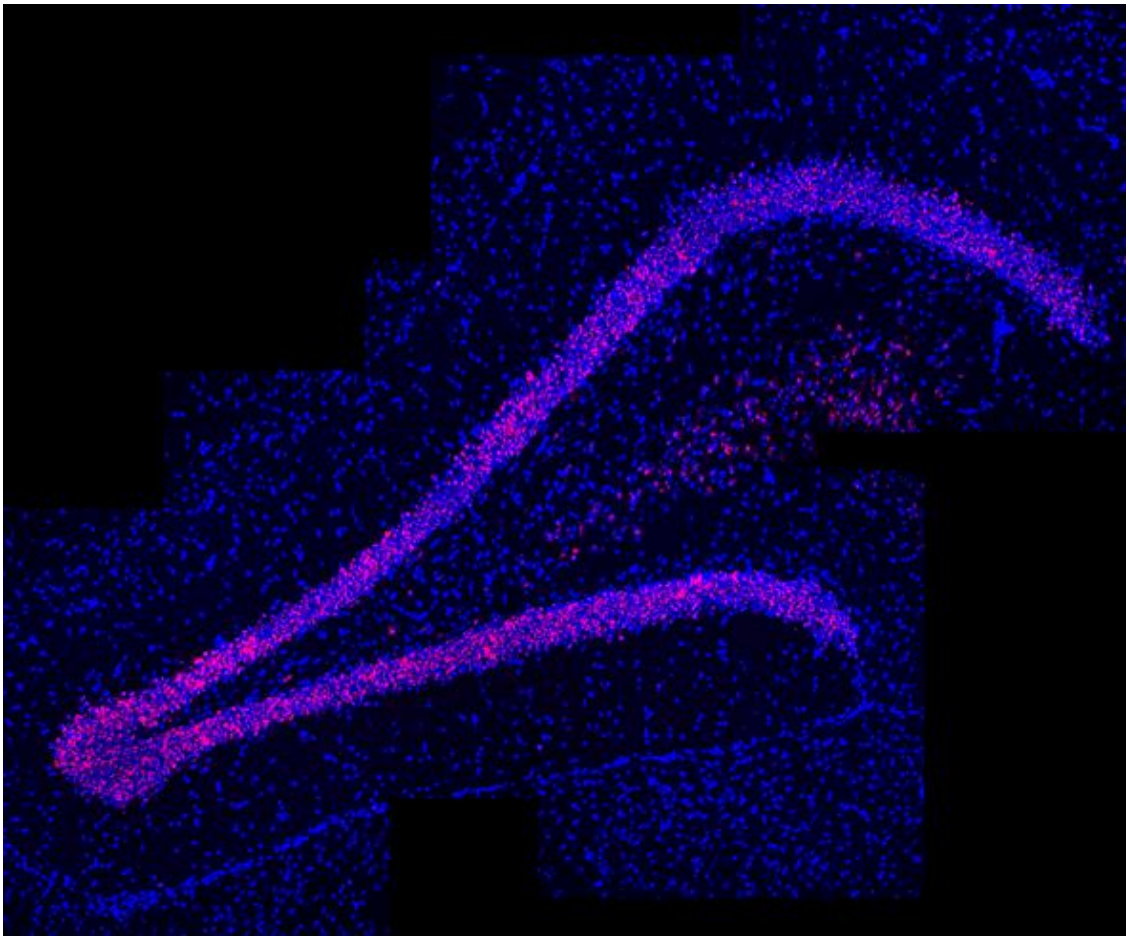
THE UNIVERSITY OF ARIZONA

Evelyn F. McKnight Brain Institute

Full Lives Through Healthy Minds

Annual Report 2021



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Life Sciences North Bldg.
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January 12, 2022

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 cognitive health.

Beginning with the challenges of 2021, this past year was difficult for many, as the pandemic continued to persist despite vaccinations being accessible, with many people (especially those over 65 years of age) getting fully vaccinated plus following up with a booster shot when they became available. The Tucson EMBI experienced no active covid-19 cases, nor were there any transmissions of the virus within laboratories across the entire University of Arizona. Obviously, the safety protocols set up by UA have been followed and have been very effective. The isolation (with most of us spending some time at home working, rather than being in the lab), and the change in social interactions this causes cannot be ignored and has had an impact on us all.

2021 was a spectacular year for the Director of the Tucson EMBI – and I believe for the McKnight Brain Research Foundation. The MBRF invested in the Tucson Director to help her achieve the 'impossible' – and for that I am grateful. The "impossible" I am referring to, is that I received 4 new grants in 2021. The first is a new NIA-supported RO1 to study NPTX2 (a possible "resilience" factor for the aging brain). The second is that my longest-running NIA-supported RO1 (since 1982) was renewed for 5 more years, and for the first time I will be studying aging rats, monkeys and humans all within the same grant. The third is that my Training Grant on the *Neurobiology of Aging and Alzheimer's Disease* got an outstanding score and will likely be approved by NIA Council this January, putting it into the group of grants that 'should be paid', assuming Congress agrees on a budget and does not drastically cut NIH funding.

Finally, the cornerstone achievement in 2021 was the funding of the $60M U19 grant, of which I am the PI. This enormous endeavor was truly a group effort – and we have 'made NIA history', in that the grant entitled "**Precision Aging Network: Closing the Gap Between Cognitive Healthspan and Human Lifespan**" is the first of its size to be supported with the primary purpose of better understanding the normative aging brain and cognition – by contrast, there are 33 Alzheimer's Research Centers supported in the US. The Precision Aging Network (PAN) aims to discover personalized solutions to maximize cognitive health in older individuals who do not have neurodegenerative diseases, and our methods are likely to also benefit those with AD and AD-related dementias. One of the PAN Projects involves in-depth assessments of individuals, based in Tucson, Miami, Baltimore, and Atlanta. Tucson and Miami EMBI faculty

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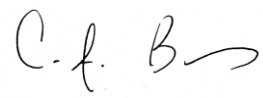
will focus on studying non-Hispanic White and Hispanic/Latino populations. We had hoped that the Birmingham EMBI would be able to participate in PAN as well, but it could not. The Baltimore and Atlanta groups will focus their in-depth testing on non-Hispanic White and Black participants in those two regions of the country. The PAN award was made at the end of September 2021, but the Executive Committee of PAN was able to have two productive monthly meetings in 2021 with the two Program Officers assigned our grant – Molly Wagster and Dana Plude. We began our monthly Steering Committee (comprised of the Executive Committee and all Leads and co-Leads of the 4 Projects and 7 Cores) meetings with our NIA Project Scientists (Jonathan King and Jennie Larkin) January 11, 2022. With these 4 NIA support staff guiding our progress, we have every reason to believe 2022 will be a productive year. The MBRF provided the foundation for the PAN award – promoting the importance of the scientific mission of understanding the normally aging brain – I am so grateful to Mrs. McKnight and her vision, and to the Trustees for their continued support!

The Tucson EMBI including its Director, co-Director and Affiliate Faculty have significant grant support, including many grants that were awarded in 2021. We will all be focusing on meeting the milestone targets for completing this funded work during 2022 and to publishing our results. Additionally, Tucson will be hosting the 13th Inter-Institutional meeting in 2022. During the past year we put together a tentative agenda for that meeting – which was reviewed by the Trustees, and by the Leadership Council. We have made appropriate revisions, and the meeting is set, with all but 2 speakers finalized. There is significant preparation that still needs to be done, and this will be a major future effort for the Tucson EMBI in 2022. The Director of the Tucson EMBI will coordinate the Leadership Council meetings through March 2022, and then will pass that duty onto the Gainesville EMBI group.

Respectfully signed January 12, 2022,



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

4. FY 2021 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.

Anandhan et al. (2021)

It is known that aging affects neural stem progenitor cell biology in fundamental ways. Madhavan has previously discovered that there is a critical period at which a decline in stem cell activity and function occurs during middle age in rats (13-15 months). This manuscript explores whether this decline in neural stem cell function in the olfactory bulb during aging can be rescued. They upregulated an important transcript factor involved in stem cell function (NRF2) at two time points, one before the critical period (11mo), and one after the critical period at 20 months. They found that stem cell proliferation, self-renewal, neurogenesis and migration to the olfactory bulb significantly increase following NRF2 upregulation in the 11-month rats past the typical critical period. By contrast, this treatment did not modulate stem cell function if given at the older age that was beyond the critical period, suggesting a critical time period for therapeutic intervention.

