spendiff, A. Lyashkov, R. Moadell, N.J. MacMillan, M-E. Filion, J.A. Morais, T. Taivassalo, L. Ferruci, and **R.T. Hepple**. Unbiased proteomics, oxphos histochemistry, and mtDNA copy number reveal better mitochondrial health in muscle of high functioning octogenarians.
ELife 11: e74355, 2022. PMID: 35404238

A full list of my publications can be found on PubMed:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=hepple+rt>

BIOGRAPHICAL SKETCH

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

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

NAME: Rossi, Eleonora

eRA COMMONS USER NAME (credential, e.g., agency login): EROSSI77

POSITION TITLE: Assistant Professor

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
University of Padua, Speech and Language Pathology, Padua, PD	BA	03/2001	Speech and Language Pathology
University of Groningen, Linguistics , Groningen, NL	MA	09/2002	Clinical Linguistics
University of Groningen, Linguistics, Groningen, NL	PHD	09/2007	Linguistics
Penn State University, State College, PA	OTH	01/2015	Psychology

A. Personal Statement

The ability to communicate is a ubiquitous experience for humans, from childhood to older age. Societies are increasingly multilingual and mobile, with most of the world's population speaking more than one language and migrating/living in different countries. At the same time, most societies are aging. In the US, by 2035, there will be 78.0 million people 65 years and older compared to 76.7 million under the age of 18. Critically, life-long bilingualism and second language learning have been shown to promote neural protection across the life-span for healthy aging and have been demonstrated to significantly delay the onset of the clinical symptoms of neurodegenerative diseases, such as Alzheimer's disease and related dementias (ADRDs). One proposed hypothesis is that active bilingualism (even at early stages of second language learning) engages language specific and cognitive domain general neural substrates to control and monitor the selection and use of the two languages. My lab at the University of Florida (Brain, Language and Bilingualism Lab -Blab-) focusses on the very nature of this bilingualism-induced neuroplasticity in younger and older adults using behavioral and neuroimaging methods including functional magnetic resonance imaging (fMRI) and electroencephalography (EEG) to study the earliest structural functional and neurophysiological changes induced by bilingualism. Since the start of my career I have supervised over 30 undergraduate students from diverse, and underrepresented backgrounds. Since joining UF in January 2019 I have supervised over 15 undergraduate students, and I am currently supervising 4 graduate students, three of whom are representatives of first-generation, underrepresented scholars. Two of my current PhD advisees, are recipients of NSF Graduate Research Fellowships. All the students in my lab present regularly at national and international conferences, and I mentor them in preparing their presentations. As such, in the context of NEURON-Aging, I feel strongly about being able to provide excellent guidance and mentorship for the students who will participate in the proposed research, from a theoretical and methodological perspective. The students who will participate in the proposed research in my lab will receive first-hand training with behavioral, EEG and MRI methodology from testing to data analysis. In addition, I strive to provide opportunities for a multi-cultural research environment in which students work together on projects with visiting scholar from other US universities, or European partners. As part of the NSF partnership in research and Education Grant -PIRE- I regularly host undergraduate students from other US Partner Institutions during the summer who can work on research projects and understand research beyond the classroom. Promoting a diverse new generation of scientist will also likely transform our understanding of

multilingual/multicultural research environments, and will foster cross-disciplinary conversation among scientists, education professionals, industry, and policy makers.

5. Rossi, E., Pereira Soares, S., Prystauka, Y., Nakamura, M., & Rothman, J. (2022). Riding the (brain) waves! Using neural oscillations to inform bilingualism research. *Bilingualism: Language and Cognition*, 1-14. doi:10.1017/S1366728922000451
6. Luk G, Pliatsikas C, Rossi E. Brain changes associated with language development and learning: A primer on methodology and applications. *System*. 2020 April; 89:102209-. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0346251X19307584> DOI: 10.1016/j.system.2020.102209
7. Rossi E, Prystauka Y. Oscillatory brain dynamics of pronoun processing in native Spanish speakers and in late second language learners of Spanish. *Bilingualism: Language and Cognition*. 2020 January 29; 23(5):964-977. Available from: https://www.cambridge.org/core/product/identifier/S1366728919000798/type/journal_article DOI: 10.1017/S1366728919000798
8. Rossi E, Newman S, Kroll JF, Diaz MT. Neural signatures of inhibitory control in bilingual spoken production. *Cortex*. 2018 Nov;108:50-66. PubMed Central PMCID: PMC6375513.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2019 -	Assistant Professor, University of Florida, Gainesville, FL
2019 -	Faculty Affiliate, Psychology department, University of Florida, Gainesville, FL
2015 - 2018	Assistant Professor in Psychology, California State Polytechnic University Pomona, Psychology, Pomona, CA
2013 - 2015	Visiting Assistant Professor, Penn State University, State College, PA
2008 - 2012	Post-doctoral associate, Penn State University, State College, PA

