Evelyn F. McKnight Brain Institute

Full Lives Through Healthy Minds

Annual Report 2017

THE UNIVERSITY OF ARIZONA

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THE UNIVERSITY OF ARIZONA

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December 18, 2017

Dear MBRF Trustees,

From everyone here at the University of Arizona, we are pleased to provide the 2017 EMBI annual report. This year we've made promising discoveries, forged new partnerships, and continued our rich tradition in neuroscience research on the normally aging brain. This year's report showcases the progress we've made toward our shared goal of healthy cognitive aging for everyone in the future. Thank you so much for your continued support. Our work would not be as impactful without your collaboration, and we're proud to have such an engaged partner in this important and challenging effort.

Sincerely,

Dr. Carol Barnes

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

THE EVELYN F. McKNIGHT BRAIN INSTITUTE
UNIVERSITY OF ARIZONA
Preserving memory, enhancing life

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December 18, 2017

Dear McKnight Brain Research Foundation Trustees,

We are honored to present this year's annual report on behalf of the University of Arizona's Evelyn F. McKnight Brain Institute. As you read, I hope you are inspired by the outstanding brain science happening here at the University of Arizona. This annual report is intended to give you a window into the progress we have made, the collaborations we have forged, and our hopes for research and translation in the future.

In the office for Research, Discovery, and Innovation, we are supporting ground-breaking UA researchers who push the boundaries of innovation and generate new knowledge. Our faculty collaborate in novel ways that yield amazing discoveries and breakthroughs both in the University and with peers across the state, nation and world. The Evelyn F. McKnight Institute is a team that embraces the UA's interdisciplinary spirit. Over the last year, Dr. Carol Barnes and her collaborators have continued their renowned tradition of excellence in neuroscience, memory and aging. This report represents the culmination of all the projects, experiments and collaborations that continue to distinguish our Institute and University.

The Institute also supports the training of the next generation of scholars and innovators. Students play a crucial role in the Institute's most innovative research and projects, and gain valuable hands-on experience in the faculty's laboratories. We are proud of the outcomes described in this report, and we are honored to be home to this robust academic center on our campus.

Thank you for your continued support of the University of Arizona Evelyn F. McKnight Institute. No doubt, our progress continues to advance because of your support, and we are grateful for the innovations and scientific insights that you are making possible. Together, we are discovering the mysteries of the brain that advance our understanding of healthy aging in new ways every year to address the ultimate goal for all of us to live their longest and healthiest lives.

Sincerely,

Robert C. Robbins, M.D.
President

Kimberly Andrews Espy, Ph.D.
Senior Vice President for Research

Andrew Comrie, Ph.D.
Senior Vice President for
Academic Affairs & Provost

Summary of scientific achievements since last report

The director and other members of the Evelyn F. McKnight Brain Institute at the University of Arizona have had another productive year. The full list of publications can be found on pages 8 through 11. The following outlines some of these accomplishments that **directly relate to mechanisms of age-related memory loss**, first from the director's and associate director's laboratories, and then from other Evelyn F. McKnight Brain Institute (**EMBI**) affiliate faculty's laboratories.

Barnes

The Barnes laboratory collaborated with Adam Gazzaley (UCSF) and Sara Burke (McKnight, UF) to examine alterations in executive function that occur in normal cognitive aging in rhesus macaques (**these data are reported in Gray et al., 2017**). The behavioral experiments were designed to assess alterations in executive function in monkeys that Gazzaley has shown to occur in older human participants. The behavioral tests given to the young and old monkeys involved assessments of attentional updating and monitoring processes to determine whether older monkeys also show multi-tasking deficits analogous to older humans. The data obtained from an interference task and a reversal learning task revealed that older animals are impaired on both of these tasks, compared to their young counterparts. Interestingly, however, the levels of performance on the object reversal task were not correlated with levels of performance in the interference task, suggesting differential effects of aging on independent prefrontal cortical circuits.

The Barnes laboratory collaborated with Meredith Hay (EMBI affiliate faculty), John Konhilas (UA), and Todd Vanderah (UA) to examine the effects of modifying inflammatory processes (via the angiotensin system) in a novel preclinical model of congestive heart failure (**these data are reported in Hay et al., 2017**). The goal of the experiment was to determine if this treatment could prevent heart failure-related cognitive decline that is common after such events in older individuals. We were able to produce myocardial infarction in the mouse, with a 50-70% decline in ejection fraction by endocardiography. The group given the angiotensin 1-7 treatment for four weeks showed significantly less cognitive impairment than did non-treated mice, but the treatment had no effect on cardiac function, suggesting specific neuroprotection of this compound.

The Barnes laboratory collaborated with Scott Moffat (Georgia Institute of Technology), Jan Wiener (Ageing and Dementia Institute, Bournemouth University, Poole, UK), and Thomas Wolbers (Aging and Cognition Research Group, Magdeburg, Germany) to produce a review of the aging navigational system literature across rodent, nonhuman primate, and humans for the prestigious journal **Neuron** (**reported in Lester et al., 2017**). The researchers each brought different expertise to the synthesis of this literature and attempted, for the first time, to define and clarify terms used to describe types of navigation used in both the human and nonhuman literature. This allowed the researchers to integrate findings more accurately across species, discuss how cognitive aging affects the brain's navigation circuits, and describe the behavioral and neural underpinnings of the deficits observed in navigational computations in old age.

The Barnes laboratory collaborated with Tom Beach (Banner Sun Health Research Institute, AZ) and Jiong Shi (Barrow Neurological Institute, AZ) to determine whether levels of pituitary adenylate cyclase activating polypeptide (PACAP) and amyloid plaque density might covary in the aging nonhuman primate brain (**these data are reported in Han et al., 2017**). The researchers hypothesized that, because PACAP has been shown to play a positive role in mitochondrial function, it may be a 'protective factor' in the presence of beta amyloid toxicity. Consistent with their hypothesis, the researchers found that plaques increased in a region-specific manner across age in these monkeys, PACAP levels decreased at older ages, and both were correlated with a decline in memory in the older monkeys.

The Barnes laboratory collaborated with Andrew Maurer (McKnight, UF) and Sara Burke (McKnight, UF) to assess the integrity of interneuron function in the perirhinal cortex of aged, cognitively characterized rats (**these data are reported in Maurer et al., 2017**). The researchers report that the lower firing rates previously observed in aged rat

Summary of scientific achievements since last report

Continued

Dr. Carol Barnes and students.

perirhinal cortical principal cells are associated with weaker interneuron activity and reduced excitatory input onto inhibitory cells in this structure. We predict that therapeutics targeting this synaptic connection may be beneficial for some of the declines in cognition observed in normal aging.

The Barnes laboratory collaborated with David Sweatt (McKnight, UAB), Matt Huentelman (EMBI affiliate faculty), and Tom Foster (McKnight, UF) on an experiment that employed next-generation RNA sequencing to examine gene expression differences related to aging-related changes in hippocampal subfields and selective cognitive declines (**these data are reported in Lanov et al., 2017**). The researchers report significant differences among hippocampus regions CA1, CA3, and dentate gyrus in the expression of specific genes and in the relationship of specific genes to cognitive decline. Importantly, the researchers used two sequencing platforms and were able to demonstrate good cross-platform concordance in the gene counts and in detecting differences in expression.

The Barnes laboratory examined amygdala cell and local field potential correlates of decision-making behaviors in young and older rats (**these data are reported in Samson et al., 2017**). Older adults tend to use strategies that differ from those used by young adults to solve decision-making tasks, and the researchers found that older rats also appear to use different strategies than their younger counterparts. Along with behavioral differences, the researchers observed age- and task-specific increases in the power of beta oscillations in the amygdala when older rats learned or decided between rewards of different size. It is thought that beta oscillations can engage a broad network across many regions of the brain. The increase in beta power in old rats (not in young) may reflect differences in strategies used by older animals in decision-making tasks and suggest a mechanism through which reward networks may be expanded during aging.

Summary of scientific achievements since last report

Continued

Ryan

The Ryan laboratory conducted a study to evaluate the effect of visual integration on memory in young and aged adults (**these data are reported in Memel and Ryan, 2017**). They report that visual integration methods benefit associative memory performance in both young and older adults similarly. Interestingly, while both younger and older adults showed increased activation of hippocampus in MRI scans during these tasks, the memory performance of older adults was most strongly predicted by prefrontal rather than temporal lobe activation, and the younger adults showed stronger temporal lobe activation than did the older participants. These data suggest a mechanism for improving associative memory in older adults.

