The Evelyn F. McKnight Brain Institute

Preserving memory, enhancing life

Annual Report

2022

Ronald M. Lazar, PhD, FAHA, FAAN
Professor of Neurology and Neurobiology
Evelyn F. McKnight Endowed Chair of Learning and Memory in Aging Director, UAB Evelyn F. McKnight Brain Institute
Director, Division of Neuropsychology (Neurology)
Department of Neurology

Kristina Visscher, PhD
Associate Professor of Neurobiology, Ophthalmology, Biomedical Engineering and Psychology
Associate Director, UAB Evelyn F. McKnight Brain Institute
Co-director, Civitan International Neuroimaging Laboratory
Department of Neurobiology

The University of Alabama at Birmingham Sparks Center – SC650K
1720 7th Avenue South Birmingham, Alabama 35294

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THE UNIVERSITY OF
ALABAMA AT BIRMINGHAM

January 9, 2023

Board of Trustees, The McKnight Brain Research Foundation

It is with great pleasure that we submit our 2022 Annual Report for the McKnight Brain Institute (MBI) at UAB.

UAB McKnight continues to emerge from the impact of the 2020 COVID-19 lockdown and 2021-2022 COVID-19 surges, with resumption of research and programmatic activities, as well as with initiation of new intra- and inter-institutional collaborations. We currently have extensive relationships across the UAB community, involving the UAB Heersink School of Medicine, Graduate School, College of Arts and Sciences, School of Engineering, School of Health Professions (SHP), School of Nursing, School of Public Health, Callahan Eye Hospital, School of Optometry, and Honors College. As a result of retirements and transitions to new institutions in the past year, we now have 46 affiliated faculty.

We continue to stress the importance of these alliances because we support the notion that innovation comes from multidisciplinary teams. Of importance, we are reconstituting the Intervention Core with the addition of Keith McGregor, PhD, a UAB SHP faculty member, who will be reaching out to the other MBIs to revitalize this critical core. We are also seeking new membership for the UAB McKnight enterprise among recently arrived faculty (particularly junior faculty), along with the newly recruited Director of the Division of Gerontology, Geriatrics, and Palliative Care. UAB is one of the most diverse research institutions in the United States, and therefore, UAB McKnight is dedicated to increasing the presence of underrepresented minorities (URMs), as both research investigators and research participants.

We remain firmly committed to aims and objectives related to age-related cognitive decline and memory loss with ongoing animal models but increased programmatic emphasis on human application, both with respect to demonstrations of proof-of-principle and clinical application. We continue to take the position initiated last year that the most effective means of mitigating cognitive and memory decline is through primary prevention. Our Brain Health Advocacy Mission (BHAM) now extends to four UAB primary healthcare clinics in our collaborations with Family and Community Medicine and General Internal Medicine. At each site, a brain health champion administers a Brain Care Score, establishes a risk factor and lifestyle profile, and implements a plan for gradual change, with patient follow-up for one year. There are several ongoing projects involving exercise and cognitive-training interventions, the REasons for GeogrAphic and Racial DifferenceS in Stroke (REGARDS) study continues to provide valuable insight into risk for cognitive decline, and there are pre-clinical models looking at the importance of the microbiome, diet, epigenetics, and the role of sex differences.

The grants in the appendix document awards that directly address McKnight goals or contribute methodologically, mechanistically, or technologically toward applications that will address McKnight objectives in the future.

We anticipate continuing within this overall framework in 2023.

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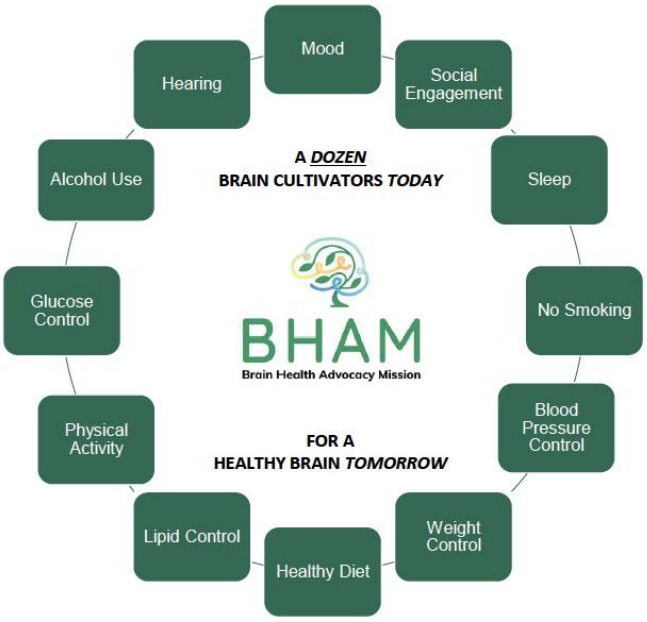
HEERSINK
SCHOOL OF MEDICINE
Department of Neurology
Ronald M. Lazar, PhD/ Evelyn F. McKnight Endowed Chair
Sparks Center – 650K | 1720 7th Avenue South | BIRMINGHAM AL 35294-0117
phone: 205.934.2334 | fax: 205.975.9034 | www.uab.edu/neurology

Institute FY22 at-a-Glance

- **Summary of Major Scientific, Programmatic, Outreach, or Training Achievements Since Last Year**.



Our most important initiative remains the UAB McKnight-funded **Brain Health Advocacy Mission (BHAM)**. Few therapeutic options are available to mitigate pathologically based memory and cognitive decline; thus, prevention is critical. With definitive evidence that a lifelong, proactive approach to risk factors and lifestyle management prevents later-life cognitive decline, a partnership with primary care represents an ideal mechanism for BHAM integration into our community. Therefore, we have established collaborations with UAB Department of Family and Community Medicine and UAB Division of General Internal Medicine in which we are implementing a phased-in process of brain care that, to our knowledge, represents the first program of its kind in the United States. The conceptual framework was derived from the American Heart Association (AHA)/American Stroke Association, which issued a 2017 Presidential Advisory on defining brain health, incorporating "Life's Simple 7" as a follow-up to an earlier statement on cardiovascular health promotion. The goal was to provide a model for defining brain health in highly quantifiable terms and to suggest specific therapeutic targets for preventive intervention that included risk factor management and lifestyle changes. In March 2021, the AHA published a Scientific Statement entitled, "A Primary Care Agenda for Brain Health," chaired by **Dr. Ronald Lazar,** amplifying "Life's Simple 7" strategy with the inclusion of alcohol consumption, social engagement, hearing, mood (depression), and education.