Honors

2020	HUMEVAL Visiting Professor, Arctic University of Norway, Tromsø
2019	Fellow of the Psychonomic Society, The Psychonomic Society

C. Contribution to Science

6. Bi-multilingualism as cognitive training: Implications for the mind and the brain in older adults

Questions about the cognitive and linguistic changes due to healthy aging in elderly adults and their social implications have been in the spotlight as one of the most relevant scientific debates about the human brain, as shown by a recent Science Special Issue on The Aging Brain (Science, 2014). My most recent line of work bridges research on bilingualism to the body of research on language processing in healthy elderly adults to ask to what extent patterns of language processing that are observed in bilinguals and elderly adults are driven by the same cognitive and neural processes. This research will advance our knowledge of whether and to what extent bilingualism modulates cognitive and neural plasticity in older adults, and will help to clarify if bilingualism could be targeted as a prime example of cognitive training. Recent findings suggest that the life-long experience of monitoring and controlling multiple languages appears to produce a range of language-independent cognitive advantages that provide protection for elderly bilinguals against

the rate of decline associated with normal and pathological cognitive aging (e.g., Bialystok et al., 2007; Craik et al., 2010; Gold et al., 2013). Also, functional and structural neural changes have been linked to second language learning past childhood (e.g., Rossi et al., 2017) and bilingual language experience. It is appealing to think that the requirement for bilinguals to juggle the competition across their two languages creates expertise that benefits general cognitive functions, and language learning abilities, across the life span, especially in healthy aging. I have advanced a number of theoretical hypotheses in two recent papers on the topic (Rossi & Diaz, 2017; Rossi, Prystauka & Diaz, 2018). At the same time, research on cognitive training has recently conveyed a lot of compelling results suggesting that the brain is more plastic than previously thought even at an older age, and has therefore provided a novel perspective to investigate cognitive functions in older adults (i.e., Rebok et al., 2014). In my lab I am exploit the hypothesis that second language learning, even for older post-critical period speakers can be viewed as one type of cognitive training that capitalizes on inhibition and other executive functions and will be at the basis of a very fruitful area of research to examine cognitive and neural plasticity in older adults. This line of research will be composed by a number of sub-projects which will investigate on the one hand, if training a specific subset of cognitive functions (among which inhibitory control, working memory -both verbal and non verbal-) will facilitate language novel language learning, and language processing (both in younger and older adults), and on the other hand, will allow investigating if and to what extent learning a new language (both intended as acquiring new vocabulary as well as leaning a new grammar) impacts more general non-linguistic cognitive functions. Changes in the behavioral and neural signatures of language learning trajectories, and cognitive abilities will be investigated using ad-hoc behavioral tests, as well as complementary neuroimaging methods that allow both excellent time (e.g., ERPs) and spatial (e.g., fMRI) resolution. Potential changes in brain structure will be analyzed looking at changes in cortical thickness, and connectivity.

- a. Luk G, Pliatsikas C, Rossi E. Brain changes associated with language development and learning: A primer on methodology and applications. *System*. 2020 April; 89:102209-. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0346251X19307584> DOI: 10.1016/j.system.2020.102209
 - b. Rossi E, Cheng H, Kroll JF, Diaz MT, Newman SD. Changes in White-Matter Connectivity in Late Second Language Learners: Evidence from Diffusion Tensor Imaging. *Front Psychol*. 2017;8:2040. PubMed Central PMCID: PMC5702476.
 - c. Rossi E, Diaz M. How aging and bilingualism influence language processing: Theoretical and neural models. *Linguistic Approaches to Bilingualism*. 2016; 6(1-2):9-42. Available from: <http://www.jbe-platform.com/content/journals/10.1075/lab.14029.ros> DOI: 10.1075/lab.14029.ros
 - d. Rossi E, Diaz M. How aging and bilingualism influence language processing. *Linguistic Approaches to Bilingualism*. 2016; 6(1-2):9-42. Available from: <http://www.jbe-platform.com/content/journals/10.1075/lab.14029.ros> DOI: 10.1075/lab.14029.ros
7. Advancing the neural bases of bilingualism: Using EEG, Time Frequency Analysis, MRI to capture the earliest changes conferred by bilingualism.