Alexander

The Alexander (EMBI affiliate faculty) laboratory along with Wright (McKnight, U Miami), Moeller (Columbia), Sacco (McKnight, U Miami), Stern (Columbia), and DeCarli (UC Davis) examined groups of individuals that received brain scans and cognitive testing (**these data are reported in Kern et al., 2017**). The participants (60 to 86 years) were split into those who had normal blood pressure, those with pharmacologically controlled hypertension, or those with uncontrolled hypertension. The uncontrolled hypertension group showed the most gray matter volume decline and white matter lesion load, and the normotensive individuals showed the least. The researchers conclude that white matter lesions from small-vessel disease are associated with reduced gray matter volume and are dependent on blood pressure management. These data provide neural documentation of the importance of maintaining a normotensive profile for promoting good executive function and memory.

The Alexander laboratory collaborated with Raichlen (UA) to propose a model of adaptive capacity of the body and brain to help explain the mechanisms underlying the exercise and brain health, which was published in the prestigious journal **TINS** (**reported in Alexander and Raichlen, 2017**). The two main questions addressed in this article are what mechanisms underlie age-related brain atrophy and how lifestyle changes influence the trajectory of healthy and pathological aging.

Brinton

The Brinton (EMBI affiliate faculty) laboratory tested the safety profile of an estrogen formulation in perimenopausal and postmenopausal women (**these data are reported in Hernandez et al., 2017**). The particular phytoestrogen chosen for this trial (an estrogen receptor beta-selective phytoestrogen) is thought to promote neuronal survival without exerting feminizing activity in the periphery. The 12-week clinical trial evaluated cognitive performance and vasomotor symptoms, but it was designed to demonstrate safety and was not powered to assess cognition. No adverse effects were noted; therefore, the researchers conclude that this formulation is well tolerated. Thus, the data support the conduct of further trials to expand the duration and number of participants tested.

The Brinton laboratory, along with a number of her collaborators at USC, edited a series of papers on the metabolic-inflammatory axis in brain aging and neurodegeneration, which included an overview of the role of changes in energy metabolism and inflammation in aging (**the introduction is Yin et al., 2017**). This series of papers explores ideas of the pivotal role that mitochondrial health and function plays in brain aging, along with inflammatory processes and microglia senescence. The goal of this series of papers is to focus efforts on effective ways to positively impact brain health.

Summary of scientific achievements since last report

Continued

Chou

The Chou (EMBI affiliate faculty) laboratory, along with collaborators from Duke University, examined the hypothesis that aging is associated with increased fronto-parietal involvement in attentional guidance (**these data are reported in Madden et al., 2017a**). Participants ranged from 19 to 78 years of age. Search reaction time measures indicated that bottom-up attentional guidance was relatively constant as a function of age, and fronto-parietal fMRI activation related to target detection was also constant as a function of age. The main difference noted in these visual search tests appeared in individuals beginning at about 35 years of age, where there was a decrease in resting state functional connectivity in visual sensory regions. These findings suggest that search reaction time changes occur relatively early in adulthood, and are maintained throughout normative aging into the eighth decade.

The Chou laboratory, along with collaborators from Duke University, examined the resting state functional connectivity and white-matter hyperintensity volumes as mediators of age-related changes in fluid cognitive processes (**these data are reported in Madden et al., 2017b**). In adults ranging in age from 19 to 79 years, the researchers found that general levels of analysis involving composite measures of fluid cognition and imaging modalities did not result in the detection of changes or significant relationships with age. The specific measure of resting-state functional connectivity of sensorimotor networks, however, was found to be a significant mediator of age-related decline in executive function. The researchers suggest that specific models of neurocognitive disconnection are needed for sensitive analyses of cognitive decline in aging.

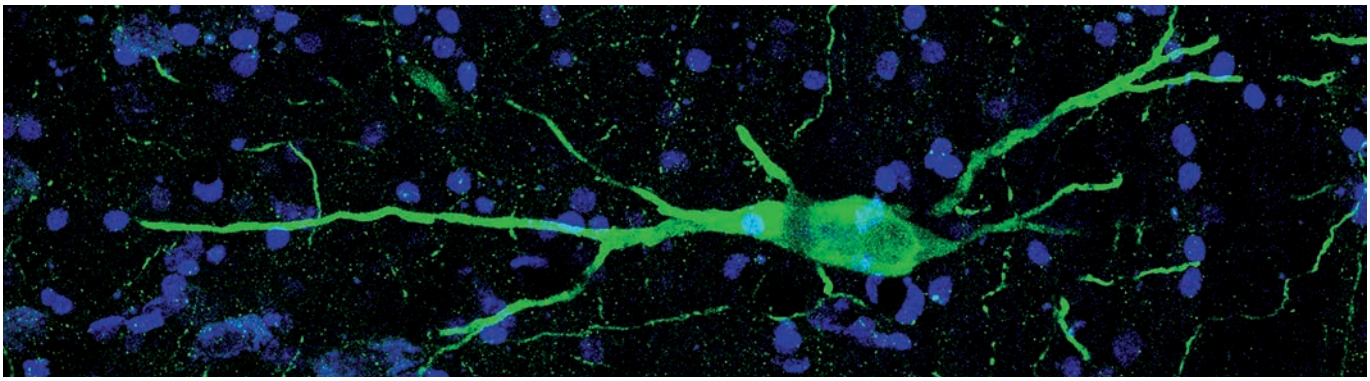
Glisky

The Glisky and Mehl (EMBI affiliate faculty) laboratories examined the efficacy of learning and using an online social networking website as an intervention to maintain or enhance cognitive function in older adults (**these data are reported in Myhre et al., 2017**). The online Facebook group showed a significant increase in an executive function associated with complex working memory tasks. No significant change in the daily diary or waitlist control groups was observed. No other measures of cognitive function or social interactions showed differential improvement as a result of this online treatment. The researchers conclude that learning and using an online social networking site can provide specific benefits for complex working memory problems in this group of healthy older adults.

Grilli

The Grilli (EMBI affiliate faculty) laboratory, in collaboration with Glisky (EMBI affiliate faculty), examined whether cognitively healthy older adults who carry the APOE4 allele of the apolipopritein E gene (a risk factor for late-onset Alzheimer's disease) benefit from sematic elaboration or imagination-generated self-reference based processing in memory for emotional and nonemotional narratives (**these data are reported in Grilli et al., 2017**). Both carriers and noncarriers of the E4 allele benefited from self-referencing methods compared to semantic elaboration methods. The older non-E4 carriers showed the expected emotional enhancement of memory effect; however, the E4 carriers did not. This suggests that deficits in emotional memory may be an early cognitive marker of abnormal decline in aging adults.

Publications in peer-reviewed journals



Dopaminergic cell in the lateral ventral tegmental area of an old, memory-impaired monkey.

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Clark, C.A.C., **Fernandez, F.,** Sakhon, S., Spanò, G., and Edgin, J.O. (2017) The medial temporal memory system in Down syndrome: Translating animal models of hippocampal compromise. Hippocampus, 27:683-691.

Cohen, R.A., and **Alexander, G.E.** (2017) Using the Telephone Interview for Cognitive Status and Telephone Montreal Cognitive Assessment for evaluating vascular cognitive impairment: Promising call or put on hold? Stroke, 48:2919-2921

Dixon, M., **Andrews-Hanna, J.R.,** Spreng, R.N., Irving, Z.C., Mills, C. Girn, M., and Christoff, K. (2017) Interactions between the default network and dorsal attention network vary across default subsystems, time, and cognitive states. Neuroimage, 147:632-649.

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Geifman, N., **Brinton, R.D.,** Kennedy, R.E., Schneider, L.S., and Butte, A.J. (2017) Evidence for benefit of statins to modify cognitive decline and risk in Alzheimer's disease. Alzheimers Research Therapeutics (2017) 9:10. doi: 10.1186/s13195-017-0237-y.

Gray, D.T., **Smith, A.C., Burke, S.N.,** Gazzaley, A., and **Barnes, C.A.** (2017) Attentional updating and monitoring and affective shifting are impacted independently by aging in the macaque monkeys. Behavioral Brain Research, 322:329-338.

Grilli, M.D., Woolverton, C.B., Crawford, M.S., and **Glisky, E.L.** (2017) Self-reference and emotional memory effects in older adults at increased genetic risk of Alzheimer's disease. Aging, Neuropsychology, and Cognition, 1-14.

Han, P., Nielsen, M., Song, M., Yin, J., Permenter, M.R., Vogt, J.A., Engle, J.R., Dugger, B.N., Beach, T.G., **Barnes, C.A.,** and Shi, J. (2017) The impact of aging on brain pituitary adenylate cyclase activing polypeptide pathology and cognition in mice and rhesus macaque. Frontiers in Aging Neuroscience, 9:180.