As a first step, we have an IRB-approved protocol to have advanced practice providers from UAB School of Nursing, under the supervision of **Pamela Bowen, PhD, CRNP, FNP-BC, BBA**, and **Roy Martin, PhD**, a neuropsychologist, serving as brain health advocates in three UAB Family Practice clinics in the Metro-Birmingham area, working with individual patients and family members for a one-year participation period. **Dr. Lazar** performs a similar role in the UAB Camellia Medical Group. As an outcome measure, we are using the McCance Brain Care Score (see below, collaborative programs with non-McKnight Institutes). With 100 participants to date, we have learned, at baseline, that our population (mean age of 45 years old) is at the high end of memory and cognitive risk, with 56% having hypertension, 17% having diabetes, and 63% considered obese. We have designed individualized programs for each participant, allowing them to choose their preferred targets at achievable starting points toward improving their brain health. We presented our first data at the 2022 meeting of the Society of Teachers of Family Medicine.

Funded by a pilot grant from the McKnight Brain Research Foundation (MBRF) (**Lazar, contact PI**), a collaboration was formed between **UAB McKnight, UAB Callahan Eye Hospital,**

UMiami McKnight, and UMiami Bascom-Palmer Eye Institute to study the effect of exercise on hypertension (HTN) in older men and women. It is well known that HTN is a major risk factor for cognitive decline, resulting from increased white matter hyperintensities and loss of microvascular density (rarefaction) in brain tissue. The premise is that exercise will increase growth factors (IGF-1), which will increase microvascular density, thereby reducing HTN and improve cognition. The innovative aspect of this project is the use of Optical Coherence Tomographic Angiography (OCT-A), a non-invasive tool to measure retinal vascular density. The study received IRB approval, a subaward agreement was executed, and the study is actively enrolling participants.

To date, there have been few prospective studies of incident silent brain infarction and cognitive trajectories. **UAB (Lazar, MPI)** and Stanford are collaborating on an NINDS-funded project to determine, in a nationwide study, whether apixaban or aspirin is more effective in reducing the number of these silent events, and in turn, result in better cognition. Silent infarction is a known risk factor for memory and cognitive decline; this project seeks to establish a primary prevention strategy to mitigate in those with known cardiac conditions. To date, 310 participants have been enrolled from 94 clinical sites around the United States, in the first known prospective study of this potentially preventable cause of memory and cognitive decline.

In an ongoing pilot grant from the MBRF, **UAB Drs. Abigail Hernandez (contact PI) and Thomas Buford** and **Drs. Jennifer Bizon and Sara Burke (UFlorida)** were funded for a project entitled, “Reuniting the Brain and Body to Understand Cognitive Aging: The Nexus of Geroscience and Neuroscience.” The project’s purpose is to study gut-brain interactions in the context of cognitive aging. Gut health influences cognitive outcomes, and alterations in brain health are often accompanied by impaired intestinal function. As gut health is likely a modifiable factor mediating cognitive resilience, several potential mechanisms of the bidirectional interactions across the gut-brain axis warrant further investigation. The goal of this study is to determine if novel therapeutic strategies targeting the gut can improve age-related cognitive decline in a validated rodent model of aging.

Dr. George Howard is the founding PI of the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study, a project originally designed to examine risk factors for incident stroke in a population-based study enriched for African American Blacks. REGARDS later generated important information relating to incident, age-related cognitive decline in the absence of frank neurological events, a focus led by **Dr. Virginia Wadley**. Since its inception in 2003 with the support of NINDS, this study has been following 30,239 participants, who are 45 years or older, living largely in the Stroke Belt across the Southeast United States and has generated more than 600 peer-reviewed papers, including more than 60 papers related to cognition. There is increasing evidence that vascular risk factors (brain health) are threats to both memory and cognitive decline and to stroke. In new work published in *Neurology*, data from REGARDS showed that the association between HTN and diabetes, traditionally among the more important risk factors for stroke, was found to be substantially less in older ages; whereas the impact of smoking, atrial fibrillation, and left ventricular hypertrophy did not decrease with age, suggesting that their relative importance in determining stroke risk likely increases with age. This finding may also pertain to age-related memory and cognitive decline, a hypothesis that will be tested.

There is also important pre-clinical work being conducted in the UAB McKnight enterprise. In a mouse-model, **Steven Austad, PhD**, UAB’s recent appointee to the Protective Life Endowed Chair in Healthy Aging Research, and colleagues are studying sex differences in the brain with

health and disease, often overlooked in experimental models. To delineate the contributions of genetic sex (XX v. XY) versus gonadal sex (ovaries v. testes) to the epigenomic regulation of hippocampal sex differences, they used the Four Core Genotypes (FCG) mouse model, which uncouples chromosomal and gonadal sex. Transcriptomic and epigenomic analyses of ~12-month-old FCG mouse hippocampus revealed genomic, context-specific regulatory effects of genotypic and gonadal sex on X- and autosome-encoded gene expression and DNA modification patterns. X-chromosomal epigenomic patterns, classically associated with X-inactivation, were established almost entirely by genotypic sex, independent of gonadal sex. Differences in X-chromosome methylation were primarily localized to gene regulatory regions including promoters, CpG islands, CTCF binding sites, and active/poised chromatin, with an inverse relationship between methylation and gene expression. Autosomal gene expression has demonstrated regulation by both genotypic and gonadal sex, particularly in immune processes. These data demonstrate an important regulatory role of sex chromosomes, independent of gonadal sex, on sex-biased hippocampal transcriptomic and epigenomic profiles.