Scientists have recently started to analyze the EEG signal in a different way, looking at the frequencies of the brain's electrical activity. Time-frequency analysis of the EEG signal has emerged

as a tool to better understand neural variability during language processing. Importantly for the scope of this proposal, time-frequency analysis of the EEG signal is a particularly valuable analysis tool to study populations that have a variable patterns of performance and neural activity, such as L2 learners (Kielar et al., 2013). In a recent number of studies I utilized TFR to investigate how native speakers of Spanish and native English speakers who are late learners of Spanish process grammar. In one study (Rossi & Prystauka, 2020) I analyzed the oscillatory signal related to Spanish pronouns, a grammatical structure that is present in Spanish but not in English. Additionally, Spanish pronouns also mark grammatical gender, a grammatical feature that is also unique to Spanish, overall making pronouns difficult to acquire for L2 learners. Our results reveal, that English L2 learners of Spanish are overall sensitive to pronouns and its gender features, as shown by similar oscillatory signal in the alpha (8-12 Hz) and beta (13-30 Hz) frequencies which have been linked to sensitivity to violations of the grammar. Crucially, the data reveal that the oscillatory signal in native Spanish speakers continues for about 1.2-1.3 seconds, while it only lasts till 1 second for L2 speakers suggesting that sensitivity to violations of grammatical structures in L2 might be shorter lived than in one's native language. We hypothesize that the length of this oscillatory reverberation signal might be connected to more domain-general cognitive resources, such as short-term memory, and maintenance in memory of the L2 (Rossi & Prystauka, 2020). The Oscillatory results are corroborated by a series of MRI and fMRI studies (Rossi et al., 2018; Rossi et al., 2017) that demonstrate that neural functional and structural measures of brain activity are shaped by learning a new language, or speaking two language, even when learned after childhood, suggesting a high level of neuroplasticity related to bilingualism.

- e. Luk G, Pliatsikas C, Rossi E. Brain changes associated with language development and learning: A primer on methodology and applications. *System*. 2020 April; 89:102209-. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0346251X19307584> DOI: 10.1016/j.system.2020.102209
- f. Rossi E, Prystauka Y. Oscillatory brain dynamics of pronoun processing in native Spanish speakers and in late second language learners of Spanish. *Bilingualism: Language and Cognition*. 2020 January 29; 23(5):964-977. Available from: https://www.cambridge.org/core/product/identifier/S1366728919000798/type/journal_article DOI: 10.1017/S1366728919000798
- g. Rossi E, Cheng H, Kroll JF, Diaz MT, Newman SD. Changes in White-Matter Connectivity in Late Second Language Learners: Evidence from Diffusion Tensor Imaging. *Front Psychol*. 2017;8:2040. PubMed Central PMCID: PMC5702476.
- h. Rossi, E., Pereira Soares, S., Prystauka, Y., Nakamura, M., & Rothman, J. (2022). Riding the (brain) waves! Using neural oscillations to inform bilingualism research. *Bilingualism: Language and Cognition*, 1-14. doi:10.1017/S1366728922000451

BIOGRAPHICAL SKETCH

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

NAME: Weisberg, Steven

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

POSITION TITLE: Assistant Professor

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
College of William and Mary, Williamsburg, VA	AB	05/2008	Psychology
Temple University, Philadelphia, PA	PHD	12/2014	Psychology
University of Pennsylvania, Philadelphia, Pennsylvania	Postdoctoral Fellow	08/2019	F32 Postdoc in Cognitive Neuroscience