Publications in peer-reviewed journals

Continued

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Krajewski-Hall, S.J., Blackmore, E.M., McMinn, J.R., and **Rance, N.E.** (2017) Estradiol alters body temperature regulation in the female mouse. Temperature, doi.org/10.1080/23328940.2017.1384090 [epub ahead of print].

Krueger, P.K., **Wilson, R.C.,** and Cohen, J.D. (2017) Directed and random exploration in the domain of losses. Judgment and Decision Making 12(2):104.

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Madden, D.J., Parks, E.L., Hoagey, D.A., Cocjin, S.B., Johnson, M.A., **Chou, Y.-H.,** Potter, G. G., Chen, N.-K., Cabeza, R., and Diaz, M.T. (2017) Sources of disconnection in neurocognitive aging: Cerebral white matter integrity, resting-state functional connectivity, and white matter hyperintensity volume. Neurobiology of Aging, 54:199-213.

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Maurer, A.P., **Burke, S.N.,** Diba, K., and **Barnes, C.A.** (2017) Attenuated activity across multiple cell types and reduced monosynaptic connectivity in the aged perirhinal cortex. Journal of Neuroscience, 37(37):8965-8974.

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Sundman, M., Chen, N.-K., Subbian, V., and **Chou, Y.-H.** (2017) The bidirectional gut-brain-microbiota axis as a potential nexus between traumatic brain injury, inflammation, and disease. Brain, Behavior, and Immunity, 66:31-44.

Thome, A., **Marrone, D.F.**, Ellmore T.M., Chawla, M.K., Lipa, P, Ramirez-Amaya, V., Lisanby, S.H., McNaughton, B.L., and **Barnes, C.A.** (2017) Evidence for an evolutionarily conserved memory coding scheme in the mammalian hippocampus. Journal of Neuroscience, 37:2795-2801.

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Warren, C.M., **Wilson, R.C.,** van der Wee, N.J., Giltay, E.J., van Noorden, M.S., Nystrom, L.E., Cohen, J.D., and Nieuwenhuis, S. (2017) The effect of atomoxetine on random and directed exploration in humans. PLOS ONE, 12(4), e0176034.

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Publications (other)

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Glisky, E.L. (2017) Forgetting. In J.S. Kreutzer, J. DeLuca, and B. Caplan (Eds.), Encyclopedia of Clinical Neuropsychology, 2nd ed. New York: Springer.

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Glisky, E.L. (2017) Incidental memory. In J.S. Kreutzer, J. DeLuca, and B. Caplan (Eds.), Encyclopedia of Clinical Neuropsychology, 2nd ed. New York: Springer.

Glisky, E.L. (2017) Memory. In J.S. Kreutzer, J. DeLuca, and B. Caplan (Eds.), Encyclopedia of Clinical Neuropsychology, 2nd ed. New York: Springer.

Glisky, E.L. (submitted) Method of vanishing cues. In J.S. Kreutzer, J. DeLuca, and B. Caplan (Eds.), Encyclopedia of Clinical Neuropsychology, 2nd ed. New York: Springer.

Rats are prepared for studies to examine the role of brain oscillations in hippocampal function and brain aging.

Presentations at scientific meetings

Andrews-Hanna, J.R. The Science of Mind-Wandering. Talk presented to the Neuroscience Cognitive Science Club, University of Arizona, Tucson, AZ, January 2017.

Barnes, C.A. Impact of aging on neural circuits critical for memory. Graduate Program in Neuroscience Seminar Series, University of Washington, Seattle, WA, January 2017.

Brinton, R.D. Regeneration in a degenerating brain. Arizona State University and Barrow Neurological Institute Neuroscience Symposium, January 2017.

Cowen, S. Brains, oscillations, aging, and memory. University of Arizona Neuroscience DataBlitz, Tucson AZ, January 2017.

Wohlford, L., Crown, L., Parent, K., Bartlett, M., Falk, T., Heien, M., and **Cowen, S.L.** Fast-Scan Controlled Adsorption Voltammetry as a Method to Measure Absolute Levels of Dopamine In Vivo. University of Arizona Undergraduate Biology Research Program Poster Session, January 2017.

Barnes, C.A. An aging delimma: Should I boost sustained or flexible attention. Winter Conference on Neural Plasticity, Grenada, Caribbean, February 2017.

Barnes, C.A. Aging is not a disease: Normal lifespan changes in brain circuits critical for memory. Distinguished Sackler Visiting Lecture, Collaborative Program in Neuroscience, University of Toronto, February 2017.

Brinton, R.D. Metabolic aging of the female brain: Risks and consequences. 9th International Meeting Steroids and Nervous System, Torino, Italy, February 2017.

Memel, M.B., and **Ryan, L.** Contributions of visual integration and frontotemporal white matter integrity on associative memory in older adults. Poster presented at the 45th Annual Meeting of the International Neuropsychological Society. New Orleans, LA, February 2017.

Moseley, S.A., Ritchie, H., Rosado-Mueller, A., and **Glisky, E.L.** Cognitive and psychosocial associations of hearing loss in older adults. International Neuropsychological Society, New Orleans, LA, February 2017.

Polsinelli, A.J., Ritchie, H., Moseley, S., Feld, S., and **Glisky, E.L.** Mindfulness training for improving cognitive and emotional functioning in healthy, nonmeditating older adults. International Neuropsychological Society, New Orleans, LA, February 2017.

Ritchie, H., Polsinelli, A.J., Moseley, S., and **Glisky, E.L.** Cognitive and emotional associations of dispositional mindfulness in older adults. International Neuropsychological Society, New Orleans, LA, February 2017.

Robbins, R., **Glisky, E.L.,** and Mehl, M. Relation between social interaction and cognitive functioning in older adults: A feasibility study using the EAR technology. International Neuropsychological Society, New Orleans, LA, February 2017.

Shinitski, N.M., Zhang, Y., Gray, D.T., **Burke, S.N., Smith, A.C., Barnes, C.A.,** and Demba, B. Can you teach an old monkey a new trick? Computational and Systems Neuroscience (Cosyne) 2017, Salt Lake City, UT, February 2017.

Andrews-Hanna, J.R. The Costs and Benefits of an Untamed Mind. Colloquium Speaker, Department of Psychology, University of Arizona, March 2017.

Andrews-Hanna, J.R. The Default Network: Emerging themes and applications to aging and Alzheimer's disease. Oral presentation given at the 2017 Arizona Alzheimer's Consortium Retreat, Phoenix, AZ, March 2017.

Presentations at scientific meetings

Continued

Brinton, R.D. Allopregnanolone as a Regenerative Therapeutic for Alzheimer's Disease: Phase 1B/2A Update. Alzheimer's and Parkinson's Diseases Congress, Vienna, Italy, March 2017.

Chou, Y.-H. Integrating TMS with Brain Imaging: Applications for Parkinson's Disease. Psychology Colloquium, University of Arizona, Tucson, AZ, March 2017.

Parent, K.L., Bartlett, M.J., Crown, L.M., Gies, K.F., Miller, M.A., Falk, T., **Cowen, S.L.,** and Heien, M.L. Longitudinal studies of tonic dopamine for investigation of neural disorders. Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy, Chicago, IL, March 2017.

Rance, N.E. The 3rd World Conference on Kisspeptin, Orlando, Florida, March 2017.

Spanò, G., Gomez, R., Demara, B., **Cowen, S.,** and Edgin J.O. Memory consolidation across polysomnography-assessed naps in preschoolers with Down syndrome. The 50th Annual Gatlinburg Conference, San Antonio, TX, March 2017.

Barnes, C.A. Brain circuit changes that contribute to age-related declines in cognition. Hagey Lecture, University of Waterloo, Waterloo, Canada, March 2017.

Barnes, C.A. The 'youngfield' of neuroscience: One senior scientists' retrospective. Student Colloquium, University of Waterloo, Waterloo, Canada, March 2017.

Barnes, C.A. Animal models of brain adaptation and compensation in aging. Cognitive Aging Summit III, Bethesda, MD, April 2017.

Barnes, C.A. Cross-species decline in cognition with aging: Why don't mammals other than humans spontaneously get Alzheimer's disease. Behavioral Models of Age-related Cognitive Decline Session. ASPET Annual Meeting at Experimental Biology 2017, Chicago, IL, April 2017.

Cowen, S. Integrated Measurement of Dopamine Release and Large-Scale Ensemble Activity in Behaving Animals. Mayo Clinic Brain Initiative Symposium, Rochester, MN, April 2017.

Spanò, G., Gomez, R., Demara, B., **Cowen, S.,** and Edgin J.O. Memory consolidation across naps in typical development and in preschoolers with Down syndrome. The 2017 SRCD Biennial Meeting, Austin, TX, April 2017.

