

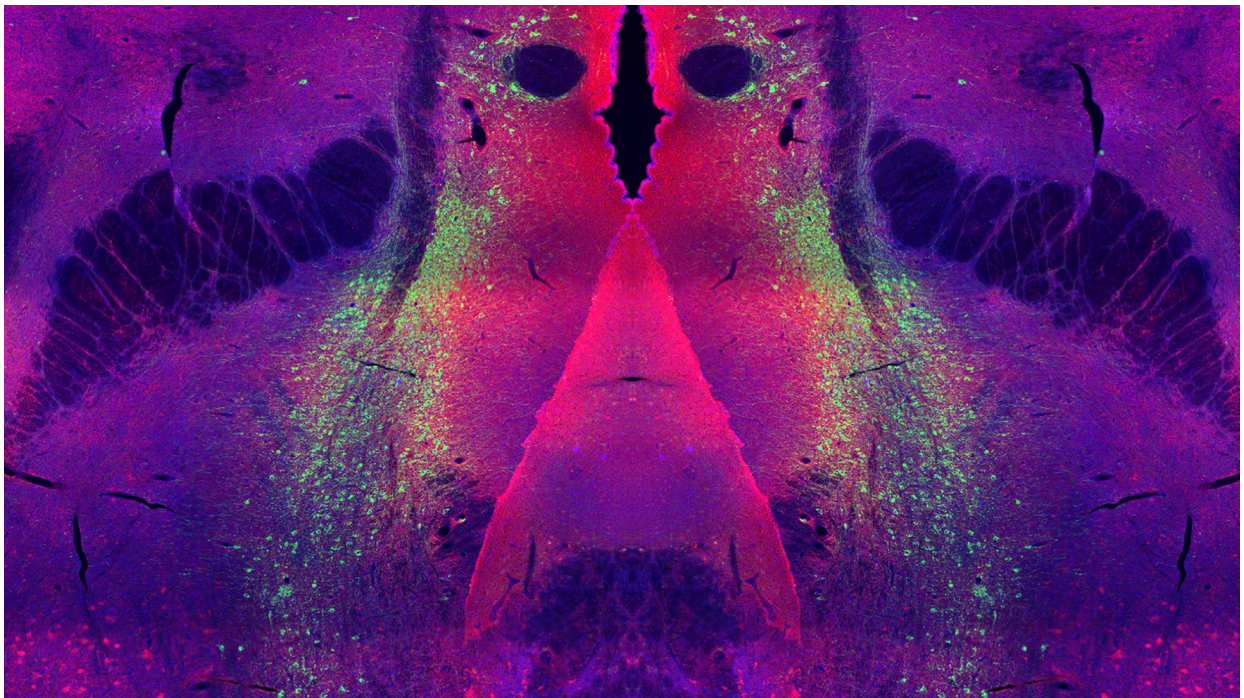


THE UNIVERSITY
OF ARIZONA

Evelyn F. McKnight Brain Institute

Full Lives Through Healthy Minds

Annual Report 2022



January 20, 2023

Trustees
The McKnight Brain Research Foundation
P.O. Box 620005
Orlando, FL 328962

Dear McKnight Brain Research Foundation Trustees,

The focus of the Tucson Evelyn F. McKnight Brain Institute (EMBI) is to promote longer and fuller cognitive lives for all. Our mission remains the same as it was when we were founded in 2006 – to discover the mysteries of the normally aging brain to achieve a lifetime of brain and cognitive health.

The challenges that arose from the pandemic in 2020 and 2021 receded somewhat in 2022, and the ‘restart’ towards more normal functioning in the personal and academic lives of the EMBI affiliate faculty was evident in the past year. This was particularly palpable in the 13th Annual McKnight Brain Research Foundation Inter-Institutional meeting held in Tucson March 23-25, 2022. There was almost a ‘giddy’ excitement at being able to be “together again” to discuss ideas, brainstorm new directions, and get caught up on recent discoveries. The theme of this 13th meeting was “*Power of Precision Aging Approaches to Brain Health and Cognition*”. In attendance were 6 MBRF Trustees, 2 MBRF staff, 17 individuals from the Birmingham EMBI, 19 from the Miami EMBI, 19 from the Gainesville EMBI, and 25 Affiliates and 7 staff from the Arizona EMBI. One aspect of the meeting that, at this moment in time, I particularly treasure is the fact that Ralph Sacco was determined not to miss this gathering in Tucson, even though he had recently undergone surgery. He was a remarkable individual – brilliant and kind, and all of the McKnight Institute family grieve his loss.

This meeting highlighted the importance of considering diverse populations in aging research made possible by novel approaches to recruitment and retention that we are exploring in the Precision Aging Network grant, and that our two keynote speakers epitomize in their research efforts. In her keynote lecture, Dr. Lisa Barnes gave multiple examples of how cognitive profiles are clearly different in aging African Americans when compared to the largely white populations studied in most experiments on aging – emphasizing the importance of expanding our studies to a more diverse group of individuals to increase our ability to sustain cognitive health in all individuals. Dr. Emily Rogalski highlighted another ‘special population’ in her keynote presentation – those individuals over 85 who have a specific kind of episodic memory that is as good as individuals 20 to 30 years younger – the so-called “SuperAgers”. These individuals are very rare, but the group at Northwestern University has pioneered efforts to find and study them so that clues to resilient and successful aging may be discovered. I have been invited to be on the External Scientific Advisory Board for a U19 grant on SuperAgers that was recently funded, that extends the recruitment of these individuals

to 5 sites, so that this population can be expanded. I look forward to sharing what I learn from their studies with the other McKnight Institution Affiliates.

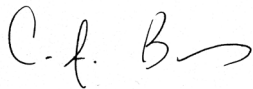
I count the 13th Inter-Institutional meeting as one of the highlights of 2022. Another highlight of the year with respect to McKnight Inter-Institutional collaborations, is the fact that Sara Burke and Carol Barnes finished their comprehensive review of “Aging” for the *Hippocampus Book* this past year, an effort that spanned a 4-year period. Oxford University Press hopes to have the final book available at the next Society for Neuroscience meeting, which will take place in Washington, DC in November. Another collaboration between McKnight Institute Affiliates resulted in the successful award of an NIH grant to Robert Wilson and Nathalie Ebner – an interaction that began at one of the McKnight Inter-Institutional meetings. Additionally, I participated with Yaakov Stern (PI) and the Executive Committee of the grant entitled “Collaboratory on Research Definitions for Cognitive Reserve and Resilience to Alzheimer’s Disease” to prepare a final white paper that arose from this project – “A framework for concepts of reserve and resilience in aging” - that will be published in the *Neurobiology of Aging* early this year. This was the culmination of 3 years of workshops and discussion with thought leaders in the field, and the NIA Program staff who wrote the RFA for this grant (Molly Wagster and Jonathan King) were very pleased with our progress, and have written an introductory commentary to this effort for the volume.

Additionally, the Director of the Tucson EMBI was awarded a competitive renewal of the NIA Training Grant entitled the “*Neurobiology of Aging and Alzheimer’s Disease*” in 2022, and another new RO1 grant entitled “*Frontal and Temporal Lobe Interactions in Rat Models of Normative Aging and Alzheimer’s Disease*” was given an outstanding priority score and will be discussed by NIA Council this January, and is likely to be funded this year. These two grants, in addition to the 2 RO1 grants and the Precision Aging Network U19 grant that were awarded in 2021, round out the Tucson Director’s portfolio, and assure a steady funding stream directed towards research on brain aging and cognition, and postdoctoral training in this area for the next 5 years. The McKnight Brain Research Foundation has significantly contributed to stabilizing resources for the Tucson EMBI, which enables collection of preliminary data for the successful acquisition of NIH awards, for which I am extremely grateful. As can be seen in **Section 4** (Institute FY22 at a Glance), **Section 13** (Top 20 publications from FY22 relevant to the MBRF), and **Section 6** (honors and awards, new grants), the Tucson EMBI Affiliates continue to be extremely productive.