Karen Gamble, PhD and her team are studying age-related cognitive decline and disruptions in circadian rhythms as growing problems related to the increase in average human life span. Multiple strains of the senescence-accelerated mouse (SAM) show reduced life span, and the SAMP8 strain, in particular, has been well documented to show cognitive deficits in behavior, as well as a bimodal pattern of circadian locomotor activity. However, little is known about circadian regulation within the hippocampus of these mouse strains. Her group tested the hypothesis that in this early senescence model, disruption of the molecular circadian clock in SAMP8 animals drives disrupted behavior and physiology. They found normal rhythms in PER2 protein expression in the suprachiasmatic nucleus 1 of SAMP8 animals at 4 months, despite the presence of disrupted wheel-running activity rhythms at this age. Her team also examined time-restricted feeding as a potential strategy to rescue disrupted hippocampal plasticity. Time-restricted feeding increased long-term potentiation at Schaffer collateral-CA1 synapses in SAMP8 mice (compared to SAMR1 controls). Overall, the Gamble group confirmed disrupted circadian locomotor rhythms in this early senescence model (as early as 4 months) and discovered that this disruption is not due to arrhythmic PER2 levels in the SCN; however, other extra-SCN circadian oscillators (i.e., hippocampus) are likely impaired with accelerated aging.

UAB is committed to diversifying the next generation of neuroscientists. **Dr. Farah Lubin** serves as Director and **Dr. Michelle Gray** as Co-Director, with 15 UAB McKnight faculty serving as mentors, of the Neuroscience Roadmap Scholars Program, supported by the National Institutes of Health (NINDS R25 NS089463), UAB Office of Diversity, Equity and Inclusion, and UAB Comprehensive Neuroscience Center. The Neuroscience Roadmap Scholars Program is designed to enhance and support the graduate experience and the scholars' respective graduate program(s) throughout the span of their PhD studies. This is accomplished through the implementation of bi-monthly lunch meetings, career coach mentoring, social and networking events, workshops, and more. In 2022, there were 27 Roadmap scholars.

- **The Most Important, Relevant Scientific Achievements of the Past Year**

Drs. Lazar and G. Howard, along with the other investigators in The Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis – Hemodynamics (CREST-H) trial for treatment of asymptomatic carotid artery disease, studied cortical thickness in 110 consecutively enrolled participants. Dynamic contrast susceptibility MR perfusion-weighted images were post-processed with quantitative perfusion maps using deconvolution of tissue and arterial signals. The protocol calculated the delay interval for blood to travel from the carotids to the cortical surface, also known as the time-to-peak (TTP) delay. Across the range of hemodynamic impairment, TTP delay independently predicted relative cortical thinning on the side of stenosis, adjusting for age, sex, hypertension, hemisphere, smoking history, LDL cholesterol, and pre-existing infarction (p=0.0032). This new finding explains our 2021 paper that showed among the first 1,000 patients in the parent CREST-2 study, there was significant decline in memory in the absence of a frank stroke event, accounting for what appears to be age-related cognitive changes. The CREST-H study will ultimately determine whether revascularization will improve memory when the stenosis is removed.

Dr. Kristina Visscher, the new Associate Director of UAB McKnight, and her PhD student (who is now Dr. Sara Nolin) were main drivers in the McKnight Brain Aging Research (MBAR) project, working on descriptions of behavior in this over 85-year-old cohort and examining how the architecture of the brain's connections predicts performance in this older age group. Dr. Visscher was the senior author on the first published paper from the MBAR project, in which the validity of the NIH toolbox cognitive battery, in the oldest-old cohort, was established (see Appendix 2 for citation). To discover new biomarkers for aging, she and her students have been studying the trajectory of eye movement changes, as people learn to use peripheral vision in simulated central vision loss conditions. Age-related macular degeneration is the most common cause of blindness in the developed world and is a major issue in older adult populations.

Co-Funded by a 2021 McKnight Intervention Core Pilot Award and an NIA grant, **Drs**. **Hernandez** and mentor, **Buford** explored rat model of declining health, gut dysbiosis, and cognitive impairments, hallmarks of advanced age. Published in *Nutrients*, their paper noted that while caloric restriction is known to robustly extend health span and alter gut microbiome composition, it is difficult to maintain. Time-restricted feeding or changes in dietary macronutrient composition could be feasible alternatives for enhancing late-life cognitive and physical health, thereby promoting compliance for extended time periods. To investigate this possibility, 8-month-old rats were placed on time-restricted feeding with a ketogenic or micronutrient- and calorically matched control diet for 13 months. A third group of rats was permitted to eat standard chow ad libitum during this time. At 22 months, all rats were tested on a biconditional association task and fecal samples were collected for microbiome composition analysis. Regardless of dietary composition, time-restricted-fed rats had better cognitive performance than ad libitum-fed rats. All baculum abundance was associated with cognitive task performance, indicating a link between gut health and cognitive outcomes in aged subjects. Overall, time restricted feeding had the largest influence on cognition performance in aged rats.

With funding from the NIA, **Michael Crowe, PhD** and colleagues examined whether pain is associated with subjective memory problems or cognition in Puerto Rican older adults. Participants came from the Puerto Rican Elderly Health Conditions (PREHCO) study, aged 60 and over (n = 2,144). Analyses assessed concurrent and longitudinal associations of pain with

subjective memory problems and cognition using a cognitive screener. Overall, participants with pain were more likely to report concurrent subjective memory problems than those without pain. Older adults with pain also exhibited slightly lower concurrent cognition. Novel pain was associated with cognitive decline and greater likelihood of incident subjective memory problems at follow-up. Persistent pain was only related to incident subjective memory problems at follow-up.