Andrews-Hanna, J.R. The Brain's Default Network: Anatomy, Function, and Relevance to Normal and Pathological Aging. Invited talk for the 2017 Arizona Alzheimer's Consortium Conference, Phoenix, AZ, May 2017.

Brinton, R.D. Advanced Training Course: Alzheimer's disease in the female brain. 2017 Pioneer Award Frontiers in Aging and Regeneration Research, Atlanta, GA, May 2017.

Chou, Y.-H. Introduction to Transcranial Magnetic Stimulation (TMS): Applications for Parkinson's Disease. Tucson Parkinson Disease Conference, Tucson, AZ, May 2017.

Chou, Y.-H. Integrating Transcranial Magnetic Stimulation with Brain Imaging. Arizona Research Institute for Biomedical Imaging (ARIBI) Workshop, University of Arizona, Tucson, AZ, May 2017.

Andrews-Hanna, J.R. and Arch, J.J. Where's My Mind? Content, Correlates, and Consequences of Daily Thinking Patterns. Oral presentation at the 2017 University of British Columbia Mind-Wandering Symposium, Vancouver, BC, Canada, June 2017.

Barnes, C.A. Session Chair: Fixing memory: Interventions that target the hippocampus. Spring Hippocampal Research Conference, Taormina, Italy, June 2017.

Presentations at scientific meetings

Continued

Brinton, R.D. Sex Steroids and the Brain. What the Brain Has Taught Us About Sex Steroids. University of California at Santa Barbara Seminar, Santa Barbara, CA, June 2017.

Brinton, R.D. Estrogenic compound trials for AD. Spring Hippocampal Research Conference, Taormina, Sicily, June 2017.

Brinton, R.D. Session Organizer: Power Hour Parkinson's Disease Genetics and Systems Biology. Parkinson's Disease Gordon Research Conference, Newry, ME, June 2017.

Brinton, R.D. Discussion Leader: The Biology of Aging and Parkinson's Disease. Parkinson's Disease Gordon Research Conference, Newry, ME, June 2017.

Madden, D.J., Parks, E.L., Hoagey, D.A., Cocjin, S.B., Johnson, M.A., **Chou, Y.-H.,** Potter, G.G., Chen, N.-K., Cabeza, R., and Diaz, M.T. Sources of disconnection in neurocognitive aging. The 2017 Annual Meeting of Human Brain Mapping, Vancouver, Canada, June 2017.

Andrews-Hanna, J.R., Wilcox, R., Renger, J., Ives, L., Sroloff, A., and Arch, J.J. Where's My Mind? A smartphone app to assess the content, consequences, and correlates of mind-wandering. Oral and Poster Presentation at the 2017 Indonesian-American Kavli Frontiers of Science Symposium, Ambon, Indonesia, July 2017.

Brinton, R.D. Catabolism of White Matter in Brain to Generate Ketone Bodies. AAIC Meeting Fueling the Glucose Starved Alzheimer's Brain, London, UK, July 2017.

Wilson, R.C. What is the nature of decision noise in random exploration? 50th Annual Meeting of the Society for Mathematical Psychology, Coventry, UK, July 2017.

Alexander G.E. Neuroimaging in brain aging, vascular health, and the risk of Alzheimer's disease. Neuroscience Community Data Blitz, University of Arizona, Tucson, AZ, August 2017.

Barnes, C.A. Temporal and frontal lobe correlates of memory decline in aging. Neal Miller Distinguished Lecture, American Psychological Association (APA) Convention, August 2017.

Alexander, G.E. Neuroimaging of the aging brain: Implications for successful aging and the risk for Alzheimer's disease. Psychiatry Grand Rounds, Department of Psychiatry, University of Arizona College of Medicine, Tucson, AZ, September 2017.

Andrews-Hanna, J.R. What's in a name? Definitions and current discourse on mind-wandering. Wandering Minds: Symposium on Spontaneous Thought in Science, Philosophy and Contemplative Traditions, Oslo, Norway, September 2017.

Andrews-Hanna, J.R. The Dynamics of Thought: Language as a Window into Meandering and Sticky Minds. Cognitive Science Colloquia, Tucson, AZ, October 2017.

Barnes, C.A. (2017) Animal models of cognition and cognitive assessment. U13 Bedside-to-Bench Conference Series. Sensory Impairment and Cognitive Decline, Bethesda, MD, October 2017.

Cowen, S. Neuro-electro-chemical transmitter analytics research. IBM Cloud University Conference, Berlin, Germany, October 2017.

Huynh, K., **Chou, Y.-H.,** Sundman, M., Chen, N.-K., and Subbian, V. Non-motor symptoms as a marker of Parkinson's disease progression: An exploratory analysis. Biomedical Engineering Society Annual Meeting, Phoenix, AZ, October 2017.

Presentations at scientific meetings

Continued

Alexander, G.E., Bharadwaj, P.K., Raichlen, D.A., Klimentidis, Y.C., Fitzhugh, M.C., Nguyen, L.A., Haws, K.A., Hishaw, G.A., Moeller, J.R., Habeck, C.G., and **Trouard, T.P.** Network covariance of hippocampal subfield volumes associated with healthy aging and the risk for Alzheimer's disease. Program No. 527.06. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Andrews-Hanna, J.R., Gardiner, C.K., Banich, M.T., and Bryan, A.D. Socioemotional and neural correlates of off-task thinking in young and old adults. Program No. 527.15. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience, November 2017.

Annadurai, A., Corenblum, M.J., Ray, S., Kirwan, K., Reed, A., **Barnes, C.A.,** and **Madhavan, L.** Enhanced Nrf2 expression improves neural stem cell function during a critical aging period. Program No. 459.08. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Bacon, E., Mishra, A., Wang, Y., Yin, F., and **Brinton, R.D.** Epigenetic control of the perimenopausal brain in hypothalamus. Program No. 678.2. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Bagevalu Siddegowda, B., Chawla, M.K., Yao, S., **Barnes, C.A.** and Zarnescu, D.C. Dynamic expression of RNA stress granule components in aging brains: From flies to rats. Program No. 712.17. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience, November 2017.

Barnes, C.A. Temporal lobe activity in nonhuman primates: Locomotion versus restraint. Program No. 265.02. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Bharadwaj, P.K., Fitzhugh, M.C., Nguyen, L.A., Haws, K.A., Hishaw, G.A., **Trouard, T.P.,** Moeller, J.R., Habeck, C.G., and **Alexander, G.E.** Multimodal neuroimaging reveals white matter microstructure related covariance networks of subcortical gray matter volumes in healthy aging. Program No. 527.05. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Brinton, R.D., Yin, F., Yao, J., Deng, Q., Mishra, A., and Mao, Z. Mechanistic role of brain hypometabolism and mitochondrial uncoupling in perimenopausal hot flash. Program No. 678.22. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Carey, N.J., Zempare, M.A., Nguyen, C.J., Bohne, K.M., Chawla, M.K., Sinari, S., **Huentelman, M.J.,** Billheimer, D., and **Barnes, C.A.** Dissociation of performance in hippocampus- and prefrontal cortical-dependent tasks in aging fisher 344 rats. Program No. 712.18. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Chawla, M.K., Zhou, Y., Wang, L., Carey, N.J., Zempare, M.A., Nguyen, C.J., Hruby, V.J., **Barnes, C.A.,** and Cai, M. Brain region-specific changes in melanocortin receptor expression in aged rat brain. Program No. 712.16. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Chen, S., Yao, J., Wong, K., and **Brinton, R.D.** Impact of allopregnanolone on the differentiation of neural stem cell. Program No. 671.13. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Comrie, A., Lister, J.P., Chawla, M.K., and **Barnes, C.A.** Sparser representation of experience by aged rat lateral entorhinal cortex. Program No. 712.14. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Presentations at scientific meetings

Continued

Cowen, S.L., Gray, D.T., Wiegand, J.-P., Schimanski, L.A., and **Barnes, C.A.** Age-associated changes in awake hippocampal sharp-wave ripples during spatial eyeblink conditioning. Program No. 712.21. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Crown, L., Nitz, D.A., and **Cowen, S.L.** Local-field oscillatory activity in the medial prefrontal cortex responds to the execution of effortful behavior but not to the anticipation of effort or reward. Program No. 250.02. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Desai, M.K., Irwin, R.W., Prajapati, M., and **Brinton, R.D.** Evaluating sex- and apoe genotype dependent response to allopregnanolone treatment. Program No. 671.1. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Do, L., Bernstein, A., Bharadwaj, P.K., **Alexander, G.E., Barnes, C.A.,** and **Trouard, T.P.** Advanced techniques for characerizing rodent brains with diffusion MRI. Program No. 706.08. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Franchetti, M., Bharadwaj, P.K., Nguyen, L.A., Klimentidis, Y.C., Haws, K.A., Fitzhugh, M.C., Hishaw, G.A., **Trouard, T.P.,** Raichlen, D.A., and **Alexander, G.E.** Relation of physical sport activity to regional white matter integrity in older adults. Program No. 527.07. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Gallegos, N.J., Stickel, A., **Ryan, L.** The impacts of family history of Alzheimer's disease and education on white matter integrity. Program No. 570.06. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Gray, D.T., **Smith, A.C., Burke, S.N.,** and **Barnes, C.A.** The alpha-2 noradrenergic receptor agonist guanfacine impairs flexible attention in young and aged macaques. Program No. 712.12. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience, November 2017.