A. Personal Statement

I am an assistant professor of psychology at the University of Florida and director of the Spatial Cognition and Navigational Neuroscience (SCANN) Lab. Our research uses neuroimaging and behavioral methods to understand the ways humans navigate and how navigation changes through aging and in age-related neurodegeneration. My research has revealed substantial variability in the accuracy with which individuals can represent large-scale space (Weisberg & Newcombe, 2016; Weisberg et al., 2014; Weisberg, Newcombe, & Chatterjee, 2018). This program of research focuses on individual differences in spatial navigation behavior, exploring the range of navigation behaviors that are supported by various cognitive traits (e.g., working memory capacity, small-scale spatial ability, etc.). A second program of research characterizes the way spatial directions are communicated through distinct formats: verbal directions, maps, vibrotactile information (Weisberg, Marchette, & Chatterjee, 2018; Weisberg, Newcombe, & Chatterjee, 2019). In these experiments, I have used behavioral measures of navigation accuracy alongside functional imaging to determine the brain regions that support the process of transforming one format of information (e.g., a map) into another (e.g., a scene). This program of research was supported by an NRSA F32 training grant through which I learned how to design, analyze, and interpret functional MRI, along with advanced analytical techniques like multi-voxel pattern analysis. This training has been instrumental in support of my ultimate goal - improving and supporting navigation behavior in impaired populations by developing a greater understanding of the brain and behavioral mechanisms that comprehend spatial directions. My ongoing work combines behavioral measurements and computational modeling of spatial navigation using lab-based and virtual reality tasks with structural and functional neuroimaging. We study spatial navigation in healthy younger and older adults (18-90) and individuals with subjective cognitive decline (SCD), a precursor state to Alzheimer's disease and related dementias (ADRD). As an independent researcher, my work focuses on

two core questions: how can we understand age- and ADRD-related behavioral and neural shifts in spatial navigation; and how can spatial navigation best be supported and enhanced across populations. This research program has been supported by substantive extramural funding, including a K01 from the NIA (mentored by co-I Dr. Natalie Ebner), an R21 from the NIMH (co-PI), and two grants from the Florida Department of Health (co-PI and co-mentor with Dr. Ebner).

In ongoing collaborations between myself and co-I Dr. Ebner, we have developed several lines of research evaluating spatial navigation behavior, and its behavioral and neural correlates in healthy older adults and . Here, we apply this training to older adults at different levels of susceptibility to developing Alzheimer's disease and related diseases (ADRD), an area in which I am currently receiving training through an NIA K01. In my collaborations with Dr. Ebner (for which we have also received external funding from the Florida Department of Health), we have explored the functional neural correlates of navigation strategy in healthy older adults, and in older adults at risk for dementia. The current R01 proposal includes a second co-investigator - Dr. Rachael Seidler - with whom we have written a review paper, which outlines the conceptual framework of our experiments. Dr. Seidler, an expert on the neural correlates of vestibular function in healthy and ADRD aging, complements our expertise by focusing on novel sensorimotor processes, which could be a vital component in explaining age- and ADRD-related spatial navigation decline. Our complementary sets of expertise make our team ideally suited to conduct the proposed research, which will yield critical data to inform future behavioral interventions as large-scale clinical trials to help prevent cognitive decline in older adults.

1. Weisberg SM, Ebner NC, Seidler RD. Getting LOST: A conceptual framework for supporting and enhancing spatial navigation in aging. *Wiley Interdiscip Rev Cogn Sci.* 2023 Nov 7; PubMed PMID: 37933623; NIHMSID: NIHMS1940503.
2. Weisberg SM, Newcombe NS, Chatterjee A. Everyday taxi drivers: Do better navigators have larger hippocampi?. *Cortex.* 2019 Jun;115:280-293. PubMed Central PMCID: PMC6513697.
3. Weisberg SM, Newcombe NS. Cognitive Maps: Some People Make Them, Some People Struggle. *Curr Dir Psychol Sci.* 2018 Aug;27(4):220-226. PubMed Central PMCID: PMC6095672.
4. Weisberg SM, Marchette SA, Chatterjee A. Behavioral and Neural Representations of Spatial Directions across Words, Schemas, and Images. *J Neurosci.* 2018 May 23;38(21):4996-5007. PubMed Central PMCID: PMC5966795.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2023 -	Affiliate Faculty, Cognitive and Aging Memory Center, University of Florida
2023 -	Affiliate Faculty, Artificial Intelligence Academic Initiative Center, University of Florida
2022 -	Fellow, Psychonomic Society
2020 -	Member, McKnight Brain Institute, University of Florida
2019 -	Assistant Professor, University of Florida, Gainesville, FL
2015 - 2019	Digital Associate Editor, Psychonomic Society, Philadelphia, PA

2015 - 2019 Post-doctoral Fellow, University of Pennsylvania, Philadelphia, PA
2010 - 2014 Graduate Student, Temple University, Philadelphia, PA