Collaborative Programs with McKnight Institutes and non-McKnight Institutes

Drs. Lazar (UAB) and Bonnie Levin (UMiami) are co-Chairs of the MBRF Cognitive Aging and Memory Intervention Core Inter-Institutional Pilot Program that is requesting Letters of Intent and Proposals for pilot studies to support interventions to reduce age-related memory loss and cognitive decline. The specific goal of these projects is to collect pilot data across two or more MBI sites to facilitate grant submissions to extramural funding sources for multi-MBI site cognitive aging and memory intervention trials.

Lazar, Ronald

McKnight Collaborations

Principal Investigator. Improving Age-Related Cognitive Decline with Exercise in Hypertensive Older Adults: A Pilot Study to Investigate A Retinal Microvascular Biomarker and the Role of IGF. McKnight Brain Research Foundation. 5/1/2021 – 4/30/2023. Collaborators: **UAB**--Lazar (PI), Buford, Girkin, Norling; **UMiami**--Wang (site-PI).

Non-McKnight Collaborations

Principal Investigator (MPI). ARCADIA CSI (Cognition and Silent Infarcts). National Institute of Neurological Disorders and Stroke (NINDS)/NIH. 4/1/2019 – 3/31/2024. Collaborators: **UAB**--Lazar (MPI), G Howard; **Stanford**—Lansberg (MPI), Wintermark; **Yale**—Sheth; **UWashington**—Tirschwell; **Cincinnati—**Broderick.

Co-Investigator. Genetic Contribution to Brain Arterial Dilatation and its Role in Cognition and Dementia. National Institute of Aging (NIA)/NIH. 7/1/2018 - 6/30/2023. Collaborator: **Columbia**—Gutierrez (PI).

Co-Investigator. AIDS and Aging Research. NIA/NIH. Collaborators: **UAB**—Austad (MPI), Saag, Willig, Porter, Thielen; **Rush**—Landay; **UWashington**—Crane (MPI), Lober, Delaney, Whitney; **Wake Forest**—Kritcvhevsky (MPI), High; **Beth Israel Lahey**—Bergeron.

A “Brain Care Score” To Predict Risk for Incident Cognitive Decline and Stroke. Collaborators: **UAB**--Lazar, G. Howard, V. Howard; **Harvard** (Mass General)—Rosand, Chemali, Westover, Sonni, Gutierrez-Martinez, Ouyang; **Yale**—Kernan.

Principal Investigator (MPI). Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Trial – Hemodynamics (CREST-H). NINDS/NIH. 7/1/2022 – 6/30/2027. Collaborators: **UAB**--G Howard; **Columbia**—Marshall (MPI); **UCLA**—Liebeskind (MPI); **Mayo/Jacksonville**—Meschia (MPI); **UWashington**—Tirschwell; **Yale**—Sheth**.**

Bolding, Mark

Director of the Neuroimaging Laboratory used by multiple McKnight members for their research.

Carter, Christy
Principal Investigator, Reuniting the Brain and Body to Understand Cognitive Aging: The Nexus of Geroscience and Neuroscience. McKnight Brain Institute Pilot - $50,000 (total). 5/2021--4/2022. This grant, supported by the MBRF, is a collaboration between UAB post-doc Abigail Hernandez and UFL MBI Sara Burke and Jennifer Bizon.

Howard, George
Dr. Ralph Sacco (UMiami MBI) is Chair of the DSMB for the REGARDS study, funded by NINDS.

Visscher, Kristina
McKnight Brain Aging Registry (MBAR) involves members from all 4 McKnight Institutes. Work is being done to analyze and publish data from a sample of healthy agers.

Working with Lesley Ross at Clemson University on a project funded by NIA/NICHD, examining the impact of speed of training on brain health and cognition for older adults.

Working with Aaron Seitz at University of California, Riverside and Nick Turk-Browne at Yale, on a study funded by NIH/NEI, examining the mechanisms of learning in adults with macular degeneration.

Honors, Awards, and New Grants

Lazar, Ronald
- Principal Investigator (MPI). Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Trial – Hemodynamics (CREST-H). NINDS/NIH. 7/1/2022 – 6/30/2027.
- Appointed to the AHA Stroke Council, Scientific Oversight Committee, Subcommittee on Brain Health.

Austad, Steven
- Principal Investigator. New Translational Rat Model for Evaluating Anti-aging Interventions. NIA/NIH, Board Of Trustees Of The University Of Oklahoma Health Sciences Center. 7/15/2022 – 6/30/2024.

Day, Jeremy
- Appointed Director of the UAB Comprehensive Neuroscience Center.
- Lab PhD student, Robert Phillips, named a 2022-2023 UAB Carmichael Scholar in recognition of his excellence in research.
- Lab postdoctoral fellow, Dr. Nathaniel Robinson, received the Whit Mallory Emerging Scholar Award from the UAB Civitan International Research Center.
- Lab postdoctoral fellow, Dr. Jen Tuscher, received a K99/R00 “Pathway to Independence” award from the National Institute of Mental Health.

Buford, Thomas
- Presentation on the impacts of antihypertensive drugs and exercise on late-life physical function at the NIA virtual workshop: Understanding heterogeneity of responses to, and optimizing clinical efficacy of, exercise training in older adults. 4/7-8/2022.
- Principal Investigator. Feasibility of High-Intensity Interval Training in Older Adults with HIV and Co-Occurring Hypertension. AIDS and Aging Research Platform (AARP). NIA/NIH. 2022-2024.

Dobrunz, Lynn
- Appointed Director of the newly established UAB Consortium for Neuroengineering and Brain-Computer Interface Initiative.

Gamble, Karen
- Appointed to the Tate Jordan Thomas Professorship in Psychiatric Medicine.

Howard, Virginia
- Co-authored a paper entitled, “Race-Dependent Association of High-Density Lipoprotein Cholesterol Levels With Incident Coronary Artery Disease,” that appeared in the November 2022 issue of the *Journal of the American College of Cardiology* and has achieved a Altmetric Score of 1252, ranking it in the top 5% of all scored research outputs (>22 million).