One comment on the U19 grant – “*Precision Aging Network: Closing the Gap Between Cognitive Healthspan and Human Lifespan*” – we finished Year 1 of the grant September 2022. Our Program Officers Molly Wagster and Dana Plude, and Project Scientists Jonathan King and Jennie Larkin were extremely pleased with our progress setting up this very complex and large effort, and we are beginning our second year on strong footing. The Precision Aging Network group is finishing up manuscripts together, and we look forward to a number of publications emanating from this work in 2023.

My plans for the upcoming year revolve around implementing the experiments proposed in my funded grants, and preparing manuscripts from the data collected. The Tucson EMBI Affiliates look forward to the upcoming 14th Inter-Institutional meeting in Birmingham and the McKnight poster session at the Society for Neuroscience that will be held again in Washington DC in 2023, which will provide more opportunity to coordinate data collection among us. We are also committed to continuing community outreach activities at which we publicize both the Tucson EMBI and the Precision Aging Network grant efforts towards understanding the aging process and optimizing cognitive health for all individuals.

Respectfully signed January 20, 2023,



Regents Professor Psychology, Neurology and Neuroscience
Evelyn F. McKnight Chair for Learning and Memory in Aging
Director, Evelyn F. McKnight Brain Institute
University of Arizona

4. FY 2022 at a Glance

Summary of Major Scientific, Programmatic, Outreach or Training Achievements

I review here the findings reported in half of the publications listed in Appendix 2, and bold authors that are Affiliate faculty.

Crown, Gray, Schimanski, **Barnes** and **Cowen (2022)**

Hippocampal oscillations and place cell activity are sensitive to sensorimotor input generated from active locomotion, yet studies of aged rodent hippocampal function often do not account for this. By considering locomotion and spatial location, we identify novel age-associated differences in the scaling of oscillatory activity with speed, spike-field coherence, spatial information content, and within-field firing rates of CA1 place cells. These results indicate that age has an impact on the relationship between locomotion and hippocampal oscillatory activity, perhaps indicative of alterations to afferent input. These data also support the hypothesis that aged hippocampal place cells, compared with young, may more often represent more general spatial information. These results may explain the observation that older adults tend to recall the gist of an experience rather than the details.

Glisky, Woolverton, McVeigh and **Grilli (2022)**

Episodic memory and executive functions are two cognitive domains that have been extensively studied in older adults, and have been shown to decline in normative aging. The strongest design to study the effect of aging cognition is a longitudinal approach, where an individual's cognitive performance is followed over time, so that "true age changes" can be separated from "cohort effects" (a factor that can contaminate cross-sectional studies). One potential drawback of longitudinal designs, however, is the potential confound of practice effects across the different testing sessions. In this study, 166 participants from the Glisky longitudinal cohort were examined with ages ranging from 65 to 91 years, and a minimum of 3 longitudinal tests. Interestingly, retest effects were only found for the "memory domain", not for the "executive functions domain". But when these practice effects were removed from the data, there still remained significant declines over time in both of these cognitive domains. Additionally, people with higher IQs showed slower age-related declines in memory, but no advantages in executive function.

Gray, Khattab, Meltzer, McDermott, Scwyhart, Hartig and **Barnes (2022)**

Synapse loss and altered plasticity of synapses are significant contributors to memory loss in aged individuals. A major question in the field of the neuroscience aging is what mechanisms exist in the brain that help 'protect synapses'. If these could be discovered, then perhaps we would gain insights into therapeutic approaches to optimize brain and cognitive health as we age. The rhesus macaque is an ideal animal model for examining the relationships between neuroanatomical properties and age associated cognitive decline, since humans and macaques share numerous homologous brain structures involved in memory function. The primary findings were that elevated microglia activity appears to regulate perineuronal net structures that are involved in regulating synapse function. Older animals with fewer perineuronal nets around synapses displayed slower learning and poorer performance on an object recognition task, implicating them in the maintenance of synapse function across age, and pointing to a potential therapeutic target for synapse health.

Harootonian, Ekstrom and Wilson (2022)

Successful navigation requires the ability to compute one's location and heading from incoming multisensory information. Previous work has shown that this multisensory input comes in two forms: body-based idiothetic cues, from one's own rotations and translations, and visual allothetic cues from the environment. How these two streams of information are integrated is unclear. In this paper they investigated the integration of body-based idiothetic and visual allothetic cues in the computation of heading, using virtual reality experimental methods. By modeling this behavior, they were able to determine that almost all participants used a strategy in which idiothetic and allothetic cues are combined when the mismatch between them is small, but that these strategies compete when the mismatch is large. The next step in this research is to examine the extent to which older adults use such hybrid strategies in solving navigation problems.

Matijevic, Andrews-Hanna, Wank, Ryan and Grilli (2022)

The ability to generate episodic details while recollecting autobiographical events are believed to depend on a collection of brain regions critical for memory. How age-related differences in episodic detail generation relate to these specific regions remains unclear. They found that older adults produced memory narratives with lower episodic specificity related to functional connectivity between the prefrontal cortex and hippocampus that differed between age groups, as well as a greater amount of semantic detail that was related to age differences in functional connectivity of other regions. They speculate that there may be a shift towards semantic retrieval strategies at older ages.

Deoni, Burton, Beauchemin, Cano-orient, De Both, Johnson, Ryan and Huentelman (2022)

Consumer wearables and health monitors, internet-based health and cognitive assessments and home biosample collection kits are increasingly used by researchers for large population-based studies in aging research. These remotely collected samples preclude powerful brain imaging methods that are typically administered at large hospitals or universities and can be difficult for some individuals to access. To offer the potential to perform neuroimaging studies at a participant's home, this manuscript reports the first use of a low-field MRI "scan van" with an online assessment of paired-associate learning to examine brain morphology and verbal memory performance in a sample of 67 individuals 18-93 years of age. Using these methods, they showed the expected associations between brain volume and verbal memory performance across age, demonstrating the feasibility of remote neuroimaging and cognitive data collection.

Jett, Malviya, Schelbaum, Jang, Jahan, Clancy, Hristov, Pahlajani, Niotis, Loeb-Zeitlin, Havryliuk, Isaacson, Brinton and Mosconi, (2022)

After advanced age, female sex is a major risk factor for late-onset Alzheimer's disease. One factor to explain this may be the hormonal transitions of endocrine aging characteristic of the menopause transition in women. Epidemiological studies have yielded contrasting results of protective, deleterious and null effects of estrogen exposure on dementia risk. This manuscript reviews the data examining the associations between female-specific reproductive health and AD risk in women, with a focus on the role of estrogen exposures as a key underlying mechanism. Reproductive lifespan, menopause status, type of menopause, number of pregnancies and exposure to hormonal therapy all turn out to be chief among the critical variables predicting vulnerability to Alzheimer's disease in women.

Kaladchibachi, Negelspach, Zeitzer and Fernandez (2022)

The central pacemaker of circadian rhythms generates less robust signals across normative aging in all species tested (humans, rodents and flies). The present study examined phase-shifts in rhythms in aged *Drosophila* locomotor activity induced from spaced episodes of blue or

green light pulses. For blue flash-exposures, older flies responses are not as efficient as younger animals, but for green light, the responses of old flies were extremely impaired compared to young in shifting circadian cycles. These data provide further support for designing trials in human participants to try different light frequencies that are tuned for wavelength, intensity, duration and frequency that may be able to entrain more optimal circadian clock function in aging.