Honors

2018 - 2018 Biomedical Postdoctoral Program Travel Award, University of Pennsylvania
2017 - 2017 Postdoctoral Fellow Award, Cognitive Neuroscience Society
2017 - 2017 Collaborative Symposium Award, Psychonomic Society
2016 - 2016 Biomedical Postdoctoral Program Travel Award, University of Pennsylvania
2014 - 2014 College of Liberal Arts Travel Award, Temple University
2013 - 2013 Collaboration Grant, Science Across Virtual Institutes, Thematic Network in Spatial Cognition, NSF
2013 - 2013 Visiting Fellowship, Martinos Center for Biomedical Imaging, MGH
2013 - 2013 Training in fMRI Fellowship, University of Michigan, NIH
2012 - 2012 Department of Psychology Travel Award, Temple University
2004 - 2008 Dean's List, College of William and Mary
2022 Society Fellowship, Psychonomic Society
2016 Ruth L. Kirschstein NRSA Postdoctoral Fellowship, F32, NIDCD

C. Contribution to Science

1. Individual variability in ecological navigation: I have used behavioral and structural neuroimaging methods in virtual environments to delineate the individual characteristics that correlate with navigation ability. My work has centered on evaluating navigation ability using a standard set of tasks (Virtual Silcton), which our lab helped developed and currently maintains. Over multiple replications, our research demonstrates wide variability in spatial navigation ability in healthy younger adults. We also show that certain aspects of spatial navigation behavior correlate with distinct cognitive processes. This research also has critical implications for the connection between individual variance in ecologically-valid behavior and macroscopic neural structure. In particular, in a large and preregistered experiment, we did not find statistically significant correlations between hippocampal volume and navigation ability - a finding that contradicts seminal experiments in navigation experts (London taxi drivers) and data from older adults (with and without ADRD-related neurodegeneration).
 - a. Weisberg SM, Ekstrom AD. Hippocampal volume and navigational ability: The map(ping) is not to scale. *Neurosci Biobehav Rev.* 2021 Jul;126:102-112. PubMed Central PMCID: PMC8402939.
 - b. Weisberg SM, Newcombe NS, Chatterjee A. Everyday taxi drivers: Do better navigators have larger hippocampi?. *Cortex.* 2019 Jun;115:280-293. PubMed Central PMCID: PMC6513697.

- c. Weisberg SM, Newcombe NS. How do (some) people make a cognitive map? Routes, places, and working memory. *J Exp Psychol Learn Mem Cogn*. 2016 May;42(5):768-785. PubMed PMID: 26595065.
- d. Weisberg SM, Schinazi VR, Newcombe NS, Shipley TF, Epstein RA. Variations in cognitive maps: understanding individual differences in navigation. *J Exp Psychol Learn Mem Cogn*. 2014 May;40(3):669-682. PubMed PMID: 24364725.
2. Supporting spatial navigation behavior: I have conducted behavioral and fMRI research that characterizes the way spatial directions are processed across formats (e.g., through verbal directions or through maps) and sensory modalities (e.g., with vibrotactile stimulation or visual and vestibular information). These results, including some in older adults with posterior cortical atrophy (PCA), a neurodegenerative variant of Alzheimer's disease, show behavioral and neural differences in how spatial directions are processed by the human brain.
- a. Weisberg SM, Ebner NC, Seidler RD. Getting LOST: A conceptual framework for supporting and enhancing spatial navigation in aging. *Wiley Interdiscip Rev Cogn Sci*. 2023 Nov 7; PubMed PMID: 37933623; NIHMSID: NIHMS1940503.
- b. Barnas AJ., Ebner NC., Weisberg SM.. Spatial direction comprehension is guided by efficient allocation of space-based attention. *Psyarxiv*. 2022 November 07. Available from: <https://doi.org/10.31234/osf.io/uwhq9>
- c. Weisberg SM, Chatterjee A. Spatial direction comprehension in images, arrows, and words in two patients with posterior cortical atrophy. *Neuropsychologia*. 2021 Jan 22;151:107697. PubMed Central PMCID: PMC7855773.
- d. Weisberg SM, Marchette SA, Chatterjee A. Behavioral and Neural Representations of Spatial Directions across Words, Schemas, and Images. *J Neurosci*. 2018 May 23;38(21):4996-5007. PubMed Central PMCID: PMC5966795.
3. Enhancing spatial navigation behavior: Our research has explored various means of improving individual navigation behavior using navigation tools - a vibrotactile compass, gestures, and maps and verbal instructions. This program of research offers new avenues toward allowing individuals to function independently or learn to use various types of navigation cues more effectively.
- a. Jaeger, Allison,, Weisberg, Steven Marc,, Nazareth, Alina,, Newcombe, Nora,. A picture or a thousand words: Neither improve spatial knowledge of a complex virtual environment. [Preprint]. 2022 November 14. DOI: 10.31234/osf.io/7grxy
- b. Weisberg SM, Badgio D, Chatterjee A. Feel the way with a vibrotactile compass: Does a navigational aid aid navigation?. *J Exp Psychol Learn Mem Cogn*. 2018 May;44(5):667-679. PubMed Central PMCID: PMC5938094.
- c. Weisberg SM, Newcombe NS. Embodied cognition and STEM learning: overview of a topical collection in CR:PI. *Cogn Res Princ Implic*. 2017;2(1):38. PubMed Central PMCID: PMC5596025.
- d. Galati A, Weisberg S, Newcombe N, Avraamides M. When gestures show us the way: Co-thought gestures selectively facilitate navigation and spatial memory. *Spatial Cognition & Computation*.