Fernandez et al. (2021)

This manuscript reviews the literature that pertains to the prevailing idea that circadian impairments associated with aging, are simply a byproduct of tissue degeneration within the central pacemaker in the brain – the suprachiasmatic nucleus. The extent to which this hypothesis is viable was examined. Contrary to this widely held view, in fact, the extant data suggest that the suprachiasmatic nucleus is a resilient brain region (little or no atrophy), which cannot be solely implicated in the behavioral manifestations of circadian disorganization often witnessed during aging. They then suggest specific experiments that can be done to examine the overall circadian system in aging in more detail, so that health outcomes can be improved in later adulthood.

Grilli et al. (2021)

This manuscript examines the increasing concern that older adults may be more susceptible to falling victim to “phishing” emails, which attempt to deceive a person into identity theft and fraud. They found that while older age was not related to a shift in overall perception of email safety, older age was related to worse discrimination between genuine and phishing emails, reflecting a difference in perceived suspiciousness. This could put older individuals at greater risk.

Liu et al. (2021)

This manuscript explored the possible mechanisms underlying interhemispheric functional connectivity that has been observed in aging individuals and aimed to determine if this difference possibly effected the inter-individual variability in response to transcranial magnetic stimulation (TMS) in older populations. They explored the baseline network properties of the sensorimotor system. In agreement with previous studies, older adults appear to recruit bilateral sensorimotor networks to maintain functionality, and thus exhibit higher levels of baseline interhemispheric functional connectivity. The pattern of results observed suggests that

those older individuals with lower interhemispheric functional connectivity might be able to elicit theta burst TMS more effectively than those with higher connectivity.

McAvan et al. (2021)

Older adults typically perform worse on spatial navigation tasks, although whether this is due to degradation of memory or an impairment in using specific strategies has yet to be determined. Most all previous studies have used desktop-based virtual reality technology that uses a mouse or joystick, that many older adults report lacking familiarity with. Here they used a wireless head-mounted display and free ambulation to create a fully immersive virtual Morris water maze to compare navigation in older and younger adults. Across different conditions tested, older adults remembered target locations less precisely compared to younger adults but used the same strategies as did younger adults to solve the problem. This finding is consistent with 'memory', not 'strategy use', being the primary driver of the age difference.

McQuail et al. (2021)

This manuscript grew out of collaborations generated at one of the NIA-sponsored Reserve and Resilience Workshops. It was clear to a group of us who study nonhuman animals that very few longitudinal experiments have been conducted in these species, while there are quite a few longitudinal studies conducted in humans. In order to 'truly define change' in an aging organism, it is optimal to study the same individual repeatedly. The goal of this review was to provide a resource for scientists using animal models of human aging who wish to implement this sort of design. These are the strongest methods to use for questions relating to cognitive reserve and brain maintenance.

Mendez et al. (2021)

This manuscript describes the results of a study on the intracellular parasite Toxoplamsa gondii, that is prevalent in people across the world, and that causes a long-term infection of neurons, that can occur across the lifespan. They developed a mouse model that allowed them to permanently mark neurons that contained parasite proteins. This allowed them to identify the cell type, and to record from neurons both 'with' and 'without' the parasite. They found that in cortex, parasite-infected neurons are primarily excitatory, while in the striatum the parasite was primarily associated with medium spiny GABAergic projection neurons. The infected neurons all had a highly aberrant electrophysiological profile. This study provides the first insights into which neurons interact with the parasite, and how neuron activity patterns are altered by this type of infection, giving clues for potential intervention strategies.

Talboom et al. (2021)

This manuscript reports the results from a large cross-sectional study of simple visual reaction time and paired associates learning. We used the MindCrowd web-based assessment tool to collect these data from 123,366 individuals between the ages of 18 and 85 years. The results demonstrate a linear decline in both reaction time and paired associates learning across the lifespan. The reaction time data from the MindCrowd cohort were validated using 247,582 individuals from the UK Biobank cohort who were between the ages of 40 and 70 years. Analyses revealed similarities between MindCrowd and the UK Biobank cohorts across most results. In the MIndCrowd cohort less education and smoking were related to additional slowing of reaction time from younger to older ages, and both cohorts replicated studies conducted in smaller populations in which men, overall, showed faster reaction times than women.

Van Etten et al. (2021)

This manuscript examined 190 cognitively healthy adults between the ages of 50 and 89 years, 60 of whom were APOE4 allele carriers. The extent to which brain volume changes are associated with the regional distribution of white matter hyperintensities was investigated. Their findings indicate that in cognitively healthy older adults, elevated white matter intensity volume, specifically in the hippocampus and temporal lobes (but not frontal, parietal or occipital lobes), was associated with reduced hippocampal volume and this effect was moderated by APOE4 status, suggesting greater vulnerability to brain aging in these individuals.

Wank et al. (2021)

It is well known that episodic autobiographical memory retrieval is reduced in older individuals. This manuscript explores the reasons for this age-related change. They found that older adults engaged in direct retrieval of the episodic autobiographical events less than did young adults and were less able to elaborate these evens with internal details. This suggests that both of these mechanisms play a role in the age-related change in retrieval of this type of memory.

Most important MBRF-relevant scientific achievements of FY21

The 20 most relevant publications from EMBI Affiliate Faculty is listed in Appendix 2, and the significant new grants that were funded to members of the Tucson EMBI are listed in Section 6 (pages 8-12).

MBI Budget and Endowment Investment Reports

See pages 17-22 for Budget and Endowment Investment Reports

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) **Cohen** (UF), **Visscher** (UF), **Wright** (UM); Collaborators: **Huentelman** (UM), **Trouard** (UA), **Woods** (UF)
Project Title: McKnight Inter-institutional Neuroimaging Core and Brain Aging Registry
Sponsor: McKnight Brain Research Foundation
Project Dates: 01/01/15 – 12/31/21
Description: The goal of this project is to establish standardized neuroimaging acquisition and a multi-institutional brain aging registry to support brain aging research.

Investigators: **Alexander** (UA) **Cohen** (UF), **Huentelman** (UM), **Wadley** (UAB); Collaborators: **Visscher** (UF), **Trouard** (UA), **Woods** (UF)
Project Title: McKnight Inter-institutional Cognitive Aging Assessment Core
Sponsor: McKnight Brain Research Foundation
Project Dates: 09/01/15 – 12/31/21
Description: The goal of this project is to provide standardized clinical and cognitive measures for multi-institutional brain aging research.

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.

6. Honors, Award and New Grants

Honors and Awards

Matthia Mehl Commencement Speaker, Department of Psychology, Friedrich-Alexander University, Erlangen, Germany, 2021

Dave Sbarra was offered and has now accepted an invitation to become the next Editor-in-Chief of the APS journal Advances in Methods and Practices in Psychological Science (AMPPS). Dave's four-year term will begin on January 1, 2022.

New Grants

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), **Levin** (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 (ADRD). 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: PI: **Barnes** (UA); Co-Investigators: **Huentelman** (TGen), Worley (JHU), Serrano (BSHRI)
Project Title: NPTX2: Preserving memory circuits in normative aging and Alzheimer's Disease
Sponsor: NIH/NIA R01 AG072643
Project Dates: 05/01/2021 – 04/30/2026
Total Award: $5,719,524
Description: We have demonstrated that NPTX2, a marker of the information storage process, correlates with cognitive performance in humans during normative aging and in the context of Alzheimer’s disease. Studies will examine the impact of NPTX2 reduction in human brain specimens and in neuronal circuits modeled in vitro using RNA and protein profiling, and the functional consequence of NPTX2 reduction on cognitive and behavior-linked circuit

function using innovative rat models, and will provide fundamental new insights into memory, cognitive resilience, aging, and Alzheimer's disease.

Investigator: PI: **Barnes** (UA); Co-Investigators: **Ekstrom** (UA), Bales (UC Davis)
Project Title: Neurobehavioral Relations in Senescent Hippocampus
Sponsor: NIH/NIA R01 AG003376
Project Period: 09/30/2021 – 05/31/2026
Total Award: $4,821,974
Description: There are three primary aims of this grant, each exploring how brain circuits responsible for spatial cognition are altered during the aging process. In rat experiments we use a novel behavioral task (the Instantaneous Cue Rotation task), and dual-structure recordings (hippocampus and medial entorhinal cortex) to examine the dynamics of the bidirectional communication between these two structures, and how this changes with age. In monkey experiments we directly compare the firing properties of ensembles of hippocampal cells using telemetric recording methods in young and old monkeys who are completely free from restraint. In the human experiments we use immersive virtual reality and high-resolution fMRI to examine hippocampal and entorhinal cortical activity in young and older adults. The overall goal of this research program is to reveal neural circuit changes that explain altered spatial cognition with age and to determine the extent to which these properties are conserved across mammals.