Palmer, **Grilli**, Lawrence, and **Ryan (2022)**

This study sought to determine whether the apolipoprotein E4 allele, a risk factor for Alzheimer's disease, impacts cognitive status of both younger and older individuals on a memory domain that is known to be impacted by age. Participants were given a continuous recognition task that required accurately separating overlapping memories when objects were presented on a white background, a familiar scene or a novel scene. Novel scenes lowered recognition scores of objects compared to all other contexts for all participants. Younger adults outperformed older adults on correctly identifying similar objects, and older adults misidentified similar objects more than did young participants. Young participants with the E4 allele made fewer false alarms than did those without, whereas this was reversed in the older participants with the E4 carriers making more false alarms. Overall, older adults underutilized details and relied more heavily on holistic information to perform the task. The data are consistent with the idea of antagonistic pleiotropy for the APOE 4 allele – it may have positive benefits early on in the lifespan, and negative consequences later in life.

Most important MBRF-relevant scientific achievements of FY22

The 20 most relevant publications from EMBI Affiliate Faculty is listed in Section 13 Appendix 2, and the significant new grants that were funded to members of the Tucson EMBI are listed in Section 6.

5. Collaborative Projects with McKnight Institutes and Non-McKnight Institutes

- Investigators:** PI: **Barnes** (UA); Project/Core Leads and Co-Leads: Albert (JHU) **Brinton** (UA), NK Chen (UA), Z. Chen (UA), **Brinton** (UA), **Huentelman** (TGen), LaFleur(UA), Lah (Emory), Levey (Emory), **Huentelman** (UM), **Ryan** (UA), **Rundek** (UM), Runyon (UA), **Sacco** (UM) Schork (TGen), Sternberg (UA), Worley (JHU)
- Project Title:** Precision Aging Network: Closing the Gap Between Cognitive Healthspan and Human Lifespan
- Sponsor:** National Institute on Aging U19 AG065169
- Project Dates:** 09/30/2021 – 08/31/2026
- Total Award:** \$59,988,951
- Description:** The strategic goal of the Precision Aging Network (PAN) is to develop the essential scientific knowledge and appropriate technologies to predict individual brain health risks and discover personalized solutions to maximize cognitive healthspan. Because of the enormous heterogeneity in brain and cognitive function among older individuals, the urgent challenge for science, medicine and healthcare providers is to discover interventions that are individually effective in delaying or preventing the onset of symptoms that arise from aging or brain disorders such as AD and AD-related dementias. To bridge existing gaps in our knowledge of the drivers of brain dysfunction, we will study very large, diverse, well-characterized and longitudinally sampled populations across the lifespan.
- Investigators:** UA Institute: **Grilli** (UA) **Huentelman** (TGen)
- Project Title:** Uncovering and Surveilling Financial Deception Risk in Aging
- Sponsor:** McKnight Brain Research Foundation
- Project Dates:** 07/01/2021 – 06/30/2023
- Description:** This study examines internet-based deception risk in aging. Grilli will examine whether individuals at higher risk for Alzheimer’s disease exhibit alterations in online scam-related decision making. **Huentelman** will provide our expertise in APOE genotyping from dried blood and saliva specimens as well as recruitment activities via the existing MindCrowd cohort.
- Investigators:** **Alexander** (UA) **Bowers, Woods** (UF)
- Project Title:** Revitalizing Cognition in Older Adults at Risk for Alzheimer's Disease with Near-Infrared Photobiomodulation
- Sponsor:** McKnight Brain Research Foundation
- Project Dates:** 08/01/19 – 04/30/24
- Description:** The goal of this project is to determine whether NIR stimulation has potential for enhancing cognition in cognitively normal but “at risk” individuals for Alzheimer’s disease.
- Investigators:** **Alexander** (UA) **Woods, Cohen, Marsiske** (UF)
- Project Title:** Augmenting Cognitive Training in Older Adults
- Sponsor:** McKnight Brain Research Foundation
- Project Dates:** 09/01/19 – 04/30/22

Description: The goals of this study are to learn ways to augment cognitive training outcomes in the elderly and to advance understanding of the underlying mechanisms associated with enhanced cognition during training.

Investigators: **Alexander (UA) Bowers (UF), Woods (UF)**
Project Title: A Pilot Intervention with Near Infrared Stimulation: Revitalizing Cognition in Older Adults

Sponsor: McKnight Brain Research Foundation

Project Dates: 09/01/18 – 04/30/22

Description: The goal of this project is to investigate whether NIR stimulation has beneficial effects on cognition, mood, and brain function.

Investigators: **Williamson (UF); Collaborators: Alexander (UA), Woods (UF)**
Project Title: Transcutaneous Vagal Nerve Stimulation and Cognitive Training to Enhance Cognitive Performance in Healthy Older Adults

Sponsor: McKnight Brain Research Foundation

Project Dates: 10/01/19 – 9/30/22

Description: The goal of this project is to determine whether tVNS augments cognitive training associated improvements in cognition.

Investigators: Co-Investigators: **Wilson, Ebner, Lighthall (UA)**
Project Title: Characterizing and modulating neurocognitive processes of learning to trust and distrust in aging.

Sponsor: NIH/NIA R01 AG072658

Project Dates: 03/01/2022 - 04/30/2027

Investigators: MPIs: **Grilli, Andrews-Hanna (UA), Co-Investigators: Mehl, Alexander (UA), Huentelman (TGen)**

Project Title: Tracking autobiographical thoughts: a smartphone-based approach to identify cognitive correlates of Alzheimer's disease biomarkers and risk factors in clinically normal older adults.

Sponsor: R01 AG068098

Project Dates: 08/15/2022-04/30/2027

Description: Tracking autobiographical thoughts: a smartphone-based approach to identifying cognitive correlates of Alzheimer's disease biomarkers and risk factors in clinically normal older adults. This proposal seeks to use mobile smartphone tools to assess cognition naturalistically, to increase accessibility of cognitive assessment, to improve early detection of preclinical Alzheimer's disease pathology, and to reveal new cognitive endpoints for prevention therapies.

6. Honors, Award and New Grants

Honors and Awards

Madeline Ally received the Alfred W. Kaszniak Graduate Fellowship for the 2022-2023 academic year.

Jessica Andrews-Hanna was the recipient of the University of Arizona Research Leadership Institute Fellowship

Carol Barnes was selected for Global Top 1,000 Female Scientists List by Research.com

Carol Barnes received the University of Arizona Office of Research, Innovation and Impact, Women of Impact Award

Roberta Brinton received Arizona Bioscience (AzBio) Researcher of the Year Award

Roberta Brinton received the University of Arizona Office of Research, Innovation and Impact, Women of Impact Award

Matthew Grilli was elected to the Memory Disorders Research Society

Matthias Mehl was the recipient of the 2022 Vontobel Award for Research on Age(ing) for the paper Ferrario et al., 2022, JMIR Aging, 5, e28333 (awarded to the first and second author)

Lee Ryan received the University of Arizona Office of Research, Innovation and Impact, Women of Impact Award

Robert Wilson was recognized as early career faculty and selected as a Scialog Fellow to participate on various Scialog Initiatives.