2017 August 16; 18(1):1-30. Available from:
<https://www.tandfonline.com/doi/full/10.1080/13875868.2017.1332064> DOI:
10.1080/13875868.2017.1332064

4. Facets of spatial navigation behavior: In addition to demonstrating individual variability in navigation behavior, my research has also revealed specific factors that correlate with this variability, including developmental processes and mnemonic processes (working and episodic memory).
 - a. Weisberg SM, Schinazi VR, Ferrario A, Newcombe NS. Evaluating the effects of a programming error on a virtual environment measure of spatial navigation behavior. *J Exp Psychol Learn Mem Cogn*. 2023 Apr;49(4):575-589. PubMed Central PMCID: PMC10714309.
 - b. Weisberg SM, Newcombe NS. Cognitive Maps: Some People Make Them, Some People Struggle. *Curr Dir Psychol Sci*. 2018 Aug;27(4):220-226. PubMed Central PMCID: PMC6095672.
 - c. Nazareth A, Weisberg SM, Margulis K, Newcombe NS. Charting the development of cognitive mapping. *J Exp Child Psychol*. 2018 Jun;170:86-106. PubMed PMID: 29453130.
 - d. Ngo CT, Weisberg SM, Newcombe NS, Olson IR. The relation between navigation strategy and associative memory: An individual differences approach. *J Exp Psychol Learn Mem Cogn*. 2016 Apr;42(4):663-670. PubMed PMID: 26501930.
5. Visual and non-visual navigational cues: In real world and virtual environments I have elucidated the mechanisms underlying how terrain slope can be used as a directional cue for spatial navigation. These experiments show substantial variability in who can use slope to navigate and how, and show novel sex differences in the use of terrain slope as a spatial cue, providing insights into non-visual sensory mechanisms supporting navigation behavior.
 - a. Nardi D, Holmes CA, Newcombe NS, Weisberg SM. Sex differences and errors in the use of terrain slope for navigation. *Cogn Process*. 2015 Sep;16 Suppl 1:323-6. PubMed PMID: 26216758.
 - b. Holmes C, Nardi D, Newcombe N, Weisberg S. Children's Use of Slope to Guide Navigation: Sex Differences Relate to Spontaneous Slope Perception. *Spatial Cognition & Computation*. 2015 March 25; 15(3):170-185. Available from:
<http://www.tandfonline.com/doi/full/10.1080/13875868.2015.1015131> DOI:
10.1080/13875868.2015.1015131
 - c. Weisberg SM, Nardi D, Newcombe NS, Shipley TF. Up by upwest: Is slope like north?. *Q J Exp Psychol (Hove)*. 2014 Oct;67(10):1959-76. PubMed PMID: 24397309.
 - d. Weisberg SM, Newcombe NS. A slippery directional slope: Individual differences in using slope as a directional cue. *Mem Cognit*. 2014 May;42(4):648-61. PubMed PMID: 24338529.

Complete List of Published Work in My Bibliography:

<https://www.ncbi.nlm.nih.gov/myncbi/steven.weisberg.2/bibliography/public/>

Appendix 2

Top 20 Publications from 2023

Albizu, A., **Indahlastari, A.**, Huang, Z., Waner, J., Stolte, S., **Fang, R.**, and **Woods, A.J.** Machine-learning defined precision tDCS for improving cognitive function. *Brain Stimulation*, June 4, 2023 16(3): 969-974.

Applebaum, J.W., McDonald, S.E., & Zsembik, B.A. (2023). Longitudinal associations between allostatic load, pet ownership, and socioeconomic position among U.S. adults aged 50+. *SSM – Population Health*, 21(3), 101344.