Investigators: Co-investigator: **Barnes** (**Reiman** PI)
Project Title: Arizona Alzheimer's Disease Core Center Administrative Core
Sponsor: NIH/NIA P30 AG072980
Project Period: 09/05/2021 – 06/30/2026
Total Award: $127,405 (UA Admin Core Subaward)
Description: Dr. Barnes will administer the Arizona Alzheimer's Disease Research Center (ADRC) Development Grant Program, coordinating the review process for funding of two development projects per year. Dr. **Barnes** also serves as Chair of the Internal Scientific Advisory Committee for the Arizona Alzheimer's Consortium which meets on a regular basis, rotating between Tucson and Phoenix area meeting sites.

Investigator: PI: **Barnes** (co-investigators: **Trouard,** Hutchison)
Project Title: An analysis of high-resolution ex vivo MRI data from aging macaque brains to estimate white matter microstructure and align histological atlases with MRI images.
Sponsor: Department of Health Services, State of Arizona
Project Period: 07/01/2021 - 06/30/2022
Total Award: $44,161
Description: This grant is to create monkey-specific quantitative anatomical maps (in MRI space) of white matter anisotropy (DTI maps), macromolecular content (BPF maps), and myelin water fraction (MWF maps) for 12 bonnet macaques across the lifespan. We are doing this on the images we have taken using high-resolution ex vivo MRI imaging procedures. With these data we will perform probabilistic tractography analyses to assess the relationship between the quantitative MRI measures listed above and our estimates of cognitive and sensory function.

Investigator: Co-investigators: **Alexander, Ahern, Rapcsak, Trouard** (**Reiman** PI)
Project Title: Arizona Alzheimer's Disease Research Center Biomarker, Clinical, Data Management and Statistics Cores
Sponsor: NIH/NIA P30 AG072980
Project Period: 09/05/2021 – 06/30/2026
Total Award: $1,856,362 (UA Subaward)
Description: The Arizona Alzheimer's Disease Core Center (ADCC) is the nation's most comprehensive example of statewide collaboration in AD research. It capitalizes on its leadership, shared scientific resources, and collaborative model to advance the study of AD, related disorders, and the aging mind and brain; Its researchers have helped to launch a new era in AD prevention research and are trying to find and support FDA approval of effective prevention therapies within the next ten years.

Investigators: Co-investigator: **Alexander** (Weinkauf,PI)
Project Title: Extracranial Carotid Atherosclerosis Contributions to Cognitive Impairment and Alzheimer's Disease Risk
Project Number: NIH/NIA R01 AG070987
Project Period: 8/15/2021-5/31/2026
Total Award: $4,900,000
Description: The goal of this project is to investigate how carotid artery disease influences the risk for Alzheimer's disease

Investigator: PI: **Alexander** (co-investigators: Atri, Beach, Caselli, Su, **Huentelman**, Klimentidis, **Rapcsak**, **Reiman**, **Trouard**)
Project Title: Lifestyle/Physical Activity Biomarkers in Brain Aging & Alzheimer's Disease Risk
Sponsor: Department of Health Services, State of Arizona
Project Period: 07/2021-06/2022
Total Award: $48,000
Description: Understanding which measures of physical activity and sleep quality provide highly sensitive lifestyle and behavioral biomarkers for brain aging and Alzheimer's disease risk..

Investigators: Multi-PI: **Andrews-Hanna, Mehl, Sbarra**
Project Title: Connected Lives - Overcoming the Self through Empathy (CLOSE): A dyadic, multi-method study
Sponsor: NIH NIMH R01MH125414
Project Period: 04/01/2021 – 01/31/2026
Total Award: $2,925,543
Description: This proposal examines a new model that combines the ideas that overall mental health depends on the extent to which repetitive negative thinking can be avoided, and high-quality social relationships promoted. By examining these factors in combination, the goal is to identify and promote healthier mental and physical outcomes, which is, of course of potential therapeutic benefit to brain and cognitive health in aging.

Investigator: PI: **Brinton**; co-investigators: Rodgers, Yin, Mosconi, Reyes-Reyes, Vitali, Wang
Project Title: Perimenopause in Brain Aging and Alzheimer's Disease
Sponsor: NIH/NIA 2P01AG026572

Project Period: 06/01/2021 – 05/31/2026
Total Award: $5,168,816
Description: Worldwide women have a 2-fold greater risk for developing Alzheimer's disease. The mission of the Perimenopause in Brain Aging and Alzheimer's Disease Program Project is to discover why women are at greater risk for Alzheimer's and based on that knowledge, create therapeutic strategies to prevent or delay development of Alzheimer's disease. Further, our strategy provides a platform for a precision medicine approach to treating Alzheimer's in both women and men.

Investigator: PI: **Chou** (PI)
Project Title: Development of MRI-Compatible TMS Protocols for Adults with Mild Cognitive Impairment
Sponsor: Core Facility Pilot Program, RII, University of Arizona
Project Period: 11/2021 - 11/2022
Total Award: $10,000
Description: Support for concurrent TMS-fMRI studies.

Investigator: PI: **Chou**
Project Title: Feasibility Study for the Mild Cognitive Impairment with Accelerated Transcranial Magnetic Stimulation
Sponsor: Department of Health Services, State of Arizona
Project Period: 07/01/2021 - 06/30/2022
Total Award: $30,000
Description: The purpose of this study is to determine the feasibility of accelerated transcranial magnetic stimulation for patients with mild cognitive impairment and test the therapeutic efficacy.

Investigator: PI: **Chou**
Project Title: Request for MRI-Compatible Transcranial Magnetic Stimulation (TMS) System: Development of a Novel Concurrent TMS-fMRI Method to Reveal Real-Time TMS-Induced Brain Activities
Sponsor: Office of Research, Innovation and Impact, University of Arizona
Project Period: 2/2021- 6/2021
Total Award: $150,000
Description: Funds for enhancement of equipment to purchase an MRI-compatible TMS system for concurrent TMS-fMRI studies.

Investigator: PI: **Cowen**
Project Title: Control of the Time Course of Dopamine Release through Optimized Electrical Brain Stimulation
Sponsor: NIH/NINDS R01 NS122725
Project Period: 09/15/21 – 08/31/24
Total Award: $1,833,908
Description: Develop new ways to use electrical deep brain stimulation for the precise control on tonic (slow) and phasic (fast) dopamine release in the brain. Disrupted tonic and phasic dopamine release underlies addiction, depression, Parkinson's disease.

Investigator: Co-investigator: **Cowen** (Miller PI)

Project Title: Alpha-Synuclein Driven Cellular Changes and Vocal Dysfunction in Parkinson's Disease
Sponsor: NIH/NINDS R21 NS123512
Project Period: 07/01/21 – 06/30/23
Total Award: $314,213
Description: Characterize the genetic and electrical brain activity during the early parkinsonian vocal deficits in an animal model.

Investigator: Co-investigator: **Cowen** (Falk PI)
Project Title: Mechanisms of Low-Dose Ketamine Treatment in Parkinson's Disease
Sponsor: NIH/NINDS RO1 NS122805
Project Period: 07/01/21 – 06/30/25
Total Award: $1,861,435
Description: Identify the circuit and single-neuron properties that drive Parkinson's disease

Investigator: Co-investigator: **Cowen** (Porreca PI)
Project Title: The Center of Excellence in Addiction Studies (CEAS)
Sponsor: NIH/NIDA
Project Period: 08/15/21 – 05/31/27
Total Award: $614,274 (Cowen component)
Description: Develop core facilities at the UA to support research at the intersection of addiction and pain management. Cowen role is to develop a pilot core that encourages de-novo research and ultimately leads to NIDA R01 applications.

Investigator: PI: **Cowen** (co-investigator: **Barnes**)
Project Title: Investigation of age-assocated changes in neural coordination and plasticity using advanced high-density neural-ensemble recording technologies
Sponsor: Department of Health Services, State of Arizona
Project Period: 07/01/2021 - 06/30/2022
Total Award: $29,000
Description: Advanced large-scale neural recording for the study of cognitive decline in aging through application of 1000-site neural recording technologies.

Investigator: PI: **Hay** (co-investigators: Konhilas, **Ryan,** Sweitzer)
Project Title: Pilot Study on the Safety and Efficacy of Angiotensin (1-7) for Cognitive Impairment in Heart Failure Patients at Risk for Vascular Dementia and Alzheimer's Disease Related Dementias
Sponsor: Department of Health Services, State of Arizona
Project Period: 07/01/2021 - 06/30/2022
Total Award: $49,300
Description: Determine if plasma neurofilament light protein (Nfl) might serve as a Prognostic Biomarker in early Vascular Cognitive Impairment and Dementia (VCID) and Alzheimer's Disease Related Dementias (ADRD) in individuals with stage II/IV heart failure (HF)

Investigator: Co-investigator: **Huentelman** (Velazquez PI)
Project Title: Identify common mechanisms of neurodegeneration between Alzheimer's disease and Down syndrome
Sponsor: NIH/NIA R01 AG059627 (TGen subaward)

Project Period: 09/01/2021 – 08/31/2022
Total Award: $101,943
Description: Dr. Huentelman and his team will perform both RNA and methylated DNA sequencing and analysis of 20 samples from experimental animals.