Edwards, Lloyd
- Principal Investigator. CREST-2 Statistical and Data Coordinating Center - (SDCC). NINDS/NIH. 9/1/2022 – 8/31/2026.

Kennedy, Richard

- Recipient of the 2022 Outstanding Academic Mentor and Outstanding Site Mentor award by the Albert Schweitzer Fellowship of Alabama.

Parpura, Vladimir

- Ranked second in the world in astrocyte expertise based on his research in the subdiscipline over the past 10 years and from an analysis of the PubMed database.

Roberson, Erik

- Named Vice-Chair for Basic and Translational Research in the UAB Department of Neurology.

Standaert, David

- Principal Investigator. UAB Research Education Program for Residents and Fellow in Neuroscience. R25, NINDS/NIH. 8/15/2022 – 6/30/2025.
- Presented with the Parkinson Association of Alabama Lifetime Achievement Award.

Thyme, Summer

- Recipient of the Director's New Innovator Award from the National Institutes of Health. The award is part of the NIH High-Risk, High Reward Research Program, supported by the Common Fund.

Visscher, Kristina

- Principle Investigator. New Methods to Quantify and Train Eye Movement Strategies in Macular Degeneration. NIH, University of California, Riverside. 2/02/2022 – 1/31/2024.

Wheeler, Pariya Fazeli

- Principal Investigator. Neurocognitive Trajectories in Older Adults with COVID-19 in the Deep South, awarded by National Academy of Neuropsychology. 2022-2023.
- Principal Investigator. Evaluation of Neurobiological Mechanisms Mediating the Effect of Immune Activation on Neurocognitive Impairment and the Role of Psychosocial Factors Among Women Living with HIV. National Institutes of Mental Health/ NIH. 9/13/2022-6/30/2027.

Technology Transfer (Patents/applications; Revenue generated from technology)

None

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

No

Do you recommend any modification to the Purpose or mandates in the Gift Agreement?

No

Did all activities during the report period further the Purpose?

Yes

Additional Comments

(items that are not covered elsewhere in the report, including any negative events, loss of full-time employees (FTEs), impending departures, space, or budget that could have an impact on carrying out the Gift Agreement.)
None

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Director, Division of Neuropsychology (Neurology)
Department of Neurology

Appendix 1 – McKnight Faculty List

List of McKnight Affiliate Faculty and their area of focus, and Department Affiliations, including a list of post-doctoral and pre-doctoral trainees involved only in the aims related to cognitive decline and memory loss, and contribute methodologically, mechanistically, or technologically toward applications that address McKnight objectives in the future.

McKnight Affiliate Faculty 2022			
Faculty	Area of Focus	Dept Affiliation	Post-Doctoral and Pre-Doctoral Trainees
Lazar, Ronald M	Cognitive Resilience and Recovery in Aging, Brain Health, Cerebral hemodynamics, Neurovascular Disease	Neurology	Pre-Doc Amani Norling, MS (Exercise) Randall Walden (Imaging) Terina Myers (Exercise) Undergrad Mary Faulkner (Heart Failure) Trevor Starling (Brain Health) Angela Ly (Exercise) Gitanjali Alapati (Exercise) Rashmi Nakkina (Brain Health)
Allendorfer, Jane jallendorfer@uabmc.edu	Exercise and epilepsy	Neurology	Pre-Doc Brandon Mitchell (Imaging & Memory)
Amara, Amy Willis aamara@uabmc.edu	Sleep disorders, movement disorders	Neurology	
Arrant, Andrew andrewarrant@uabmc.edu	Frontotemporal dementia	Neurology	
Asif, Irfan iasif@uab.edu	Primary care	Family and Community Medicine	
Austad, Steven N austad@uab.edu	Molecular and organismal biology of aging	Biology	
Ball, Karlene K kball@uab.edu	Aging-related cognitive function	Psychology	
Benveniste, Etty tika@uab.edu Emeritus	Immune/nervous system interactions	Cell, Developmental and Integrative Biology	
Bolding, Mark mark.bolding@gmail.com	Visual cognition, MRI, neuroimaging	Radiology	
Bowen, Pamela pbowen@uab.edu	Exercise and physical activity	Nursing	
Bradley, Virginia Wadley vwadley@uab.edu Emeritus	Mild cognitive impairment, comorbid cerebrovascular disease	Gerontology, Geriatrics, and Palliative Care	
Brenner, Michael michaelb@uab.edu Emeritus	Glial Cell Biology, Alexander Disease	Neurobiology	
Buford, Thomas twbuford@uab.edu	Exercise and aging	Center for Exercise Medicine	Post-Doc Abigail Hernandez (Diet) Undergrad Mercy Enogela (Exercise) Liliana Baptista (Exercise)
Carter, Christy cartercs@uabmc.edu	Exercise medicine	Gerontology, Geriatrics, and Palliative Care	Post-Doc Abigail Hernandez