Hernandez, G.D., Zhao, L., Chen, Y.-L., Franke, A., Mack, W.J., Schneider, L.S., and **Brinton, R.D.** Pharmacokinetics and safety profile of a single-dose administration of an estrogen receptor β-selective phytoestrogenic formulation (PhytoSERM) in peri and postmenopausal women. Program No. 671.12. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Irwin, R.W., Hernandez, G., Solinsky, C.M., Lopez, C.M., Kono, N., Mack, W.J., Schneider, L.S., and **Brinton, R.D.** Alzheimer's disease clinical trial recruitment and retention model in the Greater Los Angeles area. Program No. 671.09. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Kapellusch, A.J., Lester, A.W., Schwartz, B.A., Brewster, J.R., and **Barnes, C.A.** Deficits in aged rats on the W-track continuous spatial alternation task suggest impaired hippocampal-prefrontal interactions. Program No. 712.19. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Krajewski-Hall, S.J., Blackmore, E.M., Mcminn, J.R., Mcmullen, N.T. and **Rance, N.E.** Increased core temperature following ablation of neurokinin 3 receptor-expressing neurons in the mouse median preoptic nucleus and adjacent preoptic area (MnPO/POA). Program No. 414.02. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Kyle, C., **Smith, A.C.,** Gray, D.T., **Burke, S.N.,** and **Barnes, C.A.** Temporal contiguity predicts reward association learning in bonnet macaques. Program No. 712.10. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Presentations at scientific meetings

Continued

Lositsky, O., Shvartsman, M., Cohen, J.D., and **Wilson, R.C.** Contributions of working memory and across-trial probability learning to context-based decisions. Program No. 339.13. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Malem-Shinitski, N., Zhang, Y., Gray, D.T., **Burke, S.N., Smith, A., Barnes, C.A.,** and Ba, D. A separable state-space model of learning across trials and days in an aging study in macaque monkeys. Program No. 712.11. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Mishra, A., Yin, F., Mao, Z., and **Brinton, R.D.** Sex differences in metabolic and neurological outcomes in humanized APOE-E4 knock-in rats. Program No. 678.23. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Nguyen, L.A., Bharadwaj, P.K., Fitzhugh, M.C., Haws, K.A., Hishaw, G.A., Moeller, J.R., Habeck, C.G., **Trouard, T.P.,** and **Alexander, G.E.** Regional covariance patterns of white matter microstructure in healthy aging. Program No. 527.04. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Pyon, W., Gray, D.T., Chawla, M.K., and **Barnes, C.A.** An alternative to dye-based approaches to remove lipofuscin-induced background autofluorescence from primate brain tissue. Program No. 712.13. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Samson, R.D., Duarte, L., and **Barnes, C.A.** Preserved overall basal firing rates in aged rat basolateral complex of the amygdala, but neurons from aged rats are more engaged in anticipation of rewards compared to young rats. Program No. 712.20. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Solinsky, C.M., Park, J.A., Chui, H.C., Blurton-Jones, M., Ichida, J., and **Brinton, R.D.** Development of an iPSC based biomarker strategy to identify neuro-regenerative and mitochondrial responders to allopregnanolone. Program No. 671.11. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Somasundar, V., Padmanabhan, R., Roysam, B., **Barnes, C.A.,** and Lister, J.P. Semi-automated layer classification tool for defining cortical architecture. Program No. 712.15. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Stickel, A. and **Ryan, L.** Associations between cardiovascular risk factors and cognition in aging Hispanics compared to Non-Hispanic Whites. Program No. 527.26. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Wang, Y., Hernandez, G., Mack, W., Schneider, L.S., Yin, F., and **Brinton, R.D.** PhytoSERM for management of menopause-associated vasomotor symptoms -- effect of APOE genotype and mitochondrial haplogroup. Program No. 678.21. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Wiegand, J.-P., Gies, K., Bartlett, M.J., Falk, T., and **Cowen, S.L.** Altered slow-wave sleep in the LRRK2 G2019S mouse model of Parkinson's disease. Program No. 299.07. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Ye, T., Bartlett, M.J., Falk, T., and **Cowen, S.L.** Oscillatory signatures of L-DOPA-induced dyskinesia are not reduced by ketamine. Program No. 133.15. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Yin, F., Wang, Y., Mishra, A., Mao, Z., and **Brinton, R.D.** Impact of APOE genotype on the sex-differentiated bioenergetic trajectories and AD risks in aging mouse brains. Program No. 678.19. 2017 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience. Online, November 2017.

Presentations at public (non-scientific) meetings or events

Glisky, E.L. Memory Changes with Age: What to Do About It? Arizona Education Association – Retired. Tucson, AZ, January 2017.

Andrews-Hanna, J.R. Aging Gracefully: Insights from Neuroscience Research. Psychological Science of Healthy Aging: Mind, Brain and Everyday Life Speaker Series, Green Valley, AZ, February 2017.

Alexander, G.E., and **Ryan, L.** The Science of Decision Making and Aging. Co-Director. 5th Joan Kaye Cauthorn Annual Conference on Successful Aging, Tucson, AZ, February 2017.

Brinton, R.D. Part-of-the-Cloud Luncheon Speaker, Menlo Park, CA, February 2017.

Ryan, L. Decisions, Decisions, Decisions: Making Positive Choices As We Age. Co-director and presentation at the 5th Joan Kaye Cauthorn Annual Conference on Successful Aging, Tucson, AZ, February 2017.

Wilson, R.C. (2017) Making sound financial decisions. Fifth Annual Conference on Successful Aging, University of Arizona, Tucson, AZ, February 2017.

Barnes, C.A., Brinton, R.D., and **Andrews-Hanna, J.** Precision Aging, How to Keep Your Brain Healthy As You Age. UA Foundation Board of Trustees & National Leadership Council, University of Arizona, Tucson, AZ, March 2017.

Brinton, R.D. Architects of Change Luncheon Speaker, Mount St. Mary's University, Los Angeles, CA, March 2017.

Ryan, L. Mobile Devices in Clinical Trials for Neurological Diseases. Coalition Against Major Diseases, Critical Path Institute CDISC Standards Workshop, Phoenix, AZ, March 2017.

Alexander, G.E. The Brain-Exercise Connection. Tucson Medical Center Brain Week, Tucson, AZ, April 2017.

Cowen, S.L. Tucson Festival of Books Presenter. Dr. Cowen's lab developed an electronic-brain demonstration system called "Brian the Brain" for teaching K-12 students about neurophysiology (NSF funded). Dr. Cowen and his students demonstrated the device at the Festival of Books and at a local high school. Tucson, AZ, Spring 2017.

Ryan, L. Good for the heart, Good for the brain. La Posada Continuing Care Retirement Community, Green Valley, AZ, August 2017.

Andrews-Hanna, J.R. Dynamic Regulation of Internal Experience. Neuroscience of Enduring Change Symposium, Tucson, AZ, September 2017.

Ryan, L. Alzheimer's and Age-Related Memory Changes. Healthy Night Out Presentation at SaddleBrooke, Tucson, AZ, September 2017.