Investigator: PI: **Huentelman**
Project Title: MindCrowd: Development of additional internet-based cognitive tasks and enhanced recruitment of underrepresented minority groups
Sponsor: Department of Health Services, State of Arizona
Project Period: 07/01/2021 – 06/30/2022
Total Award: $100,000
Description: We plan to continue to enhance recruitment of these underserved groups and further explore novel ways to recruit additional facets of the general population into MindCrowd

Investigator: Co-investigator: **Huentelman** (Rogalski PI)
Project Title: Study to uncover pathways to exceptional cognitive resilience in aging (SUPERAging)
Sponsor: NIH/NIA U19 AG073153 (Northwestern University)
Project Period: 07/01/2021 – 06/30/2026
Total Award: $4,468,896 (TGen subaward)
Description: The goal of this grant is to identify factors that promote preservation of unusually strong memory capacity in advanced age. Dr. **Huentelman** and his team will generate and analyze molecular data from human blood and brain tissue specimens.

Investigators: co-investigator: **Huentelman** (Ebner PI)
Project Title: Uncovering and Surveilling Financial Deception Risk in Aging – Alzheimer's Disease Supplement
Sponsor: NIH/NIA R01AG057764-Supplement (University of Florida)
Project Period: 07/01/2021 – 06/30/2022
Total Award: $57,992 (TGen subaward)
Description: Perform APOE genotyping on dried blood spot or saliva specimens and enable and participate in the recruitment of MindCrowd participants into the existing study task paradigms.

Investigators: PI: **Grilli, Wilson**
Project Title: A Neuroeconomic Model of Phishing Email Susceptibility: Examining Drivers of Successful Email Attacks Across Middle to Older Age
Sponsor: UAHS Strategic Initiative 3.3, Healthy Aging Seed Grant
Project Period: 06/01/2021 - 05/31/2022
Total Award: $25,000
Description: The major goal of this project is to investigate the neural bases of email scam-related decision making

Investigators: PI: **Mehl**
Project Title: Large-scale, Long-term Data Collection and Analysis to Predict Performance and Social/Physical Activity
Sponsor: Army Research Labs CA W911NF2120197
Project Period: 09/01/2021 – 09/30/2023
Total Award: $341,982

Description: The goal of this project is to understand the dynamic patterns of behavior and decision making occurring across an individual's daily, weekly and monthly life by collecting and analyzing intensive mobile sensing data. The methods developed here will be extremely useful for collaborative experiments designed by EMBI faculty going forward.

Investigators: Co-investigator: **Mehl** (Ruiz PI)
Project Title: Ethnicity and Lung Cancer Survival: A Test of the Hispanic Sociocultural Hypothesis
Sponsor: NIH NCI R01 CA262719
Project Period: 07/01/2021 – 06/30/2026
Total Award: $3,179,543
Description: Hispanic patients with lung cancer have markedly lower age-adjusted death rates than their non-Hispanic white counterparts, in spite of being diagnosed at later stages and having broader SES and healthcare disparities. This is consistent with the so-called "Hispanic Health Paradox", characterized by Hispanic advantages in a range of health outcomes (including longevity in normative aging). This project aims to identify a range of potential protective factors that contribute to this paradox, a question that many EMBI faculty are particularly interested in.

Investigator: PI: **Ryan** (co-investigators: **Hay**, Parthasarathy, Altin, **Huentelman**)
Project Title: Evaluating Neurofilament Light Protein as a Marker of Neuronal Damage in Older Adult Survivors of SARS-CoV2
Sponsor: Department of Health Services, State of Arizona
Project Period: 07/01/2021 – 06/30/2022
Total Award: $42,000
Description: This project is designed to investigate neurofilament light protein related to cognitive function in patients who have had SARS-CoV2

Investigator: PI: **Ryan**
Project Title: Expanding Pipelines and Data Sharing Resources for MRI Analyses for Studies of Aging and Alzheimer's Disease at the University of Arizona
Sponsor: Department of Health Services, State of Arizona
Project Period: 07/01/2021 – 06/30/2022
Total Award: $92,500
Description: This project will improve the imaging resources at the University of Arizona by providing pipelines and equipment to conduct neuroimaging analysis

Investigator: Co-investigator: **Trouard** (PI: Morrison)
Project Title: NanO2 as a Cerebroprotectant in a tMCAO Stroke Model in Mice
Project Number: NIH/NINDS R41 NS124450
Project Period: 9/15/2021 - 8/31/2022
Total Award: $478,050
Description: The proposed preclinical study using a transient middle cerebral artery occlusion mouse model will address the gaps in the preclinical data for NanO2 so that the drug can be further advanced clinically and be more competitive as a candidate for organizations supported by the NIH, such as the StrokeNet.

Investigator: PI: **Trouard** (co-investigators: Alexander, Barnes, Sierks)

Project Title: Imaging and Therapy in Rodent Models of Aging, Alzheimer's Disease and Parkinson's Disease
Sponsor: Department of Health Services, State of Arizona
Project Period: 07/01/2021 – 06/30/2022
Total Award: $44,000
Description: Adapt the most promising MRI microscopy techniques from our R03 project for in-vivo human MRI as a demonstration of feasibility.

Investigator: PI: **Wilson** (co-investigators: **Grilli, Huenelman, Andrews-Hanna**)
Project Title: Phishing emails and aging: Understanding brain and cognitive factors associated with susceptibility to email scams
Sponsor: Department of Health Services, State of Arizona
Project Period: 07/01/2021 – 06/30/2022
Total Award: $30,000
Description: This project seek to advance our understanding of why older adults fall for phishing emails.

7. Technology Transfer

Brinton: US20170258810A1 was allowed this year. It doesn't have a patent number yet but the issue fee was just paid so will get a number shortly. No actual filings in 2021, just disclosures to TLA.

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

Pau S., Grandner M.A., **Fernandez F.,** and Mason B.J. Blue Enhancer Glasses.cAttorney Docket: 044974-8066.US00 (UA21-175). 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) 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) 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). U.S. Patent Application No. 63/225, 848

Madhavan: US patent no: 1109173
A biomarker platform for Parkinson's disease using patient-derived primary dermal fibroblasts"
Issue date: 08/24/21

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

No

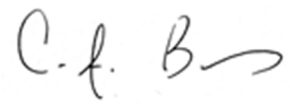
9. Do you recommend any modification to the Purpose or mandates in the Gift Agreement?

No

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

Yes

Respectfully Submitted,



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

McKnight Brain Research Foundation
Financial Summary for the

McKnight Brain Institute Endowed Chair at
The University of Arizona
As of June 30, 2022

For the period July 1, 2020 to June 30, 2021

Date of the Gift		November 1, 2006
MBRF Contribution	$	1,000,000
Match (Development Fee Paid by UA)	$	60,000 *
Transfers from other University Fund	$	N/A
For Period July 1, 2020 – June 30, 2021		
Investment Return	$	219,879
Distributions for Spending	$	35,632
June 30, 2021 Balance	$	997,179
Unmatched Balance	$	N/A

* Balance of Match ($940,000) was distributed to Quasi Endowment

Evelyn F. McKnight Chair for Learning and Memory in Aging

Summary for 12 months ending June 30, 2021

A.	Beginning Balance on July 1, 2020	$	812,932
B.	Investment Growth	$	219,879
C.	Distributions to Expendable Account	$	(35,632)
D.	Additional Contributions	$	0
E.	Ending Balance on June 30, 2021	$	997,179

McKnight Brain Research Foundation
Financial Summary for the

McKnight Brain Institute Quasi Endowment at
The University of Arizona
As of June 30, 2022

For the period July 1, 2020 to June 30, 2021

Date of the Gift		August 1, 2007 August 1, 2008 August 1, 2009 August 1, 2010
MBRF Contribution	$	$4,000,000
Match	$	$4,960,000
Transfers from other University Fund	$	N/A
For Period July 1, 2020 – June 30, 2021		
Investment Return	$	$161,070
Distributions for Spending	$	777,084
June 30, 2021 Balance	$	279,602
Unmatched Balance	$	N/A