Crowe, Michael mgcrowe@uab.edu	Gerontology, Cognitive Aging and Dementia	Psychology	Pre-Doc Cheyanne Barba (Disparities in Aging) Erin Ballard (Disparities in Aging)
Day, Jeremy jjday@uab.edu	Epigenetic mechanisms in memory formation	Neurobiology	Post-Doc Jen Tuscher (Memory) Nathanial Robinson (Memory) Saakshi Thukral (Memory)
Del Bene, Victor vdelbene@uab.edu	Cognitive impairment, dystonia, deep brain stimulation	Neurology	
DeMiranda, Briana brianademiranda@uabmc.edu	Environmental toxicants	Neurology	
Dobrunz, Lynn dobrunz@uab.edu	Regulation of short-term synaptic plasticity in the hippocampus	Neurobiology	
Edwards, Lloyd J ljedward@uab.edu	Longitudinal data analysis, health disparities	Biostatistics	
Fazeli Wheeler, Pariya plfazeli@uab.edu	Cognitive aging, gerontology	Nursing	Pre-Doc Shakaye Haase (Aging) Jeremy Delgadillo (Aging) Alexis Long (Aging)
Gamble, Karen karengamble@uabmc.edu	Environmental modulation of circadian clock function in mammalian system	Psychiatry and Behavioral Neurobiology	Post-Doc Paola Fernandes (Circadian Rhythms) Pre-Doc Jennifer Davis (Circadian Rhythms) Ananya Swaroop (Circadian Rhythms) Lacy Goode (Diet)
Gamlin, Paul pgamlin@uab.edu	Cell biology and systems neuroscience of vision and visual disorders	Ophthalmology	Post-Doc Michael McFerrin (Vision)
Gavin, Cristin cfgavin@uab.edu	Cellular and molecular mechanisms of structural and functional plasticity	Neurobiology	
Geldmacher, David dgeldmacher@uabmc.edu	Aging-related memory disorders and visual cognition	Neurology	
Gerstenecker, Adam atgers@uab.edu	Functional activity, decisional capacity, cognitive impairment dementia	Neurology	Pre-Doc Sarah Whiten (Decisional Capacity)
Goldberg, Matthew S mattgoldberg@uabmc.edu	Mechanisms of neurodegeneration	Neurology	
Gray, Michelle mccgray@uab.edu	Neurogenetics, glial function, Huntington's disease	Neurology	
Gross Gutierrez, Alecia K agross@uab.edu	Signal transduction mechanisms in the CNS	Neurobiology	Post-Doc Mary Anne Garner (CNS Signaling) Meredith Hubbard (CNS Signaling) Pre-Doc Hailey Levi (CNS Signaling) Undergrad Seth Hubbard (CNS Signaling) Anushree Gade (CNS Signaling)
Herskowitz, Jeremy H jeremyherskowitz@uabmc.edu	Amyloid beta effects on neurons	Neurology	
Howard, George ghoward@uab.edu	Stroke and aging	Biostatistics	

Howard, Virginia vjhoward@uab.edu	Cardiovascular disease, stroke and aging	Epidemiology	
Kennedy, Richard E rekenned@uab.edu	Aging	Gerontology, Geriatrics, and Palliative	
Knight, David C knightdc@uab.edu	Human imaging approach to investigating memory	Psychology	
Lahti, Adrienne alahti@uab.edu	Neuroimaging	Psychiatry and Behavioral Neurobiology	
Landefeld, Seth sethlandefeld@uab.edu	Geriatrics and Health Care Research	Medicine	
Lester, Robin A J nicotine@uab.edu	Nicotinic receptors in CNS function	Neurobiology	
Lokken, Kristine	Clinical psychology, neuropsychology	Psychiatry and Behavioral Neurobiology	
Lubin, Farah flubin@uab.edu	Signal transduction mechanisms in memory and memory disorders	Neurobiology	Post-Doc Ashleigh Irwin (Epigenetics) Rubhab Bahabry (Epigenetics) Pre-Doc Silvienne Stint Jago (Epigenetics)
Marson, Daniel C dmarson@uabmc.edu Emeritus	Neuropsychology	Neurology	
Martin, Roy rmartin@uab.edu	Neuropsychology	Neurology	Undergrad Rashmi Nakkina (Delirium)
Meador-Woodruff, Jim jimmw@uab.edu	Cellular alterations of neural circuitry and molecular expression in psych	Psychiatry and Behavioral Neurobiology	
Nakazawa, Kazutoshi nakazawk@uab.edu	Epigenetics and cognition	Psychiatry and Behavioral Neurobiology	
Parpura, Vladimir vlad@uab.edu	Imaging approaches to investigating synaptic and glial cell function	Neurobiology	
Powell, Craig M craigpow@uab.edu	Cognitive dysfunction	Neurobiology	
Pozzo-Miller, Lucas lucaspm@uab.edu	Mechanisms controlling dendritic spine morphology	Neurobiology	
Roberson, Erik eroberson@uabmc.edu	Age-related neurodegenerative disorders	Neurology	
Saag, Michael msaag@uabmc.edu	Infectious diseases, Blood equality, Hepatitis, Antiretroviral	Infectious Diseases	
Standaert, David dstandaert@uab.edu	Aging, Neurodegeneration, Translational Neuroscience	Neurology	
Theibert, Anne theibert@uab.edu	PI-3 Kinase signal transduction in neuronal cell biology	Neurobiology	
Thyme, Summer B sthyme@uab.edu	Neuropsychiatric and neurodevelopmental disorders	Neurobiology	
Ubogu, Eroboghene ubogu@uab.edu	Inflammatory neuropathies	Neurology	

Visscher, Kristina M kmv@uab.edu	Human imaging approaches to investigating memory	Neurobiology	Post-Doc Pinar Demirayak (Vision and Aging) Leland Fleming (Vision and Aging) Matt Defenderfer (Vision and Aging) Pre-doc Sara Sims (Vision and Aging) Jason Vice (Vision and Aging)
Wadiche, Jacques jwadiche@uab.edu	Synaptic plasticity and function in the cerebellum	Neurobiology	
Wadiche, Linda lwadiche@uab.edu	Adult neurogenesis in the dentate gyrus	Neurobiology	
Wilson, Scott livvy01@uab.edu	Ubiquitin/proteasome system in neuronal function	Neurobiology	

Appendix 2 – Top 20 Publications

Top 20 publications for FY22 relevant to the MBRF.

Bell TR, Pope CN, Downer B, Barba C, Crowe M. Pain associates with subjective memory problems and cognition in older Puerto Rican adults. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn.* 2022 Nov;29(6):989-99. PMID: 34187312; PMCID: PMC8716642 (available on 2023-11-01).

Boison D, Masino SA, Lubin FD, Guo K, Lusardi T, Sanchez R, Ruskin DN, Ohm J, Geiger JD, Hur J. The impact of methodology on the reproducibility and rigor of DNA methylation data. *Sci Rep*. 2022 Jan 10;12(1):380. PMID: 3501347; PMCID: PMC87487000.