New Grants

Investigator: Co-Investigators: **Wilson**, Phelps (UA)
Project Title: Testing a working memory hypothesis for the cognitive effects of chronic pain
Sponsor: CEAS Pilot Core
Project Period: 09/01/2022-08/31/2023
Total Award: \$30,000 (For research costs only, 0% effort)

Investigator: Co-Investigators: **Wilson**, Ghaderi, Lee, Sunchin, Rozenblit (UA)
Project Title: Personalized force guidance using reinforcement learning with learning optimization in surgical skills training.
Sponsor: RII Accelerate for Success Grant
Project Period: 07/01/2022-07/31/2023 (For research costs only, 0% effort)
Total Award: \$49,999

Investigator: MPIs: **Grilli, Andrews-Hanna** (UA), Co-Investigators: **Mehl, Alexander** (UA), **Huentelman** (TGen)
Project Title: Tracking autobiographical thoughts: a smartphone-based approach to identifying cognitive correlates of Alzheimer's disease biomarkers and risk factors in clinically normal older adults.
Sponsor: NIH/NIA R01 AG068098
Project Period: 08/15/2022-04/30/2027
Total Award: \$4,449, 700

Investigator: Co-Investigators: **Grilli, Sbarra** (UA)
Project Title: Genetically Informed Studies of Social Connectedness and Health
Sponsor: NIH/NIA R01 AG078361
Project Period: 08/15/2022-04/30/2027
Total Award: \$5,224,323

Investigator: Co-Investigators: **Grilli, Insel** (UA)
Project Title: Digital Technology to Support Adherence to Hypertension Medications for Older Adults with Mild Cognitive Impairment
Sponsor: NIH/NINR NR020261
Project Period: 05/08/2022-4/30/2025
Total Award: \$3,438,350

Investigator: (PI) **Grilli, Insel** (UA)
Project Title: Evaluating social and cognitive factors relevant to understanding age and Alzheimer's disease-related cognitive decline in uncontrolled environments.
Sponsor: Arizona Alzheimer's Consortium Project Grant
Department Health Services
Project Period: 07/1/22-06/30/23
Total Award: \$20,000

Investigators: **Huentelman** (TGen)
Project Title: Identification of polygenic risk scores associated with verbal memory performance in non-demented individuals.
Sponsor: Arizona DHS CTR057001
Project Dates: 07/01/2022 – 06/30/2023
Total Award: \$116,667

Investigator: Co-Investigators: **Mehl, Sbarra** (UA)
Project Title: Genetically Informed Studies of Social Connectedness and Health
Sponsor: NIA R01AG078361
Project Period: 08/01/2022-04/30/2027
Total Award: \$5,224,323

Investigator: Co-Investigators: **Mehl, Hao** (UA)
Project Title: Personal Thermal Comfort Management and Minimized Building Energy Consumption via Ambient Light Exposure for Optimal Thermal Comfort in Older Adults
Sponsor: Innovations in Healthy Aging Grand Challenges in Healthy Aging Seed Grant
Project Period: 05/01/2022-04/30/2023
Total Award: \$100,000

Investigator: PI: **Rogalski** (NW), **Huentelman** (TGen)
Project Title: Asymmetric neurodegeneration and language in primary progressive aphasia
Sponsor: NIH R01AG077444
Project Period: 06/15/2022-03/31/2027
Total Award: \$100,000

Investigators: PI: **Trouard** (UA)
Project Title: Targeted ultrasound contrast agents for the disruption of Alzheimer's plaques. This is an SBIR to develop therapy to treat Alzheimer's disease.
Sponsor: Arizona DHS CTR057001
Project Dates: 07/01/2022 – 06/30/2023
Total Award: \$478,050

Investigators: PI: **Trouard** (UA)
Project Title: Brain MRI Application and Analysis
Sponsor: Arizona Alzheimer's Consortium
Project Dates: 07/01/2022 – 06/30/2023
Total Award: \$100,000

7. Technology Transfer

Brinton - Disclosure in 2022 (not filed, under assessment by TLA):

UA22-001: Slow Release Allopregnanolone Microemulsions for the Treatment of Postpartum Depression Assessment

UA22-456: Infant formula as a nutritional neuroprotective intervention for Neurological Disease Assessment

Brinton - UA23-028: Phytoestrogenic formulations for the promotion of cognitive function, sleep quality and mood symptoms (filed Nov 7th 2022)

UA22-200: Topical Neurosteroid Formulations (Continuation-in-part filed 22nd Feb 2022) Issued (right at the end of 2021):

UA20-169: Agents, compositions, and methods for enhancing neurological function (issued as US11207331B2 28th Dec 2021)

Fernandez - International and U.S. Provisional Applications (all evenly divided attribution)

Pau S., Grandner M.A., Fernandez F., and Mason B.J. Circadian Rhythm Restoring Blue Blockers. Attorney Docket: 044974-8065.US00 (UA21-174) PCT/US2022/038207, U.S. Patent Application No. 63/225, 727

Pau S., Grandner M.A., Fernandez F., and Mason B.J. Blue Enhancer Glasses. Attorney Docket: 044974-8066.US00 (UA21-175) PCT/US2022/038215, U.S. Patent Application No. 63/225, 753

Pau S., Grandner M.A., Fernandez F., and Mason B.J. Pink Blue Blockers. Attorney Docket: 044974-8067.US00 (UA21-176) PCT/US2022/038220, U.S. Patent Application No. 63/225, 785

Pau S., Grandner M.A., Fernandez F., and Mason B.J. Green Enhancer Glasses. Attorney Docket: 044974-8068.US00 (UA21-233) PCT/US2022/038233, U.S. Patent Application No. 63/225, 806

Pau S., Grandner M.A., Fernandez F., and Mason B.J. Melanopsin Blocker. Attorney Docket: 044974-8069.US00 (UA21-234) PCT/US2022/038235, U.S. Patent Application No. 63/225, 848

8. Where any funds used for a Prohibited Purpose during the report period?

No

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

No

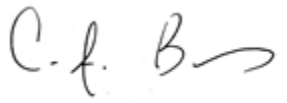
10. Did all activities during the report period further the Purpose?

Yes

11. 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

Respectfully Submitted,

A handwritten signature in black ink, appearing to read "C.A. Barnes", enclosed in a thin black rectangular border.

C.A. Barnes, Ph.D.

Regents' Professor, Psychology, Neurology and Neuroscience
Evelyn F. McKnight Chair for Learning and Memory in Aging
Director, Evelyn F. McKnight Brain Institute

12. Appendix 1

List of McKnight Affiliate Faculty and their area of focus, and Department Affiliations, including a list of post-doctoral and pre-doctoral trainees (CVs needed only for new faculty/collaborators)

No new Affiliate Faculty were appointed in the Tucson EMBI in 2022, thus there are no new curriculum vitae to append.

Primary Faculty

Gene E. Alexander, Ph.D., Professor, Psychology, UA

Area of Focus: He studies brain-behavior relationships in the context of healthy aging and age-related, neurodegenerative disease. He uses multimodal neuroimaging techniques, including structural and functional magnetic resonance imaging (MRI) and positron emission tomography (PET), in combination with measures of cognition and behavior to address research questions on the effects of brain aging and Alzheimer's disease.

Jessica Andrews-Hanna, Ph.D., Associate Professor, Psychology, UA

Area of Focus: Her research is centered on understanding the mysteries of our inner mental lives – the thoughts, memories, feelings and emotions that make us unique as individuals. Her work is particularly relevant to EMBI in that she is trying to determine how internally guided processes develop throughout adolescence and change into old age.

Carol A. Barnes, Ph.D., Regents Professor, Psychology, UA

Area of Focus: Her research has focused on the aging brain, and how cognition changes during the course of normal aging. She uses animal models of human aging (rodents and nonhuman primates) that allow a detailed examination of the brain mechanisms of age-related changes in learning and memory, and the circuits responsible for complex cognitive functions. More recently she is also studying normative age-related cognitive changes in humans.

Robbie Brinton, Ph.D., Regents Professor, Pharmacology, UA

Area of Focus: She investigates the mechanisms of bioenergetic and regenerative aging of the brain. Translationally, the pathways involved in these mechanisms that are activated by neurosteroids provide the basis for personalized interventions that target stages of bioenergetic aging in both female and male brains to prevent and delay brain aging and susceptibility to Alzheimer's disease.