Evelyn F. McKnight Brain Institute Quasi Endowment

Summary for 12 months ending June 30, 2021

A.	Beginning Balance on July 1, 2020	$	895,616
B.	Investment Growth	$	161,070
C.	Distributions to Expendable Account	$	(777,084)
D.	Additional Contributions	$	0
E.	Ending Balance on June 30, 2021	$	279,602

McKnight Brain Research Foundation
Financial Summary for the

McKnight Brain Institute Permanent Endowment at
The University of Arizona
As of November 30, 2021

For the period July 1, 2021 to November 30, 2021

Date of the Gift		September 30, 2015 September 30, 2016 September 30, 2017 September 30, 2018 September 30, 2019
MBRF Contribution	$	$5,000,000
Match	$	$4,026,973
Transfers from other University Fund	$	42,767
For Period July 1, 2021 – June 30, 2021		
Investment Return	$	$505,540
Distributions for Spending	$	157,072
June 30, 2021 Balance	$	10,858,211
Unmatched Balance	$	973,027

THE UNIVERSITY OF ARIZONA
Foundation

University of Arizona Foundation
Evelyn F. McKnight Brain Institute Endowed

SCNC - College of Science
0423 – Psychology

Financial Report for the 2022 Fiscal Year
Activity for the Period July 01, 2021 - November 30, 2021

Fund Number: 40-10-4500

Fund Performance

Financial Summary

Beginning market value at 7/1/2021	$	10,414,353.74
Investment performance		505,540.44
Endowment payout		(157,072.07)
Endowment fee		(49,732.29)
New gifts and additions		145,121.03
Ending market value at 11/30/2021	**$**	**10,858,210.85**
Historical gift value at 11/30/2021	**$**	**8,852,973.18**

Historical Gift Value consists of:

McKnight Foundation Gifts Net of UDF	4,826,000.00
UAF/Matching Gifts Net of UDF	4,026,973.18
	8,852,973.18

University Earnings Shortfall Match made in FY 2021 **42,767**

12. Appendix 1

List of McKnight Affiliate Faculty and their area of focus and Department Affiliations.

No new Affiliate Faculty were appointed in the Tucson EMBI in 2021, 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., Assistant 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 bioenergtic 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., Assistant 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., Assistant 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., Head, Neurobehavioral Research Unit, 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.

David A. Sbarra, Ph.D., Professor, Psychology, UA

Area of Focus: He studies how high-quality social relationships are positively associated with increased life satisfaction and psychological wellbeing across the lifespan, and are negatively associated with illness and death from a range of diseases. His laboratory studies why, and in what contexts relationships promote or hinder good health.

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

Geoffrey L. Ahern, M.D., Ph.D., Professor, Neurology, Psychology and Psychiatry, UA
Heather Bimonte-Nelson, Ph.D., Associate Professor, Psychology, ASU
Paul Coleman, Ph.D., Research Professor, Biodesign Institute, 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., Assistant Professor, Neurology, UA
Lalitha Madhavan, M.D., Ph.D., Assistant 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., Sage Therapeutics, Massachusetts

Predoctoral Trainees

Monica Acevedo-Molina (Grilli)
Area of interest: Role of bilingualism in cognitive aging.

Jesse Altemus (Brinton)
Area of interest: Role of autoantibodies and microbiomes in pathogenesis.

Eric Andrews (Andrews-Hanna)
Area of Interest: Emotion-cognition interactions at differing levels of brain and behavior.

Kelsey Bernard (Madhavan)
Area of Interest: Glycosylated peptides as therapeutic candidates for Parkinson's disease.

Pradyumna Bharadwaj (Alexander)
Area of Interest: Applications of multimodal brain imaging in the study of cognitive aging.

Avnish Bhattrai (Brinton)
Area of interest: Utilizing neuroimaging and informatics tools to study the metabolic as well as structural changes in the brains of translational animal models for Alzheimer's disease.

Greg Branigan, (Brinton)
Area of interest: MD, PhD Program: Medical informatics and systems biology for estrogen biology in Alzheimer's disease prevention.

Yu-Chin Chen, (Chou)
Area of Interest: Development of image-guided TMS treatment for mild cognitive impairment.

Yu Jung Chen (Barnes)
Area of Interest: Assessing network stability in the aging hippocampus and entorhinal cortex using molecular imaging methods.

Patricia Chilton (Grilli, Mehl)
Area of interest: The cognitive aging of wisdom.

Lizzie Church (Barnes)
Area of interest: Electrophysiology of memory and aging.

Andrea Coppola (Andrews-Hanna and Sbarra)
Area of Interest: Neural underpinnings of self and other-focused thought, with relation to mental health

Helena Cortes Flores (Brinton)
Area of interest: Sex differences in mechanisms underlying prodromal late-onset Alzheimer's disease endophenotype.

Nicole Delatorre (Brinton)
Area of interest: Alzheimer's Disease biomarkers and immune infiltration into the brain.

Loi Do (Trouard)
Area of interest: Anatomical and diffusion MRI of rodent models of aging.

Hannah Dollish (Fernandez)
Area of Interest: Seasonality of circadian photo-responses.

Sydney Friedman (O'Connor)
Area of interest: Anatomical and Diffusion MRI of rodent models of hypertension.

Nathaniel Gallegos (Ryan)
Area of Interest: Family history of Alzheimer's disease among Hispanics.

Gabriel Holguin (Cowen)
Area of Interest: Neural systems involved in memory formation and motor control.

Mariam Hovhannisyan (Andrews-Hanna and Grilli)
Area of interest: Cognition and brain aging.

Hannah Johnson (Koshy)
Area of Interest: Understanding *in vivo* neuron immune responses using *Toxoplasma gondii*.

Josh Kochanowsky (Koshy)
Area of Interest: Role of ROP16 in lytic and latent cycles of type III *T. gondii* strain.

Yilin Liu (Chou)
Area of Interest: Development of image-guided TMS treatment for memory enhancement.

Stephanie Matijevic (Ryan)
Area of Interest: Genetic, health and socio-motivational factors influencing neurocognitive changes in normal aging.

Kelsey McDermott (Barnes)
Area of interest: Understanding how the locus coeruleus contributes to age-related cognitive deficits in an aging nonhuman primate model.

Will McLean (Brinton)
Area of interest: Genetic, gender, and metabolic risk contributors to Alzheimer's disease pathology from the single-cell to systems biology level and potential therapeutic interventions based on those approaches.

Aiden McRobbie-Johnson (Madhavan)
Area of Interest: Phenotyping Parkinson's disease in patient-derived cells.

Katie McVeigh (Grilli)
Area of interest: Social and cognitive aging.

Oscar Mendez (Koshy)
Area of interest: Defining neuronal subtypes and electrophysiological properties of *Toxoplasma gondii* interacted neurons (Ph.D. received 2021).

Emily Merritt (Koshy)
Area of interest: Role of GRA15 in driving type II survival *in vivo.*

Jack-Morgan Mizell (Wilson)
Area of interest: Decision making and aging.

Devin Murphy (Trouard)
Area of interest: Enhancing drug delivery to the brain using MRI-guided focused ultrasound.

David C. Negelspach (Fernandez)
Area of Interest: Scaling circadian responses to millisecond administration of LED light – implications for aging.

Justin Palmer (Ryan)
Area of Interest: Understanding how genetic and health factors impact cognitive and brain aging.

Quentin Raffaelli (Andrews-Hanna)
Area of Interest: Spontaneous thought and creativity.

Ramamoorthy Rajashree (Cowen)
Area of interest: Advanced technologies for the measurement of neural activity and dopamine release.

Hyun Song (Alexander)
Area of Interest: Neural mechanisms of individual differences in cognitive aging.

Samantha Smith (Alexander)
Area of Interest: Actigraphy and cognition in normal and pathological aging.

Sahana Srivathsa (Barnes).
Area of interest: Age-related changes of signals involved in spatial memory and decision making.

Mark Sundman (Chou)
Area of Interest: Cortical excitability and plasticity in adults with and without cognitive impairment.

Georgina Torrandell Haro (Brinton)
Area of interest: Statin therapy and risk of Alzheimer's and age-related neurodegenerative diseases.

Emily Van Etten (Alexander)
Area of Interest: Effects of healthy aging on memory and brain structure.

Hannah Van Rossum (Brinton)
Area of interest: Activation of the neuroimmune system in midlife aging and Alzheimer’s disease.

Abhilasha Vishwanath (Cowen)
Area of interest: Neural basis of Parkinson's disease and its treatment with L-DOPA and ketamine.

Aubrey Wank (Grilli)
Area of interest: Autobiographical memory and aging.

Da'Mere Wilson (O'Connor)
Area of interest: Interactions between social stress, grief, and health outcomes.

Jingming Xue (Wilson)
Area of interest: Computational modeling of perceptual decisions.