Awards

Rat tissue stained with a substance that selectively labels neurons

Gene Alexander, Ph.D., Elected Fellow of the American Psychological Association, Division 40, Society for Clinical Neuropsychology (2017)

Jessica Andrews-Hanna, Ph.D., Kavli Foundation/National Academy of Science Frontiers of Science Fellow (2017)

Carol Barnes, Ph.D., University of New Mexico Department of Psychology Quad-L Award in recognition of significant scientific contributions in the areas of learning, memory, and cognition (2017)

Roberta Brinton-Diaz, M.D., Ph.D., Alzheimer's Drug Discovery Foundation Melvin R. Goodes Prize for Excellence in Alzheimer's Drug Discovery (2017)

Roberta Brinton-Diaz, M.D., Ph.D., NIA MERIT (Method to Extend Research in Time) Award, R37AG053589, Aging and Estrongenic Control of the Bioenergetic System in Brain (2017-2022)

Lalitha Madhavan, M.D., Ph.D. University's Visionary Leadership Maria Teresa LVelez Outstanding Faculty Mentor Award (2017)

Lynn Nadel, Ph.D., American Psychological Foundation Gold Medal for Life Achievement in the Science of Psychology (2017)

Mary-Francis O'Conner, Ph.D., American Psychosomatic Society 75th Anniversary Award for recognition of contributions to our understanding of the integration of emotion, social relationships, and health (2017)

Faculty

Continued

Complete Faculty List

Director

- Carol A. Barnes, Ph.D., Regents' Professor, Psychology, Neurology and Neuroscience; Director, Evelyn F. McKnight Brain Institute; Evelyn F. McKnight Chair for Learning and Memory in Aging; Director, Division of Neural Systems, Memory and Aging

Associate Director

- Lee Ryan, Ph.D., Professor and Head, Psychology; Director, Cognition and Neuroimaging Labs, University of Arizona

Strategic Advisory Committee

- Martha A. Brumfield, Ph.D., President and Chief Executive Officer, Critical Path Institute; Research Professor, Pharmacology and Toxicology, University of Arizona
- Eric M. Reiman, M.D., Ph.D., Professor, Psychiatry; Associate Head for Research and Development (Phoenix Campus), University of Arizona; Director, Arizona Alzheimer's Disease Consortium; Executive Director, Banner Alzheimer's Institute; Clinical Director, Neurogenomics Program, Translational Genomics Research Institute (TGen)
- Leslie P. Tolbert, Ph.D., Regents' Professor, Neuroscience and Cellular and Molecular Medicine, University of Arizona

Scientific Advisory Committee

(Biographical sketches included in following pages; all scientific advisors are also affiliate faculty)

- Geoffrey L. Ahern, M.D., Ph.D., Professor, Neurology, Psychology and Psychiatry; Medical Director, Behavioral Neuroscience and Alzheimer's Clinic; Bruce and Lorraine Cumming Endowed Chair in Alzheimer's Research, University of Arizona
- Gene E. Alexander, Ph.D., Professor, Psychology, Psychiatry and Neuroscience; Director, Brain Imaging, Behavior and Aging Lab, University of Arizona
- Carol A. Barnes, Ph.D., Regents' Professor, Psychology, Neurology and Neuroscience; Director, Evelyn F. McKnight Brain Institute; Evelyn F. McKnight Chair for Learning and Memory in Aging; Director, Division of Neural Systems, Memory and Aging, University of Arizona
- Roberta Diaz Brinton, Ph.D., Professor, Pharmacology, Neurology and Psychology; Director, Center for Innovation in Brain Science
- Stephen L. Cowen, Ph.D. Assistant Professor, Psychology, Division of Neural Systems, Memory and Aging, Evelyn F. McKnight Brain Institute, University of Arizona
- Elizabeth Glisky, Ph.D., Professor, Psychology, University of Arizona
- Naomi E. Rance, M.D, Ph.D., Professor, Neurology, Cell Biology and Anatomy, and Pathology; Associate Head, Pathology, University of Arizona
- Lee Ryan, Ph.D., Professor, Psychology; Director, Cognition and Neuroimaging Labs, University of Arizona

Faculty

Continued

Additional Affiliate Faculty

- Jessica Andrews-Hanna, Ph.D., Assistant Professor, Psychology, University of Arizona
- E. Fiona Bailey, Ph.D., Associate Professor, Physiology, University of Arizona
- Heather Bimonte-Nelson, Ph.D., Associate Professor, Honors Disciplinary Faculty; Behavioral Neuroscience Program Director, Arizona State University
- Ying-hui Chou, Ph.D., Assistant Professor, Psychology, University of Arizona
- Paul Coleman, Ph.D., UA Associate, Evelyn F. McKnight Brain Institute, University of Arizona; Research Professor, The Biodesign Institute, Neurodegenerative Disease Research Center, Arizona State University
- Fabian Fernandez, Ph.D., Assistant Professor, Psychology, University of Arizona
- Ralph F. Fregosi, Ph.D., Professor, Physiology, University of Arizona
- Andrew J. Fuglevand, Ph.D., Associate Professor, Physiology, University of Arizona
- Katalin M. Gothard, M.D., Ph.D., Professor, Physiology, University of Arizona
- Matt Grilli, Ph.D., Assistant Professor, Psychology, University of Arizona
- Meredith Hay, Ph.D., Professor, Physiology, University of Arizona
- Matthew J. Huentelman, Ph.D., UA Associate, Evelyn F. McKnight Brain Institute, University of Arizona; Associate Professor, Neurogenomics Division, Translational Genomics Research Institute
- Anita Koshy, M.D., Assistant Professor, Neurology, University of Arizona
- Lalitha Madhavan, MBBS, Ph.D., Assistant Professor, Neurology, University of Arizona
- Diano Marrone, Ph.D., UA Associate, Evelyn F. McKnight Brain Institute; Assistant Professor, Psychology, Wilfrid Laurier University
- Matthias R. Mehl, Ph.D., Professor, Psychology, University of Arizona
- Lynn Nadel, Ph.D., Regents' Professor, Psychology, University of Arizona
- Janko Nikolich-Zugich, M.D., Ph.D., Professor and Chairman, Immunobiology; Co-Director, Arizona Center on Aging, University of Arizona
- Mary-Frances O'Conner, Ph.D., Assistant Professor, Psychology, University of Arizona
- Mary Peterson, Ph.D., Professor, Psychology, University of Arizona
- Steve Rapcsak, M.D., Professor, Neurology, Psychology and Speech, Hearing and Language Pathology, University of Arizona; Chief, Neurology Section, VA Medical Center
- Linda L. Restifo, M.D., Ph.D., Professor, Neurology, Neuroscience, Cell Biology and Anatomy, and BIO5 Institute, University of Arizona
- David A. Sbarra, Ph.D., Professor and Director of Clinical Training, Psychology, University of Arizona
- Anne C. Smith, Ph.D., Associate Research Scientist, Evelyn F. McKnight Brain Institute, University of Arizona
- Ted P. Trouard, Ph.D., Professor, Biomedical Engineering, University of Arizona
- Robert C. Wilson, Ph.D., Assistant Professor, Psychology, University of Arizona
- Pixuan 'Joe' Zhou, Ph.D., Adjunct Research Professor, Optical Sciences, University of Arizona

Biographical Sketch

Geoffrey Lawrence Ahern, M.D., Ph.D.
Professor

Education/Training

Institution & Location	Degree	Year(S)	Field Of Study
SUNY, Purchase College	B.A.	1976	Psychology
Yale University, New Haven	M.S.	1978	Psychology
Yale University, New Haven	Ph.D.	1981	Psychology
Yale University, New Haven	M.D.	1984	Medicine
Waterbury Hospital, Waterbury	Intern	1984 – 1985	Medicine
Boston University, Boston	Resident	1985 – 1988	Neurology
Beth Israel Hospital, Boston	Fellow	1988 – 1990	Behavioral Neurology

Positions

1977 – 1980	Lab Director, Human Psychophysiology Laboratory, Yale University, New Haven
1985 – 1988	Teaching Fellow, Department of Neurology, Boston University School of Medicine, Boston
1988 – 1990	Instructor, Department of Neurology, Harvard Medical School, Boston
1988 – 1990	Attending Neurologist, Beth Israel Hospital, Boston
1990 – 1996	Assistant Professor, Neurology and Psychology, University of Arizona, Tucson
1990	Attending Neurologist, University Medical Center, Tucson, Arizona
1990 – 1996	Medical Director, Behavioral Neurology Unit, University of Arizona, Tucson
1990	Director, Neurobehavioral Laboratory, University of Arizona, Tucson
1990	Member, Committee on Neuroscience, University of Arizona, Tucson, Arizona
1996 – 1999	Associate Professor, Neurology and Psychology, University of Arizona, Tucson
1996	Director, Behavioral Neuroscience & Alzheimer's Clinic, University of Arizona, Tucson
1999 – 2002	Associate Professor, Neurology, Psychology, Psychiatry, University of Arizona, Tucson
2002	Professor, Neurology, Psychology, and Psychiatry, University of Arizona, Tucson
2007	Professor, Evelyn F. McKnight Brain Institute, University of Arizona, Tucson
2007	Bruce and Lorraine Cumming Endowed Chair in Alzheimer's Research

Biographical Sketch

Geoffrey Lawrence Ahern, M.D., Ph.D.