Bottari S.A., **Cohen R.A.**, Friedman J., **Porges E.**, Chen A., Gunstad J., **Woods A.J.**, Britton M., **Williamson J.B.** (2023). Change in cerebral metabolite concentrations following bariatric surgery. *NMR in Biomedicine*, epub ahead of print <https://doi.org/10.1002/nbm.4897>

Budamagunta V., **Kumar K.**, Rani A., Bean L., Manohar-Sindhu S., Yang Y., Zhou D., **Foster T.C.**, Effect of peripheral cellular senescence on brain aging and cognitive decline, *Aging Cell*, 2023, e13817, PMID: 36959691.

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Appendix 3

Top 10 Presentations at Scientific or Public Meetings

- Burke, S.N.** Plenary Lecture. Targeting metabolism to improve cognitive resilience during aging. International Meeting on Learning and Memory. April 28, 2023.
- Woods A.J.** Invited Lecture. Principles and application of transcranial direct current stimulation. International Brain Stimulation Conference, Lisbon, Portugal. February 21, 2023.
- Foster, T.** Invited Talk. Transcriptional Resilience Mechanisms for Cognitive Reserve. The American Society for Neural Therapy and Repair. April 27-30, 2023.
- Alvina, K.** Invited Speaker. Muscle-Brain Axis: New Insights from Preclinical Investigations. Catholic University of the North, Coquimbo, Chile. September 2023.
- Applebaum, J.W.** .Presenter. Use of natural language processing to identify patient human-animal interactions in human electronic health records, International Society for Anthrozoology Edinburgh, Scotland, 2023.
- Cruz-Almeida, Y.** Lecture. Feasibility of clinical brain age predictions: Toward MR protocol-agnostic, and unbiased brain age predictions
- Ebner, N. C.** Understanding and promoting social-cognitive and affective aging. School of Gerontology Colloquium, University of Southern California, Los Angeles, CA, USA. February, 2023.
- Indahlastari, A, Salehinejad, M, Soleimani, G., and Schmidt, N.** Variability in transcranial electrical stimulation results: The role of circadian factors, aging, anatomical difference, and stimulation parameters. On-demand Symposium at the 5th International Brain stimulation Conference. Portugal. February, 2023.
- Setlow, B.** Effects of acute and chronic cannabis/cannabinoids on cognition across the lifespan. Annual Meeting of the Gerontological Society of America, Tampa, FL, November 8, 2023.
- Someya, R.** Invited Talk. Sex Differences in Hearing and Aging. University of Louisville Audiology. 2023

Appendix 4

Communications

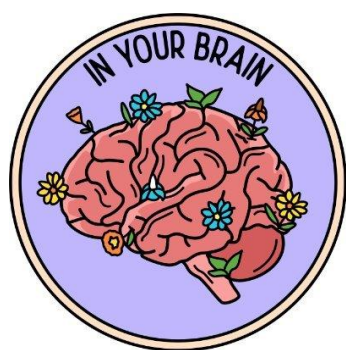
Website Development

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

The number of visits to the CAM website for 2023 was 6,459 – which is 13% over the previous year. The page that was visited the most on our site was Dr. Burke’s article from *The Conversation* about ultra-processed foods.

Social Media: **Twitter** - @UF_CAMcenter. Our account currently has over 500 followers; however, Twitter has taken a hit over the last year with many scientists leaving it for other services. In 2024 we have decided to create a center **LinkedIn** account and build a network through that platform.

Podcasts: CAM graduate student, Cristina Besosa, hosts a neuroscience podcast entitled *In Your Brain*. Many CAM researchers have been featured on the podcast. In 2023, there were 782 downloads of podcast episodes. Over 200 of those downloads have been from outside of the United States.



Media Coverage

1-10-23 – Dr. Ruogu Fang ‘s work in medical AI is featured in *Computer Vision News*.
<https://www.rsipvision.com/ComputerVisionNews-2023January/32/>

1-31-23 – Dr. Sara Burke discusses how the science shows that ultra-processed foods may contribute to cognitive decline. <https://theconversation.com/ultraprocessed-foods-like-cookies-chips-frozen-meals-and-fast-food-may-contribute-to-cognitive-decline-196560>

2-13-23 – Dr. Jen Bizon has been named the new director of the MBI.
<https://mbi.ufl.edu/2023/02/13/dr-jennifer-bizon-named-director-of-ufs-mcknight-brain-institute/>

2-24-23 – CAM center helps support 2023 Luttge Lecturer Dr. Joshua A. Gordon, director of the National Institute of Mental Health. <https://mbi.ufl.edu/2023/02/24/national-institute-of-mental-health-director-delivers-2023-luttge-lecture/>

3-6-23 – Dr. Alejandro Albizu, recent graduate from Dr. Adam Woods’s lab, is quoted in UF article about the College of Medicine’s 2023 Celebration of Research.