Ying-hui Chou, Ph.D., Associate Professor, Psychology, UA

Area of Focus: She works in the area of cognitive and clinical neuroscience of aging and neurodegenerative disorders. Within this framework, her laboratory is particularly interested in integrating brain imaging and transcranial magnetic stimulation (TMS) techniques to develop therapeutic TMS protocols for individuals with mild cognitive impairment and potentially normative aging. The development of TMS-derived and image-based biomarkers for early diagnosis and prediction of therapeutic outcomes will be important to many EMBI faculty.

Stephen Cowen, Ph.D., Associate Professor, Psychology, UA,

Area of Focus: His interest is in understanding how interacting groups of neurons represent the value of anticipated outcomes, planned actions, and physical space. He is specifically interested in determining the neural origins of age-associated memory loss and the role of sleep in the memory formation process.

Arne Ekstrom, Ph.D., Professor, Psychology, UA

Area of Focus: His work revolves around the important question of the neural basis of human memory, with a particular interest in spatial navigation. With respect to aging, the hippocampus is critical for spatial navigation, and he is conducting experiments using high resolution MRI and immersive VR technologies to examine how spatial navigation changes during aging in humans.

Fabian Fernandez, Ph.D., Associate Professor, Psychology, UA

Area of Focus: His laboratory is interested in circadian timekeeping, which is fundamental to human health. He is particularly interested in how chronic and quick, sequenced light exposure can be designed to promote normal healthy aging and strengthen adaptive cognitive/emotional responses to being awake in the middle of the night.

Matt Grilli, Ph.D., Associate Professor, Psychology, UA

Area of Focus: His primary interest is in understanding how we store and retrieve memories, with an emphasis on autobiographical memory, which refers to memories of personal experiences. Ongoing projects are investigating how autobiographical memory is affected in several populations, including older adults, as well as how decision-making operations are altered in aging.

Meredith Hay, Ph.D., Professor, Physiology, UA

Area of Focus: Her interests are in cardiovascular neurobiology and aging, and in the development of novel peptides that are neuroprotective. She is particularly interested in peptides that inhibit inflammatory cascades and improve brain blood flow, which has applications in both normative aging and in age-related diseases.

Matthew Huentelman, Ph.D., Division Director and Professor, Neurogenomics Division, TGen

Area of Focus: His lab is using genomics and transcriptomics to better understand why some individuals exhibit better cognitive aging when compared to others. The hope is that through the better understanding of these differences we may someday be able to develop therapeutics that could enable a larger portion of the population to exhibit better cognitive aging.

Matthias Mehl, Ph.D., Professor, Psychology, UA

Area of Focus: He is a health psychologist who is interested in the psychological implications of our daily lives. He develops behavioral assessment methods for studying everyday life using naturalistic observation of social interactions and quantitative text analysis of natural language use across the lifespan.

Mary-Frances O'Connor, Ph.D., Associate Professor, Psychology UA

Area of Focus: She is interested in understanding individual differences in response to loss, especially the death of a loved one, both psychologically and physiologically. For the latter, she examines neurobiological, immune and autonomic parameters that vary between individual grief responses, and across age.

Lee Ryan, Ph.D., Professor and Head, Psychology, UA

Area of Focus: Her research focuses on the neural basis of memory, age-related changes in memory, and how these changes relate to brain functioning. She has a special interest in the impact of cardiovascular health for maintaining memory function as we age, and decreasing risk for age-related disorders.

Ted P. Trouard, Ph.D., Professor, Biomedical Engineering, UA

Area of Focus: His interests involve the development and biomedical application of magnetic resonance imaging technologies to experiments that seek to monitor brain changes over time – whether it is in normative aging, or in age-related diseases, such as AD. He is also expert in small animal imaging and collaborates with several EMBI faculty on such studies. Additionally, he is working on a project involving focused ultrasound for drug delivery that has many potential applications.

Robert Wilson, Ph.D., Associate Professor, Psychology

Area of Focus: His research interests mix theoretical and computational modeling, psychophysics, pupillometry, EEG and fMRI to probe the neuroscience of learning and decision making in humans, and across the lifespan.

Secondary Faculty

Heather Bimonte-Nelson, Ph.D., Professor, Psychology, ASU

Paul Coleman, Ph.D., Research Professor, Neurodegenerative Disease Research Center, ASU

Ralph F. Fregosi, Ph.D., Professor, Physiology, UA

Andrew J. Fuglevand, Ph.D., Professor, Physiology, UA

Elizabeth L. Glisky, Ph.D., Professor Emeritus, Psychology, UA

Katalin M. Gothard, M.D., Ph.D., Professor, Physiology and Neurology, UA

Asta Håberg, M.D, Ph.D., Professor, NTNU, Norway

Al Kaszniak, Ph.D., Professor Emeritus, Psychology, UA

Anita Koshy, M.D., Associate Professor, Neurology, UA

Lalitha Madhavan, M.D., Ph.D., Associate Professor, Neurology, UA

Diano Marrone, Ph.D., Professor, Psychology, Wilfrid Laurier Univ.

Elliott Mufson, Ph.D., Professor, Neurobiology, Dignity Health, Phoenix

Lynn Nadel, Ph.D., Regents' Professor, Emeritus, UA

Janko Nikolich-Zugich, M.D., Ph.D., Department Head, Immunobiology, UA

Mary Peterson, Ph.D., Professor, Psychology, Director Cognitive Science Program, UA

Naomi E. Rance, M.D., Ph.D., Professor Emeritus, Pathology, UA

Steven Z. Rapcsak, M.D., Professor, Neurology, Psychology, and Speech, Language and Hearing Sciences, UA

Eric Reiman, M.D., Executive Director, Banner Alzheimer's Institute, Phoenix

Linda L. Restifo, M.D., Ph.D., Professor, Neurology, UA

Anne Smith, Ph.D., Associate Director, Sage Therapeutics, Massachusetts

Predocctoral Trainees

Monica Acevedo-Molina (Grilli)

Eric Andrews (Andrews-Hanna)

Monica Acevedo-Molina (Grilli)

Kelsey Bernard (Brinton)

Vehanshi Bhargava (Brinton)

Avnish Bhattra (Brinton)

David Bradford (Brinton)

Greg Branigan, (Brinton)
Yu-Chin Chen, (Chou)
Yu Jung Chen (Barnes)
Patricia Chilton (Grilli, Mehl)
Lizzie Church (Barnes)
Andrea Coppola (Andrews-Hanna and Sbarra)
Helena Cortes Flores (Brinton)
Nicole Delatorre (Brinton)
Loi Do (Trouard)
Hannah Dollish (Fernandez)
Lesley Espinosa (Ryan)
Sydney Friedman (O'Connor)
Nathaniel Gallegos (Ryan)
Brittany Gratreak (Brinton)
Gabriel Holguin (Cowen)
Mariam Hovhannisyan (Andrews-Hanna and Grilli)
Yinqi Huang (Wilson and Eckstrom)
Hannah Johnson (Koshy)
Josh Kochanowsky (Koshy)
Michelle Krumm (Barnes)
Yilin Liu (Chou)
Stephanie Matijevic (Ryan)
Kelsey McDermott (Barnes)
Will McLean (Brinton)
Katie McVeigh (Grilli)
Oscar Mendez (Koshy)
Simona Merlini (Brinton)
Emily Merritt (Koshy)
Jack-Morgan Mizell (Wilson)
Alana Mueller (Eckstrom)
Devin Murphy (Trouard)
David C. Negelspach (Fernandez)
Justin Palmer (Ryan)
Colin Potter (Brinton)
Quentin Raffaelli (Andrews-Hanna)
Ramamoorthy Rajashree (Cowen)
Evie Robinson (Eckstrom)
Sameer Sabharwai-Siddiqi (Eckstrom)
David Scott (Brinton)
Sarah Seger (Eckstrom)
Sahana Srivathsa (Barnes)
Mark Sundman (Chou)
Katrina Teer (Brinton)
Coco Tirambulo (Brinton)
Georgina Torrandell Haro (Brinton)
Emily Van Etten (Alexander)
Barbora Vagnerova (Brinton)
Abhilasha Vishwanath (Cowen)
Zach Webber (Brinton)
Da'Mere Wilson (O'Connor)
Cristi Williams (Brinton)