Marc Zempare (Barnes)
Area of interest: Understanding the role of NPTX2 as a resilience factor in the aging rat brain.

Postdoctoral Trainees

Anandhan Annadurai, Ph.D. (Madhavan)
Area if Interest: Role of Nrf2 in Aging and Parkinson's disease.

Monica Chawla, Ph.D. (Barnes)
Area of Interest: Immediate early gene expression in aging in the rat medial temporal lobe.

Daniel Gray, Ph.D. (Barnes)
Area of Interest: Circuits and synapses involved in cognitive decline in a non-human primate model of aging.

Wayne Jepsen, Ph.D. (Huentelman)
Area of Interest: Genetic factors associated with familial late-onset Alzheimer's disease.

Adam Lester, Ph.D. (Barnes)
Area of Interest: Spatial computations made by the hippocampus and entorhinal cortex and how this changes in aging rats.

Candace Lewis, Ph.D. (Huentelman)
Area of Interest: Genetic, epigenetic, and environmental factors associated with differential trajectories of childhood cognitive development.

Koeun Lim, Ph.D. (Chou)
Area of Interest: Development of data analysis pipeline for TMS studies.

Erin Maresh, Ph.D. (Andrews-Hanna)
Area of interest: Neural underpinnings of self and other-focused thought, with relation to mental health.

Kathyrn McGovern, Ph.D. (Koshy)
Area of interest: Using Toxoplasma gondii to define neuroinflammatory responses in the aging brain.

Caroline Phelps, Ph.D. (Wilson)
Area of Interest: Decision making and aging.

Kathryn Post, Ph.D. (Huentelman)
Area of Interest: High-throughput and high-content screening of genomic factors that modify mitochondrial disease cellular phenotypes.

Chandrasekaran Sambamurthy, Ph.D. (Koshy)
Area if Interest: Using Toxoplasma gondii to define neuroinflammatory responses in the aging brain.

Irina Sinakevitch, Ph.D. (Barnes)
Area of Interest: Understanding the role of different subcomponents of the locus coeruleus to cognitive changes that occur in an aging nonhuman primate model.

Teodora Stoica, Ph.D., (Andrews-Hanna, Grilli)
Area of interest: Emotion, aging and brain network connectivity.

Joshua Talboom, Ph.D. (Huentelman)
Area of Interest: Demographic, lifestyle, environmental, and medical factors associated with differential cognitive aging in non-demented individuals.

13. Appendix 2

Top 20 publications from FY 21 relevant to MBRF

These 20 publications include 19 Affiliate Faculty from the Tucson EMBI, and 9 faculty from the other EMBI Institutes, attesting to the collaborative nature of McKnight Faculty.

Anandhan A, Kirwan KR, Corenblum MJ, and **Madhavan L**. (2021) Enhanced Nrf2 expression mitigates the decline in neural stem cell function during aging. **Aging Cell**. Jun;20(6):e13385. PMCID: PMC8219498.

Boutzoukas EM, O'Shea A, Albizu A , Evangelista ND, Hausman HK, Kraft JN, Van Etten E, Bharadwaj PK, Smith SG, Song H, Porges E, Hishaw A, Dekosky S, Wu SS, Marsiske M, **Alexander GE, Cohen R, Woods AJ.** (2021) Frontal white matter hyperintensities and executive functioning performance in older adults. **Frontiers in Aging Neuroscience**, 13, 338.

Dagliati A, Peek N, **Brinton RD,** Geifman N. (2021) Sex and APOE genotype differences related to statin use in the aging population. Alzheimers Dement (NY). May 2;7(1):e12156. doi: 10.1002/trc2.12156. **eCollection** 2021. PMID: 33969178. PMCID: PMC8088592

Evangelista ND, O'Shea A, Kraft JN, Hausman HK, Boutzoukas EM, Nissim NR, Albizu A, Hardcastle C, Van Etten EJ, Bharadwaj PK, Smith SG, Song H, Hishaw GA, **DeKosky S**, Wu S, Porges E**, Alexander GE,** Marsiske M, **Cohen R, Woods AJ. (**2021) Independent contributions of dorsolateral prefrontal structure and function to working memory in healthy older adults. **Cerebral Cortex**, 31, 1732-1743.

Fernandez F-X., Kaladchibachi S., and Negelspach D.C. (2021) Resilience in the suprachiasmatic nucleus: Implications for aging and Alzheimer's disease. **Experimental Gerontology**, 147: 111258.

Flores M, Ruiz JM, Butler EA, **Sbarra DA,** Garcia DO, Kohler L, Crane TE, Corbie-Smith G, Benavente V, Kroenke CH, Saquib N, Thomson CA Does the Hispanic Mortality Advantage Vary by Marital Status Among Postmenopausal Women in the Women's Health Initiative? **Ann Behav Med.** 2021 Jun 28;55(7):612-620. doi: 10.1093/abm/kaaa113.

Glisky, E.L., Alexander, G.E., Hou, M., Kawa, K., Woolverton, C.B., Zigman, E.K., Nguyen, L.A., Haws, K., Figueredo, A.J., **Ryan, L.** (2021). Differences between young and older adults in unity and diversity of executive functions. **Neuropsychol Dev Cogn B Aging Neuropsychol Cogn**. 8:1-26.

Grilli, M.D., McVeigh, K.S., Wank, A.A., Hakim, Z.M., Getz, S.J., **Levin, B.E., Ebner, N.C., & Wilson, R.C.** (2021). Is this phishing? Older age is associated with greater difficulty discriminating between safe and malicious emails. **Journal of Gerontology: Psychological Sciences,** 76 (9), 1711-1715.

Grilli MD, Wank AA, **Huentelman MJ, Ryan L.** Autobiographical Memory Fluency Reductions in Cognitively Unimpaired Middle-Aged and Older Adults at Increased Risk for Alzheimer's Disease Dementia. **J Int Neuropsychol Soc.** 2021 Oct;27(9):905-915. doi: 10.1017/S1355617720001319. Epub 2021 Jan 29

Hooyman A, Talboom JS, DeBoth MD, **Ryan L**, **Huentelman MJ,** Schaefer SY. (2021) Remote, Unsupervised Functional Motor Task Evaluation in Older Adults across the United States Using the MindCrowd Electronic Cohort. **Dev Neuropsychol.** 2021 Oct 6:1-12. doi: 10.1080/87565641.2021.1979005.

Liu, Y., Lim, K., Sundman, M., Ugonna, C., That, V. T., **Cowen, S., & Chou, Y**. (2021). Interhemispheric functional connectivity of sensorimotor cortex predicts responsiveness of transcranial magnetic stimulation in older adults. **Brain Stimulation**, 14(6), 1683. https://doi.org/10.1016/j.brs.2021.10.303

Matijevic, S. and **Ryan, L.** (2021). Tract Specificity of Age Effects on Diffusion Tensor Imaging Measures of White Matter Health. **Frontiers in Aging Neurocience**.March 13:628865.

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14. Appendix 3

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

Scientific Presentations

Alexander GE, Application of multivariate network covariance for neuroimaging biomarkers of aging and alzheimer's disease risk, NACC Data Core Webinar, May 2021. (Invited)
Barnes, C.A. Keynote Address: Region-selective hippocampal contributions to altered cognition in aging. Cajal Course: Ageing Cognition, Bordeaux School of Neuroscience, Bordeaux, France, September 2021. (Invited)
Barnes, C.A. Precision aging network (PAN): Closing the gap between cognitive healthspan and human lifespan. Center to Stream Healthcare in Place (C2SHIP), California Institute of Technology, Pasadena, CA, December 2021. (Invited)
Brinton: Session Chair: National Institute on Aging (NIA) Division of Neuroscience (DN) Lipids in brain aging and AD/ADRD workshop: Myelin as a ketone reservoir: feeding a starving brain April 28-29, 2021 (Invited)
Burns, H. Griffith, C., Cegavske, C., Andrews, E., Nye, P., Vega-Reid, J., Strojek, D., Spillman, A., Raffaelli, Q., Wilcox, R., **Ryan, L., Grilli, M.D. & Andrews-Hanna, J.R**. (2021). Age-related differences in resting-state cognition: An adapted think-aloud paradigm, Arizona Alzheimer's Consortium, Tucson, A.Z.
Do, L., Zempare, M.A., Bernstein, A.S., Bharadwaj, P., Carey, N., **Alexander, G.E., Barnes, C.A**. and **Trouard, T.** Global and regional and diffusion weighted MRI analysis of rodent brains as a function of age and cognition. Session # 894.06, Society for Neuroscience Annual Meeting, November 2021. (Abstract)
Gray, D.T., Do, L., Khattab, S.O., Sinakevitch, I., **Trouard, T.P., and Barnes, C.A.** A test of the hypothesis that factors acting to protect synapse function are at the core of the biological basis of cognitive reserve. Session # 894.02, Society for Neuroscience Annual Meeting, November 2021. (Abstract)
Liu, Y., Lim, K., Sundman, M., Ugonna, C., Ton That, V., **Cowen, S.,** and **Chou, Y.-H.** (2021). Interhemispheric functional connectivity of sensorimotor cortex predicts responsiveness of transcranial magnetic stimulation in older adults. Poster presented at the 4th International Brain Stimulation Conference. Charleston, SC.
McDermott K., Sinakevitch, I., Gray, D.T., Khattab, S., Pyon, W.S., and **Barnes, C.A.** Locus coeruleus neuronal, glial, and vascular populations remain stable with age in cognitively impaired rhesus macaques. Session # 894.08, Society for Neuroscience Annual Meeting, November 2021. (Abstract)
McVeigh, K.S., **Mehl, M.R.,** Wank, A.A., Polsinelli, A.J., Moseley, S.A., **Glisky, E.L., & Grilli, M.D.** (February 2021). Loneliness and aging: Manifestations of loneliness in everyday conversations among older adults. Poster presented at the Annual Meeting of the International Neuropsychological Society. (virtual meeting)