<https://news.drgator.ufl.edu/2023/03/06/faculty-and-trainee-investigations-and-art-showcased-during-2023-celebration-of-research/>

3-7-23 – Dr. Sara Burke named co-director of UF’s CAM Center. <https://mbi.ufl.edu/2023/03/07/sara-burke-ph-d-named-co-director-of-ufls-cam-center/>

4-28-23 – Dr. Joseph Gullett’s study that uses AI to predict who may benefit from cognitive training to stave off dementia is featured. <https://phhp.ufl.edu/2023/04/28/new-study-uses-ai-to-predict-who-may-benefit-from-cognitive-training-to-stave-off-dementia/>

5-1-23 – Dr. Jessica Kraft, recent graduate from Dr. Adam Woods’s lab, is UF’s latest MBI Rising star. <https://mbi.ufl.edu/2023/05/01/mbi-rising-stars-jessica-kraft/>

5-9-23 – Dr. Natalie Ebner is featured in University of Florida’s Women in Neuro series. #UFWomenOfNeuro.

6-6-23 – Dr. Jen Bizon is featured in a Q&A as the new MBI director. <https://mbi.ufl.edu/2023/06/13/qa-with-mbi-director-dr-jen-bizon/>

6-23-23 – Dr. Adam Woods has been named co-director of CAM center. <https://mbi.ufl.edu/2023/06/23/adam-woods-ph-d-named-co-director-of-ufls-cam-center/>

8-2-23 – Drs. Ron Cohen’s and Brain Ho’s study looking into the benefits to aerobic and strength training in people over 85 is highlighted in *The Conversation*. <https://theconversation.com/aerobic-and-strength-training-exercise-combined-can-be-an-elixir-for-better-brain-health-in-your-80s-and-90s-new-study-finds-212433>

9-29-23 – Dr. Sara Burke is featured on the podcast In Your Brain to discuss What is Memory? <https://open.spotify.com/episode/73PPWCMY1cLCJRJbnliJtY?si=9881f9e0a85548cd&nd=1&dlsi=7b6f939aef8d4f9c>

10-19-23 – UF’s McKnight Brain Institute celebrates 25 years with a glance back and a look forward. <https://news.ufl.edu/archive/1998/10/national-brain-institute-to-open-this-week-at-university-of-florida.html>

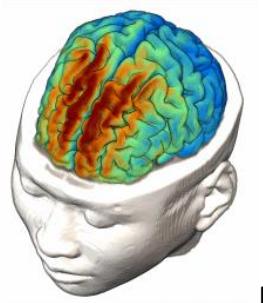
10-30-23 – Dr. Ruogu Fang’s research is highlighted in UF’s Biomedical Engineering’s annual magazine. https://issuu.com/ufbme/docs/crosslink_2023?fr=xKAE9_zU1NQ

10-30-23 – Dr. Aaron Colverson, a recent graduate from Dr. John Williamson’s lab, is featured in UF’s College of the Arts magazine for his research in rhythmic music and the aging brain. <https://arts.ufl.edu/in-the-loop/news/uf-school-of-music-ethnomusicologist-studies-rhythmic-music-and-the-aging-brain/>

11-4-23 – Team CAM raised over \$2400 for suicide prevention, research, and awareness by participating in Out of the Darkness Gainesville Walk.

11-13-23 – Dr. Sara Burke featured in an article about mentorship in UF’s College of Medicine. <https://news.drgator.ufl.edu/2023/10/16/uf-college-of-medicine-mentorship-platform-connects-faculty/>

12-5-23 – Dr. Aprinda Indahlastari wins the CASC Coalition for Academic Scientific Computation’s image contest with an illustration depicting electrical current distributed across the brain during an experimental treatment aimed at improving cognitive health. <https://php.ufl.edu/2023/11/28/aprinda-indahlastaris-art-shines-in-annual-scientific-computation-image-contest/?fbclid=IwAR0j-OruYbTtqcs6Gavble8XmpF5vJ6jpLF1OqwCrlyXk4-92GlzSMvm7IQ>



Dr. Indahlastari’s winning illustration.



Cam social. A chance for center members to get out of the lab and enjoy each other’s company.