continued

Honors and Awards

1994	Cited in S Naifeh and GW Smith (eds.) The Best Doctors in America	1994 – 1995
1996	Cited in S Naifeh and GW Smith (eds.) The Best Doctors in America, Pacific Region	1996 – 1997
1998	Cited in S Naifeh and GW Smith (eds.) The Best Doctors in America	1998 – 1999
2003	Cited in S Naifeh and GW Smith (eds.) The Best Doctors in America	2003 – 2004
2005	Cited in S Naifeh and GW Smith (eds.) The Best Doctors in America	2005 – 2006
2007	Cited in S Naifeh and GW Smith (eds.) The Best Doctors in America	2007 – 2008
2009	Cited in S Naifeh and GW Smith (eds.) The Best Doctors in America	2009 – 2010
2010	Cited in S Naifeh and GW Smith (eds.) The Best Doctors in America	2011 – 2012
2013	Cited in S Naifeh and GW Smith (eds.) The Best Doctors in America	2013
2014	Cited in S Naifeh and GW Smith (eds.) The Best Doctors in America	2014
2015	Cited in S Naifeh and GW Smith (eds.) The Best Doctors in America	2015 – 2016

Publications

Beach, T.G., Adler, C.H., Sue, S.I., Serrano, G., Shill, H.A., Walker, D.G., Lue, L.F., Roher, A.E., Dugger, B.N., Maarouf, C., Birdsill, A.C., Intorcia, A., Saxon-Labelle, M., Pullen, J., Scroggins, A., Filon, J., Scott, S., Hoffman, B., Garcia, A., Caviness, J.N., Hentz, J.G., Driver-Dunckley, E., Jacobson, S.A., Davis, K.J., Belden, C.M., Long, K.E., Malek-Ahmadi, M., Powell, J.J., Gale, L.D., Nicholson, L.R., Caselli, R.J., Woodruff, B.K., Rapcsak, S.Z., Ahern, G.L., Shi, J., Burke, A.D., Reiman, E.M., Sabbagh, M.N. (2015) Arizona study of aging and neurodegenerative disorders and brain and body donation program. Neuropathology, 35:354-389.

Filon J., Intorcia, A., Sue, L.I., Vazquez Arreola, E., Wilson, J., Davis, K.J., Sabbagh, M.N., Belden, C.M., Caselli, R.J., Adler, C.H., Woodruff, B.K., Rapcsak, S.Z., Ahern, G.L., Burke, A.D., Jacobson, S.A., Shill, H.A., Driver-Dunckley, E., Chen, K., Reiman, E.M., Beach, T.G., Serrano, G. (2016) Gender differences in Alzheimer's disease: Brain atrophy, histopathology burden, and cognition. Journal of Neuropathology and Experimental Neurology, 75 (8) 748-754.

Biographical Sketch

Gene E. Alexander, Ph.D.

Education/Training

Institution & Location	Degree	Year(S)	Field Of Study
Pomona College, Claremont, CA	B.A.	5/1983	Psychology
Loyola University of Chicago, Chicago, IL	M.A.	5/1987	Clinical Psychology
Loyola University of Chicago, Chicago, IL	Ph.D.	1/1992	Clinical Psychology

Personal Statement

Gene E. Alexander, Ph.D., is professor in the Departments of Psychology and Psychiatry, in the Evelyn F. McKnight Brain Institute, and in the Neuroscience and Physiological Sciences Graduate Programs of the University of Arizona. He is director of the Brain Imaging, Behavior and Aging Lab; a member of the Scientific Advisory Committee for the Arizona Evelyn F. McKnight Brain Institute; chair of the Research Committee in the Department of Psychology; and a member of the BIO5 Institute and the MRI Operations Committee at the University of Arizona. Prior to coming to Arizona, Dr. Alexander was chief of the Neuropsychology Unit in the Laboratory of Neurosciences in the Intramural Research Program at the NIA. Dr. Alexander is a fellow of the American Psychological Association (Division 40) Society for Clinical Neuropsychology and the Association for Psychological Science. His research has been supported by grants from the National Institutes of Health, McKnight Brain Research Foundation, and the state of Arizona. Dr. Alexander has more than 20 years of experience as a neuropsychology and neuroimaging researcher on the effects of aging and risk factors for age-related neurodegenerative disease. He uses structural and functional magnetic resonance imaging (MRI) and positron emission tomography (PET) with novel network analyses to investigate the effects of multiple health and lifestyle factors on the cognitive and brain changes associated with healthy and pathological aging, with the goal of developing new interventions for the effects of cognitive aging.

1. Kern KC, Wright CB, Bergfield KL, Fitzhugh M, Chen K, Moeller JR, Nabizadeh N, Elkind MSV, Sacco RL, Stern Y, DeCarli C, & Alexander GE. (2017) Blood pressure control in aging predicts cerebral atrophy related to small-vessel white matter lesions. Frontiers in Aging Neuroscience, 9, 132.

2. Cohen RA & Alexander GE. Using the Telephone Interview for Cognitive Status and Telephone Montreal Cognitive Assessment for evaluating vascular cognitive impairment: Promising call or put on hold? Stroke, in press. (Invited editorial)

3. Alexander GE. (2017) An emerging role for imaging white matter in the preclinical risk for Alzheimer disease: Linking ß-amyloid to myelin. JAMA Neurology, 74(1), 17-19. (Invited editorial)

4. Raichlen DA & Alexander GE. (2017) Adaptive Capacity: An evolutionary neuroscience model linking exercise, cognition, and brain health. Trends in Neurosciences, 40(7), 408-421.

Research and Professional Experience

1988 – 1989	Clinical Psychology Intern, Dept. of Psychiatry & Behav Sci, Univ of Washington, Seattle, WA
1989 – 1992	Research Fellow, Dept. of Brain Imaging, NYSPI and Columbia University, NY, NY
1991 – 1993	Research Scientist I, Dept. of Brain Imaging, NYSPI and Columbia University, NY, NY
1993 – 1999	Staff Fellow to Sr. Staff Fellow, Laboratory of Neurosciences, NIA, NIH, Bethesda, MD
1993 – 1999	Chief, Neuropsychology Unit, Laboratory of Neurosciences, NIA, NIH, Bethesda, MD
1999 – 2003	Research Associate Professor, Dept. of Psychology, Arizona State University, Tempe, AZ
2001 – 2009	Director, Data Management and Statistics Program/Core, Arizona ADC, AZ

Biographical Sketch

Gene E. Alexander, Ph.D.

continued

2003 – 2007	Assoc. Professor with Tenure to Professor, Psychology Dept., Arizona State University, Tempe, AZ
2007 – Present	Professor, Psychology Dept & Evelyn F McKnight Brain Institute, University of Arizona, Tucson, AZ
2007 – Present	Director, Brain Imaging, Behavior & Aging Lab, Psychology Dept, University of Arizona, Tucson, AZ
2007 – Present	Professor, Neuroscience Graduate Interdisciplinary Program, University of Arizona, Tucson, AZ
2008 – Present	Member, Scientific Advisory Board, Evelyn F. McKnight Brain Inst., University of Arizona, Tucson, AZ
2011 – Present	Professor, Physiological Sciences Graduate Interdisciplinary Program, University of Arizona, AZ
2017 – Present	Member, BIO5 Institute, University of Arizona, Tucson, AZ
2017 – Present	Professor, Department of Psychiatry, College of Medicine Tucson, University of Arizona, AZ

Honors and Awards

1995 – Present	Ad Hoc Reviewer, over 20 journals in Neuropsychology, Psychiatry, Neurology, and Neuroscience.
1996 – 1999	Staff Recognition Awards (annual), Laboratory of Neurosciences, IRP, NIA, NIH
2000 – Present	Reviewer, Alzheimer's Association Research Grant Program
2003 – 2007	Member, Study Section, Clinical Neuroscience and Disease, IRG, CSR, NIH
2003	Member, SEP, Women's Health Initiative Memory Study, Review Branch, NHLBI, NIH
2004	Member, Special Emphasis Panel, Alzheimer's Disease Center Grant Review, NIA, NIH
2004 – 2009	External Advisor, Aging Brain: Vasculature, Ischemia & Behav. Prog. Proj., UCSF/Davis
2005 – 2007	Member, Specialist Review Cmte, Psychology: Exp/Clinical, Fulbright Scholar Program
2006	Chair, SEP, Clinical Neuroscience & Disease, ZRG1 BDCN-E, IRG, CSR, NIH
2008	Member, SEP, Prog Proj Review Group, Recovery from Illness, ZAG1 ZIJ-8 O1, NIA, NIH
2008	Member, Study Section, Brain Injury & Neurovasc. Path., ZRB 1 BDCN-L (07), CSR, NIH
2008	Member, SEP, SPRINT Center Review, ZHL1 CCT-B C2 1, NHLBI, NIH
2008 – Present	Member, Neuroimaging Workgroup, International Conf. on Alzheimer's Disease/ISTAART
2009	Reviewer, SEP, Challenge Grant Panel #10, ZRG1 BDA-A 58 R, CSR, NIH
2009	Member, SEP, P30 Faculty Recruitment in Biomedical Research Core Centers, NIA, NIH
2009	Member, SEP, RC2 Grand Opport. Grants in Genetics, Epigenetics & Genomics, NIA, NIH
2009	Member, SEP, Program Project Review Group, Brain Dopamine, ZAG1 ZIJ-8 J3, NIA, NIH
2009	Member, SEP, Prog. Proj. Rev. Group, Neuroimaging and Aging, ZAG1 ZIJ-5 JF, NIA, NIH
2010	Member, Neurological Sciences & Disorders K Review Committee, NSD-K, NINDS, NIH
2010 – 2012	Member, Neuroscience of Aging Review Committee, NIA-N, NIA, NIH
2010	Member, SEP, Prog. Proj. Rev., Exercise, Motor Deficits, & Aging, ZAG1-ZIJ-9, NIA, NIH
2010	Member, SEP, Prog. Proj. Rev., Dopaminergic Dysfunct. Aging, ZAG1 ZiJ-6 J3, NIA, NIH
2011	Chairperson, Member Special Emphasis Panel, ZAG1 ZIJ-7 (J1), NIA, NIH