Haley Wiskoski (Trouard)
Hanbo Xie (Wilson)
Jingming Xue (Wilson)
Marc Zempare (Barnes)
Huadong Ziong (Wilson)

Postdoctoral Trainees

Monica Chawla, Ph.D. (Barnes)
Yu (Karen) Du, Ph.D. (Eckstrom)
Febrizio Ecce, Ph.D. (Huentelman)
Daniel Gray, Ph.D. (Barnes)
Gerson Hernandez, Ph.D. (Brinton)
Paul Hill, Ph.D. (Eckstrom)
Atsushi Ishii, Ph.D. (Madhavan)
Sevag Kaladchibachi, Ph.D. (Fernandez)
Aigerim Kamzina, Ph.D. (Huentelman)
Adam Lester, Ph.D. (Barnes)
Koeun Lim, Ph.D. (Chou)
Erin Maresh, Ph.D. (Andrews-Hanna)
Kathryn McGovern, Ph.D. (Koshy)
Yashi Mi, Ph.D. (Brinton)
Caroline Phelps, Ph.D. (Wilson)
Guoyuan Qi, Ph.D. (Brinton)
Adam Raikes, Ph.D. (Brinton)
Chandrasekaran Sambamurthy, Ph.D. (Koshy)
Irina Sinakevitch, Ph.D. (Barnes)
Teodora Stoica, Ph.D., (Andrews-Hanna, Grilli)
Francesca Vitali, Ph.D. (Brinton)
Fei Yin, Ph.D. (Brinton)
Nahla Zaghoul, Ph.D. (Brinton)
Li Zheng, Ph.D. (Eckstrom)

13. Appendix 2

Top 20 publications from FY 21 relevant to MBRF

These 20 publications include Affiliate Faculty from the Tucson EMBI, and faculty from the other EMBI Institutes, attesting to the collaborative nature of McKnight Faculty.

Boutzoukas E.M., O'Shea A., Kraft J.N., Hardcastle C., Evangelista N.D., Hausman H.K., Albizu A., Van Etten E.J., Bharadwaj P.K., Smith S.G., Song H., Porges E.C., Hishaw G.A., DeKosky S.T., Wu S.S., Marsiske M., **Alexander G.E.**, Cohen R., Woods A.J. (2022) Higher white matter hyperintensity load adversely affects pre-post proximal cognitive training performance in healthy older adults. *GeroScience*, 1-15.

Crown, L.M., Gray, D.T., Schimanski, L.A., **Barnes, C.A., Cowen, S.L.** (2022) Aged rats exhibit altered behavior-induced oscillatory activity, place cell firing rates, and spatial information content in the CA1 region of the hippocampus, *Journal of Neuroscience*, 42: 4505-4516.

Deoni S.C.L., Burton P., Beauchemin J., Cano-Lorente R., De Both M.D., Johnson M., **Ryan L., Huentelman M.J.** Neuroimaging and verbal memory assessment in healthy aging adults using a portable low-field MRI scanner and a web-based platform: results from a proof-of-concept population-based cross-section study. *Brain Struct Funct.* 2022 Nov 9:1–17. doi: 10.1007/s00429-022-02595-7. Epub ahead of print. PMID: 36352153; PMCID: PMC9646260.

Ferrario, A. Luo, M., Polsinelli, A. J., Moseley, S. A., **Mehl, M. R.**, Yordanova, K., Martin, M., Demiray, B., (2022). Predicting working memory in healthy older adults using real-life language and social context information: A machine learning approach. *JMIR Aging*, 5, e28333. doi: 10.2196/28333

Glisky, E.L., Woolverton, C.B., McVeigh, K.S., **Grilli, M.D.** (2022). Episodic memory and executive function are differentially affected by retests but similarly affected by age in a longitudinal study of normally-aging older adults. *Frontiers in Aging Neuroscience*, 14, 863942.

Gray, D.T., Khattab, S., Meltzer, J., McDermott, K., Schwyhart, R., Sinakevitch, I., Härtig, W., **Barnes, C.A.** (2022) Retrosplenial cortex microglia and perineuronal net densities are associated with memory impairment in aged rhesus macaques. Oxford University Press, DOI: 10.1093/cercor/bhac366

Grilli, M.D., Sheldon, S. (2022). Autobiographical event memory and aging: Older adults get the gist. *Trends in Cognitive Sciences*, 26(12), 1079-1089.

Gust, C.J., Moe, E.N., Seals, D.R., Banich, M.T., **Andrews-Hanna, J.R.**, Hutchison, K.E., Bryan, A.D. (2022) Associations between age and resting state connectivity are partially dependent upon cardiovascular fitness. *Frontiers in Aging Neuroscience*, 20(14), 858405.

Haas, M., **Mehl, M. R.**, Ballhausen, N., Zuber, S., Kliegel, M., & Hering, A., (2022). The sounds of memory: Exploring the age-prospective memory paradox in everyday behavior and conversations. *The Journals of Gerontology Series B Psychological Sciences and Social Sciences*, 77, 695-703. doi: 10.1093/geronb/gbac012

Harootonian, S. K., **Ekstrom, A. D., Wilson, R. C.** (2022). Combination and competition between path integration and landmark navigation in the estimation of heading direction. *PLoS computational biology*, 18(2), e1009222.

Heath, L., Earls, J.C., Magis, A.T., Kornilov, S.A., Lovejoy, J.C., Funk, C.C., Rappaport, N., Logsdon, B.A., Mangravite, L.M., Kunkle, B.W., Martin, E.R., Naj, A.C., Ertekin-Taner, N., Golde, T.E., Hood, L., Price, ND; **Alzheimer's Disease Genetics Consortium**. Manifestations of Alzheimer's disease genetic risk in the blood are evident in a multiomic analysis in healthy adults aged 18 to 90. *Sci Rep.* 2022 Apr 12;12(1):6117. doi: 10.1038/s41598-022-09825-2. PMID: 35413975; PMCID: PMC9005657

Hausman, H.K., Hardcastle, C., Kraft, J.N., Evangelista, N.D., Boutzoukas, E.M., O'Shea, A., Albizu, A., Langer, K., Van Etten, E.J., Bharadwaj, P.K., Song, H., Smith, S.G., Porges, E., Hishaw, G.A., Wu, S., DeKosky, S., **Alexander, G.E.**, Marsiske, M., Cohen, R., Woods, A.J. (2022) The association between head motion during functional magnetic resonance imaging and executive functioning in older adults. *Neuroimage: Reports*, 2 (2), 100085.

Lester, A.W., Jordan, G.A., Blum, C.J., Philpot, J.P., **Barnes, C.A.** (2022) Differential effects in young and aged rats' navigational accuracy following instantaneous rotation of environmental cues. *Behavioral Neuroscience* 136 (6), 561

Matijevic, S., **Andrews-Hanna, J.R.**, Wank, A.A., **Ryan, L., Grilli, M.D.** (2022). Individual differences in the relationship between episodic detail generation and resting state functional connectivity vary with age. *Neuropsychologia*, 166, 108138.

McAven A.S., Wank A., Rapcsak S.Z., **Grilli M.D., Ekstrom, A.D.** (2022). Largely intact memory for spatial locations during navigation in an individual with dense amnesia. *Neuropsychologia*. 170: 108225. PMID: 35367237.