Public Presentations related to COVID

Ryan, L. Web-Based Evaluations of Cognitive Aging in the Time of COVID. Aging research on COVID-19: a NIA investigators' workshop. June 18th, 2021. Online presentation.

Daniel Taylor, **Mary-Frances O'Connor** and **Dave Sbarra**, moderated by **Lee Ryan**
Wonder at home: maintaining well-being in an uncertain world

Mary-Frances O'Connor was the special guest speaker for the Webinar: Grief in the time of COVID: understanding the biology of bereavement

15. Appendix 4

Highlights of website development, media coverage and social media audience

Website Development

During the past year the Tucson EMBI has made a significant effort to update and improve its website content, adding more laboratory pictures, updating current presentations and new publications. The last phase of this buildout has involved a significant section on our newest project – *The Precision Aging Network.* The new website went live January 11, 2022.

Social Media Summary

Facebook: 674 likes, 794 followers

Instagram: 753 followers

LinkedIn: 590 followers, 418 connections

Monthly website visitors: average of 9-10K users per month

Media Coverage

Gene E. Alexander

- **Energizing Aging Brains**, Feature in *Alumni Association Magazine.*

Could near-infrared light give aging brains a boost? A team of researchers from the University of Arizona thinks so. Along with partners at the University of Florida, they are investigating whether near-infrared light could help enhance cognition and reduce Alzheimer's disease risk in older adults.

With the support of a $3.8 million grant from the National Institute on Aging — $1.8 million of which was distributed to the University of Arizona — researchers are exposing study participants to near-infrared light via caps placed on participants' heads and devices inserted in the nose.

"We think near-infrared light can help enhance energy metabolism and mitochondrial function; mitochondria are essentially the engines in the cell that produce energy," says Gene Alexander, one of the project's principal investigators and a professor in the UArizona departments of psychology and psychiatry, the Evelyn F. McKnight Brain Institute and the BIO5 Institute.

Near-infrared light has shown promise as a cognitive intervention in animal studies and in smaller human studies. If proven successful, this intervention could be a safe, low-cost tool in the battle against cognitive decline and Alzheimer's disease.

The two universities are enrolling participants now and will include 168 over the course of the five-year study. They will focus on older individuals who are cognitively healthy but have increased risk for Alzheimer's disease.

"There's a lot of interest now in trying to identify people who are in the preclinical stages of Alzheimer's disease, because we think that's when we have the best chances of intervening and being able to prevent or delay its development," says Alexander, who also is director of the Brain Imaging and Fluid Biomarkers Core for the Arizona Alzheimer's Disease Center.

Participants will be randomly assigned to either the study group, which will receive the light treatment, or the control group, which will use the same equipment and procedures but will not receive any near-infrared light exposure. Because near-infrared light can't be seen and doesn't emit heat, participants won't know whether they are getting the treatment.

Before and after the intervention, participants will complete neuropsychological tests and undergo MRI scans to measure resting state connectivity in the brain. Researchers also will use a special type of MRI scan known as magnetic resonance spectroscopy to measure aspects of mitochondrial brain function. Participants will be tested again three months after the intervention to determine whether there were any lasting effects.

Jessica Andrews-Hanna, Ph.D.

- **Daily doses of brief mindfulness meditation reduce the negative mental health impact of COVID-19,** *National Post*.

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The uncertainties, loss and isolation of the COVID-19 pandemic and its associated restrictions have disrupted many people's emotional well-being. This has been exacerbated by the constantly evolving public health guidelines and news stories, which increase anxiety and fear in many people.

The urgency of this problem has led mental health professionals and scientists to call for the further development of mental health science and intervention during the pandemic. As vaccination rates increase, there is an opportunity to redirect public health efforts to manage the mental health consequences of the pandemic.

As a team of cognitive neuroscientists and a clinical health psychologist studying mind wandering and ways to improve well-being in vulnerable populations, we responded to the call for action for mental health interventions. Specifically, we studied mindfulness meditation as a potential coping strategy for these mental health adversities.

- **University of Arizona researchers search for meaning behind idle thoughts**, *AZPM News.*

University of Arizona researchers are following the path our mind travels during our wandering thoughts.

Psychology professor Jessica Andrews-Hanna co-authored a study that asked subjects to say what they were thinking in-the-moment and determining how those thoughts unfold and develop over time.

"Our question was can we determine something about the mental health of different people by capturing those internal thoughts and quantifying certain characteristics of those thoughts?" she said.

Seventy-eight people, mostly college students, took part in the study. They were trained to voice their thoughts aloud for 10 minutes while sitting alone. The researchers found negative patterns of thinking lasted longer than positive thoughts.

The findings also revealed a possible link to pandemic-related behavior.

Study co-author Quentin Raffaelli believes COVID-related isolation combined with idle thoughts led some people to turn to addictive drugs.

“It suggests that a significant portion of the population did not handle the anxiety of the situation, as well as being left alone with their thoughts," he said.

More than 2,000 thoughts were analyzed in the study. The findings were published in the journal Scientific Reports last month.

- **What Our Wandering Thoughts Can Teach Us About Mental Health, *UA News*.**

University of Arizona researchers recorded idle thoughts for 10 minutes. What they learned may be useful in the diagnosis and treatment of mental health issues such as depression.

Where does your mind wander when you have idle time? A University of Arizona-led study published in Scientific Reports may offer some clues, and the findings reveal a surprising amount about our mental health.

The study's 78 participants were trained to voice their thoughts aloud for 10 minutes while sitting alone in a room without access to electronic devices. Researchers used audio equipment to record those thoughts, then transcribed the recordings and analyzed them for content. In total, more than 2,000 thoughts were analyzed.

"We wanted to mimic the small breaks we have throughout the day, such as when waiting in line at a café, taking a shower, lying in bed at night and so on. These are all times during which external demands are minimal and internal thoughts tend to creep in," said first author Quentin Raffaelli, a graduate student in the UArizona Department of Psychology.

Most psychology research addressing human thought either tells people what to think about, asks participants to remember what they were thinking about minutes before, or uses self-report questionnaires to capture freeze-frame snapshots of thoughts at different moments in time, according to the authors.

"While insightful in its own right, this snapshot approach doesn't tell us much about how thoughts unfold and transition over time – features of thinking that we think are important for our mental health. To capture these dynamic properties of thinking, we need a method that records thoughts in real time and for extended periods," said co-author Jessica Andrews-Hanna, an assistant professor of psychology who oversaw the research in her lab.

Jessica Andrews-Hanna, Ph.D. *and* **Dave Sbarra**

- **UArizona Psychologists Receive $2.9M to Study Neural Mechanisms of Emotions in Couples**, *UA News*.

The study will help researchers better understand how difficulties in romantic relationships affect mental health and well-being.

COVID-19 has illuminated the importance of social connections, but it's also placed a strain on some relationships, which can in turn impact mental health.

University of Arizona psychologists are launching a new study to better understand how difficulties in romantic relationships affect mental health and well-being.

With support from a $2.9 million grant from the National Institute of Mental Health, UArizona psychology professors Jessica Andrews-Hanna and David Sbarra will conduct a neuroimaging study of 200 romantic couples, looking at how both members of a couple process social information, and the ways in which these neural responses may affect risk for depression.

Carol A. Barnes, Ph.D. and **Lee Ryan, Ph.D.**

- **UArizona Awarded $60 Million to Lead Precision Aging Network,** *UA News.*

The network, established with funding from the National Institutes of Health, has the the ultimate goal of developing more effective brain-aging treatments and interventions targeted to the individual.