Bowen PG, Affuso O, Opoku-Agyeman W, Mixon VR, Clay OJ. Texting Older Sisters to Step to Manage Obesity in Older Black Women: A Feasibility Study. *Am J Prev Med*. 2022 Jul;63(1 Suppl 1):S56-S66. doi: 10.1016/j.amepre.2022.03.014. PMID: 35725141.

Davis JA, Paul JR, Mokashi MV, Yates SA, Mount DJ, Munir HA, Goode LK, Young ME, Allison DB, Gamble KL. (2022). Circadian disruption of hippocampus in an early senescence male mouse model. *Pharmacol Biochem Behav*. 2022 Jun;217:173388. PMID: 35447158; PMCID: PMC9422145.

Enogela EM, Buchanan T, Carter CS, Elk R, Gazaway SB, Goodin BR, Jackson EA, Jones R, Kennedy RE, Perez-Costas E, Zubkoff L, Zumbro EL, Markland AD, Buford TW. Preserving independence among under-resourced older adults in the Southeastern United States: existing barriers and potential strategies for research. *Int J Equity Health*. 2022 Aug 27;21(1):119. PMID: 36030252; PMCID: PMC9419141.

Fazeli PL, Hopkins C, Vance DE, Wadley V, Li P, Turan B, Bowen PG, Clay OJ. Rationale and protocol for a pilot randomized controlled trial of a cognitive prescription intervention for reducing dementia risk factors among African Americans. *Nursing (Auckl).* 2022;12:1-15. PMID: 35079596; PMCID: PMC8783962.

Hansen B, Allendorfer JB. Considering social determinants of health in the relationship between physical activity and exercise engagement and cognitive impairment among persons with epilepsy. *Front Rehabil Sci.* 2022 Jul 26;3:923856. PMID: 36188918; PMCID: PMC9397670.

Hernandez AR, Watson C, Federico QP, Fletcher R, Brotgandel A, Buford TW, Carter CS, Burke SN. Twelve Months of Time-Restricted Feeding Improves Cognition and Alters Microbiome Composition Independent of Macronutrient Composition. *Nutrients*. 2022 Sep 24;14(19):3977. PMID: 36235630; PMCID: PMC9572159.

Hooker SP, Diaz KM, Blair SN, Colabianchi N, Hutto B, McDonnell MN, Vena JE, Howard VJ. Association of Accelerometer-Measured Sedentary Time and Physical Activity With Risk of Stroke Among US Adults. *JAMA Netw Open*. 2022 Jun 1;5(6):e2215385. PMID: 35657625; PMCID: PMC9166254.

Howard G, Banach M, Kissela B, Cushman M, Muntner P, Judd SE, Howard VJ. Age-Related Differences in the Role of Risk Factors for Ischemic Stroke. *Neurology.* 2022 (in press).

Goode LK, Fusilier AR, Remiszewski N, Reeves JM, Abiraman K, Defenderfer M, Paul JR, McMahon LL, Gamble KL. Examination of diurnal variation and sex differences in hippocampal neurophysiology and spatial memory. *eNeuro.* 15;9(6):ENEURO.0124-22.2022. PMID: 36265903; PMCID: PMC9668349.

Marshall RS, Liebeskind DS, Huston III J, Edward LJ, Howard G., Meschia JF, Brott TG, Heck D, Lanzino G, Sangha N, Kashyap VS, Morales CD, Cotton-Samuel D, Rivera AM, Brickman AM, Lazar RM. Cortical Thinning in High-grade Asymptomatic Carotid Stenosis. *Journal of Stroke*. 2022 (in press).

Martin RC, Gerstenecker A, Hebert K, Triebel K, Marson DC. Assessment of Testamentary Capacity in Older Adults: Description and Initial Validation of a Standardized Interview Instrument. *Arch Clin Neuropsychol*. 2022 Aug 23;37(6):1133-1147. PMID: 35596954; PMCID: PMC9396451 (available on 2023-05-22).

McDonough IM, Nolin SA, Visscher KM. 25 years of neurocognitive aging theories: What have we learned? *Front Aging Neurosci*. 2022 Sep 23;14:1002096. PMID: 36212035; PMCID: PMC9539801.

Nolin SA, Cowart H, Merritt S, McInerney K, Bharadwaj PK, Franchetti MK, Raichlen DA, Jessup CJ, Hishaw GA, Van Etten EJ, Trouard TP, Geldmacher DS, Wadley VG, Porges ES, Woods AJ, Cohen RA, Levin BE, Rundek T, Alexander GE, Visscher KM. Validity of the NIH toolbox cognitive battery in a healthy oldest-old 85+ sample. *J Int Neuropsychol Soc.* 2022 Oct 14;1-10. doi: 10.1017/S1355617722000443. Online ahead of print. PMID: 36239453.

Ocañas SR, Ansere VA, Tooley KB, Hadad N, Chucair-Elliott AJ, Stanford DR, Rice S, Wronowski B, Pham KD, Hoffman JM, Austad SN, Stout MB, Freeman WM. Differential regulation of mouse hippocampal gene expression sex differences by chromosomal content and gonadal sex. *Mol Neurobiol.* 2022 Aug;59(8):4669-4702. PMID: 35589920; PMCID: PMC9119800.

Peper KM, Guo B, Leann Long D, Howard G, Carson AP, Howard VJ, Judd SE, Zakai NA, Cherrington A, Cushman M, Plante TB. C-reactive Protein and Racial Differences in Type 2 Diabetes Incidence: The REGARDS Study. Hypertension. 2022 Jan;79(1):196-206. doi: 10.1161/HYPERTENSIONAHA.120.15196. Epub 2021 Nov 17.PMID: 34784734.