Nolin, S., Cowart, H., Merritt, S., McInerney, K., Bharadwaj, P., Franchetti, M., Raichlen, D.A., Jessup, C.J., Hishaw, G.A., Van Etten, E J, **Trouard, T.P.**, Geldmacher, D.S., Wadley, V.G., Porges, E.S., Woods, A.J., Cohen, R.A., Levin, B.E., Rundek, T, **Alexander, G.E.**, Visscher, K. (2022). Validity of the NIH toolbox cognitive battery in a healthy oldest-old 85 sample. *Journal of the International Neuropsychological Society*, 1-10. doi:10.1017/S1355617722000443

O'Connor, M.F., Seeley, S. H. (2022). Grieving as a form of learning: Insights from neuroscience applied to grief and loss. *Current Opinion in Psychology*, 43, 317–322. <https://doi.org/10.1016/j.copsyc.2021.08.019>

Palmer, J.M., **Grilli, M.D.**, Lawrence, and **Ryan, L.** (2022). The impact of context on pattern separation for objects among younger and older APOE $\epsilon 4$ carriers and noncarriers. *J Int Neuropsychol Soc.* 23:1-11.

Raikes, A.C., Hernandez, G.D., Matthews, D.C., Lukic, A.S., Law, M., Shi Y., Schneider L.S., **Brinton, R.D.** Exploratory imaging outcomes of a phase 1b/2a clinical trial of allopregnanolone as a regenerative therapeutic for Alzheimer's disease: Structural effects and functional connectivity outcomes. *Alzheimers Dement (N Y)*. 2022 Mar 14;8(1): e12258.doi: 10.1002/trc2.12258.eCollection 2022. PMID: 35310526; PMCID: PMC8919249

Smith, R., Taylor, S., **Wilson, R. C.**, Chuning, A. E., Persich, M. R., Wang, S., & Killgore, W. D. (2022). Lower levels of directed exploration and reflective thinking are associated with greater anxiety and depression. *Frontiers in Psychiatry*, 12, 782136.

14. Appendix 3

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

Scientific Presentations

Barnes, C.A., Region-Selective Hippocampal Contributions to Altered Cognition in Aging. (Invited) Collaborative Research Center Neural Resources of Cognition Retreat, Burg Wanzleben, Germany, 2022

Barnes, C.A. Region-Selective Hippocampal Contributions to Altered Cognition in Aging. (Invited) 6th Annual Rodolfo Llinás Lecture, NYU School of Medicine, NY, 2022

Brinton, R. The Great Neuro Reunion Aging and Dementia: Neuroimaging, Aging and Alzheimer's Disease, Exploratory Imaging Outcomes of a Phase 1B/2A Clinical Trial of Allopregnanolone as a Regenerative Therapeutic for Alzheimer's Disease: Structural and Functional Outcomes. (Invited) American Academy of Neurology (AAN) 2022 Annual Meeting

Do, L, Zempare, MA, Bernstein, AS, Bharadwaj, P, Carey, N, Nguyen, C , **Alexander, GE, Barnes, CA,** and **Trouard, TP.** Volumetric MRI Analysis of Rodent Brains as a Function of Age and Cognition. Society for Neuroscience, San Diego, 2022.

Grilli, M.D. Tracking the temporal unfolding of autobiographical remembering in older adults. Memory Disorders Research Society Annual Meeting, Philadelphia, Pennsylvania, 2022.

Hill, P, McAvan, A. S., **Barnes, C. A., Eckstrom, A. D.**, Age-related spatial navigation impairments are moderated by testing modality. Society for Neuroscience, San Diego, 2022.

Huentelman, M. Genome-wide DNA methylation analysis suggests lower CD8+ T cell proportions in SuperAgers. Society for Neuroscience, San Diego, 2022.

Mehl, M. R. The sounds of healthy aging: Naturalistic observation of aging-related social and cognitive processes in daily life. (Invited keynote) Geneva Aging Series, Geneva, Switzerland, 2022.

Stoica, T., **Grilli, M.D.**, Andrews, E.S., Burns, H., Wilcox, R., & **Andrews-Hanna, J.R.** Resting State Connectivity of Affective Linguistic Expression during Naturalistic Speech. Organization for Human Brain Mapping Meeting, Glasgow, Scotland, 2022.

Van Etten, E. J., Bharadwaj, P. K., Hishaw, G. A., **Trouard, T. P., & Alexander, G. E.** Influence of age and apolipoprotein E ϵ 4 status on regional white matter hyperintensity volume and cognition in healthy aging. International Neuropsychological Society. New Orleans, LA, 2022

15. Appendix 4

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

Website Development

During the past year the Tucson EMBI continues to make a significant effort to continue to update and improve its website content, adding more laboratory pictures, updating current presentations and new publications. The last phase of the buildout involved a significant section on our newest project – *The Precision Aging Network*. The new website went live in January.

The Department of Psychology launched a new website in September. A few highlights of the new website include improved mobile friendliness, accessibility, new content, improved menu structure and many new images.

Social Media Summary EMBI Website Tucson

Total Users: 817

New Users: 421

Average Visit (Min) : 5:34

Psychology Department Website

Total Users: 31,021

New Users: 20,289

Average Visit (Min) : 9:11

Media Coverage

Fabian-Xosé Fernandez. NPR, Arizona Public Media, Determining the real cost of loss of sleep (Arizona Science Episode 336)

Carol Barnes, Lee Ryan. Seeking Better Brain Health: Precision Aging Network to Research How Brains Age. Biz Tucson. April 11, 2022.

Carol Barnes. Unlocking the mystery of the aging brain. Arizona Science Radio, Episode 339, September 16, 2022.

Mary-Frances O'Connor. Inspire the Mind, “The Surprisingly Comforting Science Behind Grief,” Livia Dyring, October 24, 2022: <https://www.inspirethemind.org/blog/the-surprisingly-comforting-science-behind-grief>

Mary-Frances O'Connor. Nature, “Millions Are Mourning The Queen—What’s The Science Behind Public Grief?” Katharine Sanderson, September 14, 2022: <https://www.nature.com/articles/d41586-022-02945-9#correction-0>

Mary-Frances O'Connor. Crocuses in the Snow, “Why Do We Grieve Celebrities?” Catriona Innes, September 14, 2022: <https://catrionainnes.substack.com/p/why-do-we-grieve-celebrities>

Mary-Frances O'Connor. Financial Times, “What Grief Does to Those Left Behind,” Nicola Davis, September 12, 2022: <https://www.theguardian.com/society/2022/sep/11/mourning-rituals-help-people-cope-with-grief-scientists>

Mary-Frances O'Connor. The Guardian, “Morning Rituals Help People Cope with Grief, Say Scientists,” Nicola Davis, September 11, 2022: <https://www.theguardian.com/society/2022/sep/11/mourning-rituals-help-people-cope-with-grief-scientists>

Mary-Frances O'Connor. The Next Big Idea Club, “3 New Books on Grief, Heartbreak, and Carrying On,” August 28, 2022: <https://nextbigideaclub.com/magazine/3-new-books-grief-heartbreak-carrying/35506/>

Mary-Frances O'Connor. Psychology Today, “The Practice of Mourning and Living Life Now,” Deborah Cabaniss, August 18, 2022: <https://www.psychologytoday.com/us/blog/finding-mind/202208/the-practice-mourning-and-living-life-now>

Mary-Frances O'Connor. Psychology Today, “Rewiring the Brain in Grief,” Sophia Dembling, August 18, 2022: <https://www.psychologytoday.com/us/blog/widows-walk/202208/rewiring-the-brain-in-grief>

Mary-Frances O'Connor. Behavioral Scientist, “Walking in the Dark: Creating a New Virtual Map in Your Brain After Loss,” August 2, 2022: <https://behavioralscientist.org/walking-in-the-dark-creating-a-new-virtual-map-in-your-brain-after-loss/>