The University of Arizona has been awarded a five-year $60 million grant from the National Institutes of Health to create and lead a Precision Aging Network that could transform the way we think about the aging brain.

The network will bring together researchers from across the country to better understand how and why people experience brain aging differently, with the ultimate goal of developing more effective treatments and interventions targeted to the individual.

Led by neuroscientist Carol Barnes, a UArizona Regents Professor of psychology, neurology and neuroscience and a national leader in brain aging research, the program was inspired by the field of precision medicine, which takes into account a person's genetics, lifestyle, environment and other factors to customize care rather than relying on a one-size-fits-all approach.

- **University of Arizona to create and lead Precision Aging Network**, *Clinical OMICs.*

University of Arizona to Create and Lead Precision Aging Network

The University of Arizona will receive a $60M five-year grant from the National Institutes of Health to develop and run a Precision Aging Network to investigate the aging brain and help develop more effective treatments for conditions such as dementia.

Diseases of the aging brain impact many people –50 million people around the world live with some form of dementia and this is predicted to double every 20 years– and are hard to treat. Precision medicine has already had success in other areas, such as cancer, and the aim of the new network is to try and apply these principles to diseases of the aging brain and neurological system.

In addition to the University of Arizona, which has a strong history of aging research, the network will include researchers from Arizona State University, Emory University, Johns Hopkins University, Baylor College of Medicine, the Georgia Institute of Technology, the University of Miami and the Phoenix-based Translational Genomics Research Institute, or TGen.

“You’re going to age differently from me, and I’m going to age differently from someone else. We all need a prescription that fits us individually if we are to optimize our cognitive health,” said project leader Carol Barnes, a University of Arizona professor in the field of psychology, neurology and neuroscience, in a press statement discussing the new network.

“We’re interested in exploring more deeply: What is a normative aging brain? What are the fundamentals? Because we can’t understand the diseases that happen in an aging brain until we understand the fundamentals of what is a generally normative aging brain.”

- **This $60M project will study why brains age differently**, *KJZZ 91.5*

This $60M project will study why brains age differently

The National Institutes of Health has awarded a five-year, $60 million grant to a national project for studying why people's brains age differently.

The University of Arizona will lead the Precision Aging Network, which will include scientists and technologies from TGen and Arizona State University.

"So the questions are, what does impact healthy brain function as we age? And the answer that we're trying to get to is for a given individual to predict, prevent, or slow the progress of these unwanted changes," said Carol Barnes, the UA neuroscientist who leads the project.

"If we can do this, we can probably also slow the onset of neurodegenerative diseases that also occur in aging."

Around 50 million people worldwide live with dementia, and normal age-related declines affect many times that number.

Arne Ekstrom, Ph.D.

- **Ever Been Lost in the Grocery Store? Researchers are Closer to Knowing Why it Happens**. *UA News.*

Ever Been Lost in the Grocery Store? Researchers are Closer to Knowing Why it Happens

A new study led by UArizona psychologists suggests that the brain differentiates very similar environments – such as two stores from the same supermarket chain – as if they were even more different than two places that are nothing alike.

imagine you're walking through a chain supermarket, headed for the dairy section.

You've done it a million times: Take a right at the entrance, away from the produce, and walk past two-dozen aisles of canned soups, boxed macaroni and other staples. The rows of industrial refrigerators should be right … about … here.

But they're not.

And then you remember: You're at the supermarket across town, not the one in your neighborhood. Everything else looks the same, but the dairy section's location is flipped, and you're at the wrong end of the store.

Researchers have long struggled to learn how the brain remembers spatial environments, especially those that are similar – such as two stores from the same supermarket chain – and how the brain avoids confusion, or doesn't.

- **Why an unexpected store layout messes with your brain.** ***Interview with 91.5 KJZZ.***

Why an unexpected store layout messes with your brain

Have you ever walked into an environment that seems familiar — let's say it's a chain store that you go to on a regular basis — but you're temporarily confused because the items and departments aren't where you expected them to be?

That probably has happened, because though it's the same store name, it's in a different part of town or even in a different state and not laid out in the exact same way. That reaction by your brain is known as "repulsion."

A new study by the University of Arizona looks more closely into how and why that happens — in part by using virtual stores.

Professor Arne Ekstrom led the study, and The Show spoke with him to learn more about the concept.

- **What can supermarkets tell researchers about older brains?** *Green Valley News.*

What can supermarkets tell researchers about older brains?

One key to unlocking what's happening inside the brain of an Alzheimer's patient could be hiding in the grocery store.

That's according to a new study by University of Arizona psychologists who looked at how the brain remembers spatial environments, especially those that are similar – such as two grocery stores from the same supermarket chain.

Dr. Arne Ekstrom, senior study author and professor of psychology at the UA Human Spatial Cognition Laboratory, helped direct the study, which led participants through virtual stores in three virtual cities.

Each of the stores and cities shared similarities and had some differences. Participants were then tested on their knowledge of the virtual layouts.

Matthias R. Mehl, Ph.D.

- **How to have more meaningful conversations**, *Psyche.*

Be brave enough to share, kind enough to listen, and you can escape the shallows of small talk to dive deep with another.

Have you ever had a decent conversation in a lift? If not, join the club – being in a lift with a stranger is a universally awkward experience. One reason is the typical duration of a lift journey – long enough to feel the social pressure to say something, anything, but never long enough to say something worthwhile. The world over, lifts are a microcosm of that most pained aspect of social interaction – small talk.

The psychologist Matthias Mehl at the University of Arizona studies conversations, and he defines small talk on the basis of how much information is exchanged. 'If afterwards I know nothing more about you than I knew before,' he tells me, 'then that will be small talk.'

The vacuousness of small talk helps to explain why it's often so boring, but it can be worse than that. Thanks to more lift journeys than I care to remember, I can vouch that some small talk is, unfortunately, both boring and awkward. And it's not just in lifts: whether we're at the

hairdresser's, in a taxi, or even with our best friend, sometimes it can be painful to figure out what to say, how exactly to hit upon a topic to fill the silent, stale air between us. Many of us are crying out for help with small talk, and the internet has answered with countless articles suggesting solutions and offering advice.

Mary-Frances O'Connor, Ph.D.
COVID Has Put the World at Risk of Prolonged Grief Disorder, *Scientific American*
The deaths of more than 586,000 people in the U.S. from COVID since the spring of 2020 have left many millions grieving. A sizable number of these bereaved individuals will find their anguish lasts an unusually long time, does not diminish and renders their life almost unbearable, mental health specialists [such as Mary-Frances O'Connor] say.

People who sufferer this intense bereavement are frequently unable to keep their job, leave their home or care for other loved ones. Even those who are able to navigate some of everyday life describe their agonized existence as just waiting to die. Their continued high level of stress can damage the body, increasing inflammation and risks for associated illnesses such as heart disease. This condition, a psychiatric state called prolonged grief disorder, typically lasts for many months after a loss—defined as one year in the United States, or six months in international criteria.

Grief can be terrible. Most people, however, eventually integrate their loss and find a way forward, even as they continue to mourn their loss. Mary-Frances O'Connor, a clinical psychologist at the University of Arizona specializing in grief and its physiological impacts, likens this process to healing a broken leg: For the majority of people, rest and a cast will allow it to return to normal. Yet for a subset, a complication will arise—an infection or secondary trauma to the area—that prevents it from healing properly without more intensive intervention. In bereavement, those are the people with prolonged grief.

O'Connor found that people experiencing grief have higher levels of inflammation, particularly the cytokine interleukin-6, which has been linked to increased risk of cardiovascular disease and greater susceptibility to infections. O'Connor notes that long-term psychological and social distress leads to a harmful "weathering" in the body, a well-established state of prolonged biological stress that predisposes people to greater disease risk and earlier health decline.

Lee Ryan, Ph.D.

- **Memory Problems: Forgetfulness, Stress or Alzheimer's Dementia**, *MindCrowd.*

What causes memory problems as we age? Are we experiencing mild cognitive impairment? Or is it the early stages of Alzheimer's?

As we age, we face what we perceive as memory problems.

We have memory lapses, we may have a hard time remembering someone's name, or the title of a favorite song. To add fuel to the fire, we may have family members who suffer or suffered with Alzheimer's or another form of dementia.

What causes these memory problems? Are they part of aging? Is our memory failing? Can these memory issues be fixed? Are they signs and symptoms of Alzheimer's?

In a previous article, memory expert Lee Ryan, Ph.D. dispelled some myths about memory and explained 10 facts about what is normal in brain aging. If you haven't read it yet, please, do.