Steinberg N, Parisi JM, Feger DM, Clay OJ, Willis SL, Ball KK, Marsiske M, Harrell ER, Sisco SM, Rebok GW. Rural-Urban Differences in Cognition: Findings From the Advanced Cognitive Training for Independent and Vital Elderly Trial. *J Aging Health*. 2022 May 23;8982643221102718. doi: 10.1177/08982643221102718. PMID: 35604034.

Vance DE, Del Bene VA, Kamath V, Frank JS, Billings R, Cho DY, Byun JY, Jacob A, Anderson JN, Visscher K, Triebel K, Martin KM, Li W, Puga F, Fazeli PL. Does olfactory training improve brain function and cognition? A systematic review. *Neuropsychology Review*. 2022 (in press).

Yacoubian TA., Fang Y-H, Gerstenecker A, Amara A, Stover N, Ruffrage L, Collette C, Kennedy R, Zhang Y, Hong H, Qin H, McConathy J, Benveniste EN, Standaert DG. Brain and systemic inflammation in de novo Parkinson's disease. *medRxiv*. 2022.09.21.22280194; doi:https://doi.org/10.1101/2022.09.21.22280194.

Appendix 3 – Top 10 Presentations

Top 10 presentations at scientific or public meetings relevant to the MBRF.

Annual UAB McKnight Lecture (2/3/2022)
Olajide Williams, MD, MS, Professor and Chief of Staff, Department of Neurology, Columbia University Vagelas College of Physician & Surgeons.
“Racism and Stroke Disparities: Centering the Margin”
Link: Dr. Olajide Williams - "Racism and Stroke Disparities.."

Austad S. “Sex differences in aging and disease: a role for transposable elements?” FASEB Scientific Research Conference on The Mobile DNA Conference: Evolution, Diversity, and Impact. Malahide, Ireland. July 2022.

Bowen PG, Delaney E, Boyd F, Shedlarski A, Lane JB, Starling TR, Asif I, Lazar RM, Davuluri S. Brain Health Advocacy Mission (BHAM). Society of Teachers of Family Medicine, Conference on Practice and Quality Improvement. Savannah, GA. September 2022

Baptista LC, Graham ZA, Hernandez AR, Carter CS, Buford TW. “Impact of a genetically modified Lactobacillus paracasei probiotic designed to express Angiotensin 1(-7) combined with exercise training in an aging male rat model: evidence for altered neuro-remodeling and inflammatory gene expression.” 15th Symposium of the International Society of Exercise and Immunology. Tucson, AZ. 10/24-27/2022.

Browning W, Atkins G, Bowen PG, Crowe M, Dreer L, Ruggiano N, Clay O. **“**Adverse Social Experiences, Social Support, and Health Outcomes Among Black and White Caregivers.” Gerontological Society of America, 2022 Embracing Our Diversity, Enriching Our Discovery, Reimagining Aging. November 2022.

Gamble KL. “Dysregulated Physiology in the Brain: It’s a Matter of Time.” Experimental Biology, American Physiological Society Presidential Symposium. Philadelphia, PA. March 2022.

Howard VJ. “Seeking factors contributing to disparities in stroke mortality and cognitive function: The REasons for Geographic and Racial Differences in Stroke (REGARDS) Study.” Boston University Clinical Neuroscience Grand Rounds. November 15, 2022.

Lazar RM, Lansberg MG, Howard G, Sheth K, Tirschwell DL, Wintermark M, Harris T, Myers T, Kemp SM, Cassarly C, Elkind M, Kamel H. Arcadia CSI (Cognition And Silent Infarcts). International Stroke Conference. New Orleans, LA. February 2022.

Lazar RM. “A Brain Health Agenda for Primary Care.” Rutgers, The State University of New Jersey, Neurology Grand Rounds. Newark, NJ. 7/8/2022

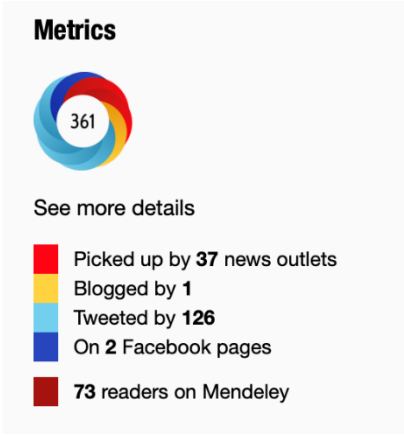
Lubin F. Presentation at the Diversity Symposium focused on Immunology and Neuroscience, University of Virginia School of Medicine. Charlottesville, VA. 6/30/2022.

Appendix 4 – Highlights of website, media, and social media

Highlights of website development, media coverage, and/or social media audience development.

- The UAB McKnight website, updated regularly, received 5,012 hits in FY2022.

- Dr. Lazar's paper, "A Primary Care Agenda for Brain Health," first published online in March 2021, resulted in the following 2022 Altmetric Attention Scores and prominence:
    - In the top 5% of all research outputs scored by Altmetric High Attention Score compared to outputs of the same age (99th percentile).
    - High Attention Score compared to outputs of the same age and source (99th percentile).



- Lazar R. Brain Health Program can Help Prevent Dementia. Birmingham Medical News, 8/2022.

- Gamble K. How does daylight saving time affect health? Brain & Life, October/November 2022.

- Austad S. Interview in Washington Post: "Turning 80, faces renewed age questions as he weighs reelection." 11/11/2022.

- Parpura V. News: Heersink School of Medicine. "Parpura ranked second in the world in astrocyte expertise; leads the way for gliotransmission research in the Central Nervous System." 8/17/2022.

- Allendorfer J. UAB Studies Whether Exercise Can Boost Epileptics Memory. Birmingham Medical News, May 2022.

- Lubin F. lncRNA Mediated Epigenetic Mechanisms in Memory Formation and Age-Related Memory Deficits. Recommended Readings, The Rockefeller University, The Markus Library News. 10/14/2022.

Appendix 6 – New Faculty CVs

No New Faculty in 2022