Mary-Frances O'Connor. Psychology Today, “Is the Afterlife All in Our Heads?” Sophia Dembling, July 29, 2022: <https://www.psychologytoday.com/us/blog/widows-walk/202207/is-the-afterlife-all-in-our-heads>

Mary-Frances O'Connor. The Next Big Idea Club, “Heartbroken? These 5 Books Will Help You Move Forward,” July 27, 2022: <https://nextbigideaclub.com/magazine/heartbroken-5-books-will-help-move-forward/34992/>

Mary-Frances O'Connor. The Bottom Line, “The Science of Grief,” July 24, 2022: <https://bottomlineinc.com/life/emotional-health/the-science-of-grief>

Mary-Frances O'Connor. The Low Calorie, High Fibre, High Calcium, Tech Geeks Don't Have Any Time Cookbook Blog, “Review of ‘The Grieving Brain,’ by Mary-Frances O'Connor,” July 9, 2022: <https://fibrecookery.blogspot.com/2022/07/review-of-grieving-brain-by-mary.html>

Mary-Frances O'Connor. The Behavioral Scientist, “Behavioral Scientist’s Summer Book List 2022,” Antonia Violante and Evan Nesterak, June 30, 2022: <https://behavioralscientist.org/behavioral-scientists-summer-book-list-2022/>

Mary-Frances O'Connor. CancerToday, "The Pain of Grief," Charlotte Huff, June 22, 2022: <https://www.cancertodaymag.org/summer-2022/the-pain-of-grief/>

Mary-Frances O'Connor. How To Live Blog, "The Five Stages of Grief Are a Myth; Grief is a Process," Amanda Stern, June 1, 2022: <https://amandastern.bulletin.com/grief>

Mary-Frances O'Connor. New York Times, "The Arrow in America's Heart," Elizabeth Dias, May 31, 2022: <https://www.nytimes.com/2022/05/31/us/america-life-uvalde-covid.html>

Mary-Frances O'Connor. Fortune, "We're Living In An Era Of Daily Trauma: Here's How To Cope," Kells McPhillips, May 27, 2022: <https://fortune.com/2022/05/27/vicarious-trauma-how-to-cope/>

Mary-Frances O'Connor. Psyche, "Seeing grieving as learning explains why the process takes time," Saren Seeley and Mary-Frances O'Connor, May 26, 2022: <https://psyche.co/ideas/seeing-grieving-as-learning-explains-why-the-process-takes-time>

Mary-Frances O'Connor. The Marginalian, "Your Brain On Grief, Your Heart On Healing," Maria Popova, May 25, 2022: <https://www.themarginalian.org/2022/05/25/the-grieving-brain-mary-frances-o-connor/>

Mary-Frances O'Connor. Next Avenue, "When Grief Doesn't Go Away," Barbra Williams Cosentino, May 23, 2022: <https://www.nextavenue.org/when-grief-doesnt-go-away/>

Mary-Frances O'Connor. The Guardian, "What Made America's Covid Death Toll Even Worse: The Gnawing Pain Of Human Separation," Eric Berger, May 15, 2022: <https://www.theguardian.com/world/2022/may/15/covid-coronavirus-1m-deaths-separation-isolation>

Mary-Frances O'Connor. UArizona News, "Understanding Black Grief," Alexis Blue, April 28, 2022: <https://news.arizona.edu/story/understanding-black-grief>

Mary-Frances O'Connor. GriefHaven, "The Grieving Brain Interview: Part I and Part II 2022," Susan Whitmore, April 23, 2022: <https://griefhaven.org/the-grieving-brain-interview-part-i-and-part-ii-2022>

Mary-Frances O'Connor. UCLA Health, "Long-Term Grief Gets the Attention It Deserves," Tina Daunt, April 19, 2022: <https://connect.uclahealth.org/2022/04/19/long-term-grief-gets-the-attention-it-deserves>

Mary-Frances O'Connor. Seven Ponds Blog, "The Grieving Brain and How Our Minds Are Changed by Loss," Suzette Sherman, April 19, 2022: <https://blog.sevenponds.com/professional-advice/the-grieving-brain-and-how-our-minds-are-changed-by-loss>

Mary-Frances O'Connor. TODAY, "'Bridgerton' Season 2 Explores The Grief Of Losing A Parental Figure As A Young Adult," Nicoleta Richardson, April 18, 2022: <https://www.today.com/health/health/bridgerton-season-two-explores-grief-of-young-adult-losing-parent-rcna23548>

Mary-Frances O'Connor. Mad In America, "Books Under Review: Spring 2022," Amy Biancolli, April 16, 2022: <https://www.madinamerica.com/2022/04/books-under-review-spring-2022/>

Mary-Frances O'Connor. Outside Magazine, "What I've Learned from Loving a New Dog While Grieving Another," Annette McGivney, April 4, 2022: <https://www.outsideonline.com/culture/essays-culture/pet-loss-dog-grief-attachment-theory/>

Mary-Frances O'Connor. Stuff, "What Grief Really Does To Your Brain—And How It Changes It Forever," Anna Maxted, March 30, 2022: <https://www.stuff.co.nz/life-style/wellbeing/300553476/what-grief-really-does-to-your-brain--and-how-it-changes-it-forever>

Mary-Frances O'Connor. The Psychologist, The British Psychological Society, "You Can't Really Study Grief Without Studying Love," Jon Sutton, March 24, 2022: <https://www.bps.org.uk/psychologist/bereavement-and-grief>

Mary-Frances O'Connor. The Telegraph, "What Grief Really Does to Your Brain—And How It Changes It Forever," March 19, 2022: <https://www.telegraph.co.uk/health-fitness/mind/grief-really-does-brain-changes-forever/>

Mary-Frances O'Connor. The Guardian, "Mary-Frances O'Connor: 'People Struggle to Understand Grief, But It Is a Byproduct of Love'," Ian Tucker, March 5, 2022: <https://www.theguardian.com/science/2022/mar/05/mary-frances-oconnor-the-grieving-brain-grief-psychology>

Mary-Frances O'Connor. Book Bite, Next Big Idea Club, "The Grieving Brain: The Surprising Science of How We Learn from Love and Loss," March 1, 2022: <https://nextbigideaclub.com/magazine/grieving-brain-surprising-science-learn-love-loss-bookbite/32708/>

Mary-Frances O'Connor. Katie Couric Media, "5 Things You Should Know about Grief," Ryan Buxton, February 26, 2022: <https://katiecouric.com/health/mental-health/what-to-know-about-grieving-process/>

Mary-Frances O'Connor. TODAY, "The Grieving Brain: How Your Mind Deals with a Loved One's Death and How to Heal," Agnes Pawlowski, January 26, 2022: <https://www.today.com/health/mind-body/grief-changes-brain-rcna13613>

Mary-Frances O'Connor. NPR's Shots "How Your Brain Copes with Grief, and Why It Takes Time to Heal," Berly McCoy, December 20, 2021: <https://www.npr.org/sections/health-shots/2021/12/20/1056741090/grief-loss-holiday-brain-healing>

Mary-Frances O'Connor. Scientific American, "COVID Has Put the World at Risk of Prolonged Grief Disorder," Katherine Harmon Courage, May 19, 2021: <https://www.scientificamerican.com/article/covid-has-put-the-world-at-risk-of-prolonged-grief-disorder/>

Mary-Frances O'Connor. WBRC Mike Behind the Mic, "Mike Talks To Author Of "The Grieving Brain," Mike Dubberly, June 7, 2022: <https://www.wbrc.com/2022/06/07/mike-behind-mic-mike-talks-author-grieving-brain/>

Mary-Frances O'Connor. WBRC, "Psychology Professor on How Our Brains Cope with Loss and Grief," May 31, 2022: <https://www.wbrc.com/video/2022/05/31/psychology-professor-how-our-brains-cope-with-loss-grief/>

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