Biographical Sketch

Gene E. Alexander, Ph.D.

continued

2011 – 2014	Advisory Editor, Neurobiology of Aging, Elsevier
2011	Member, VA MHBB Merit Review Subcommittee, Veterans Administration
2011	Member, SEP, Biobehav Res Award Innovat New Scientists (BRAINS), ZMH1ERBL04, NIMH, NIH
2011 – Present	Reviewer, Alzheimer's Disease Pilot Grant Program, Arizona Alzheimer's Disease Center
2011 – Present	Fellow, Association for Psychological Science
2012	Member, Neurological Sciences & Disorders K Review Committee, NSD-K, NINDS, NIH
2012 – Present	Member, Cognitive Workgroup, Evelyn F. McKnight Brain Institute
2012 – Present	Member, MRI Standardization Workgroup, Evelyn F. McKnight Brain Institute
2012 – Present	Co-Director, Annual Conference on Successful Aging, University of Arizona
2013	Member, SEP, Neurodegen. & Neurodevelopmental Dis., ZRG1BDCN-Y(02), NIA, NIH
2013	Member, SEP, Psychol. Health, Development & Aging, 10 ZRG1 BBBP-D (02), NIA, NIH
2013	Member, Alzheimer's Disease Research Centers Review, ZAG1ZIJ4J1, NIA, NIH
2013 – Present	Member, Neuroscience of Aging Review Committee, NIA-N, NIA, NIH
2014	Member and Chairperson, Biobehav & Behav. Processes Rev. Group, ZRG1BBBPY04, CSR, NIH
2015 – Present	Guest Assoc. Editor, Neuroimaging Approaches to Cognitive Aging, Frontiers Aging Neuroscience
2015 – Present	Chair, Research Committee, Department of Psychology, University of Arizona
2016	Member, SEP, Alzheimer's Disease Center Review, ZAG1 ZIJ-1 M1, NIA, NIH
2016	Member, SEP, Prevention Trial Review, ZAG1 ZIJ-1 M2, NIA, NIH
2017 – Present	Fellow, American Psychological Association Division 40, Society for Clinical Neuropsychology

Contribution to Science

Brain Imaging and Cognitive Effects of Age-Related Dementia. My early research interests focused on understanding brain-behavior relationships in the context of Alzheimer's dementia with the use of functional and structural neuroimaging methods combined with measures of cognition and demographic characteristics. My initial work in this area, with Dr. Yaakov Stern, led to the first functional neuroimaging findings to suggest the potential for a brain-based, cognitive reserve against the effects of Alzheimer's disease. My research then expanded to include measures of cerebral metabolism with PET, further supporting the concept of cognitive reserve and the use of PET as a method to evaluate treatments to delay or diminish declines in cerebral metabolism over time in Alzheimer's dementia.

1. Stern Y, Alexander GE, Prohovnik I, Mayeux R. (1992) Inverse relationship between education and parietotemporal perfusion deficit in Alzheimer's disease. Ann Neurol, 32, 371-5.
2. Alexander GE, Prohovnik I, Stern Y, Mayeux R. (1994) WAIS-R subtest profile and cortical perfusion in Alzheimer's disease. Brain and Cognition, 24, 24-43.
3. Alexander GE, Furey M, Grady CL, Pietrini P, Brady D, Mentis MJ, Schapiro MB. (1997) Association of premorbid function with cerebral metabolism in Alzheimer disease: Implications for the cognitive reserve hypothesis. Am J Psychiatry, 154, 165-172. (Article featured in journal editorial)
4. Alexander GE, Chen K, Pietrini P, Rapoport SI, Reiman EM. (2002) Longitudinal PET evaluation of cerebral metabolic decline in dementia: A potential outcome measure in Alzheimer's disease treatment studies. Am J Psychiatry, 159, 738-745. (Article featured on journal cover and editorial)

Biographical Sketch

Gene E. Alexander, Ph.D.

continued

Brain Imaging and Cognitive Effects of Healthy Aging: In more recent years, my research program has focused on the effort to better understand heterogeneity across the spectrum from successful to pathological aging. This work includes studies of healthy aging across the adult age range using structural and functional brain imaging methods combined with standardized and computerized measures of cognition. Additionally, I have an interest in extending my research in humans to nonhuman animal models of aging and age-related disease. The following publications provide examples of my work using both univariate and novel multivariate network analysis methods to evaluate patterns of brain structure in older adults, as well as functional brain regions and cognitive processes impacted by brain aging.

1. Alexander GE, Chen K, Merkley TL, Reiman EM, Caselli RJ, Aschenbrenner M, Santerre-Lemmon L, Lewis DJ, Pietrini P, Teipel SJ, Hampel H, Rapoport SI, Moeller JR. (2006) Regional Network of MRI Gray Matter Volume in Healthy Aging. NeuroReport, 17, 951-6.
2. Bergfield KL, Hanson KD, Chen K, Teipel SJ, Hampel H, Rapoport SI; Moeller JR, Alexander GE. (2010) Age-related networks of regional covariance in MRI gray matter: Reproducible multivariate patterns in healthy aging. NeuroImage, 49, 1750-9.
3. Alexander GE, Ryan L, Bowers D, Foster TC, Bizon JL, Geldmacher DS, Glisky EL. (2012) Characterizing Cognitive Aging in Humans with Links to Animal Models. Frontiers in Aging Neuroscience, 4, 21.
4. Ryan L, Cardoza JA, Barense MD, Kawa KH, Wallentin-Flores J, Arnold WT, Alexander GE. (2012) Age-related impairment in a complex object discrimination task that engages perirhinal cortex. Hippocampus, 22, 1978-89.

Method Development, Evaluation, and Implementation for Neuroimage Analysis Approaches: My work also includes the development, evaluation, and implementation of novel analysis methods for neuroimaging data. Early in the course of my research, I recognized the importance of applying analysis methods that have the potential to more fully capture the rich regional information obtained within functional and structural brain images. My work in this area has focused on the application of novel multivariate network analysis methods to characterize regional patterns of covariance in brain scans to better understand the effects of brain aging and age-related disease. I have applied this approach to PET cerebral metabolism, functional MRI, and multimodal approaches that combine across imaging modalities. I have also performed the first application of this approach to structural MRI in both humans and in a nonhuman primate model of aging. The example publications below illustrate my research efforts in this area.

1. Alexander GE, Moeller JR. (1994) Application of the Scaled Subprofile Model to functional imaging in neuropsychiatric disorders: A principal component approach to modeling regional patterns of brain function in disease. Human Brain Mapping, 2, 79-94. (Article featured on journal cover)
2. Chen K, Reiman EM, Zhongdan H, Caselli RJ, Bandy D, Alexander GE. (2009) Linking functional and structural brain images with multivariate network analyses: A novel application of the partial least square method. Neuroimage, 47, 602-10.
3. Smith JF, Chen K, Johnson SC, Morrone-Strupinsky J, Reiman EM, Nelson A, Moeller JR, Alexander GE (2006) Network analysis of single-subject fMRI during finger opposition task. Neuroimage, 32, 325-32.
4. Alexander GE, Chen K, Aschenbrenner M, Merkley TL, Santerre-Lemmon LE, Shamy JL, Skaggs WE, Buonocore MH, Rapp PR, Barnes CA. (2008) Age-related regional network of magnetic resonance imaging gray matter in the rhesus macaque. Journal of Neuroscience, 28, 2710-8.

Biographical Sketch

Gene E. Alexander, Ph.D.

continued

Large Multi-Institutional Collaborative Projects: Additionally, my research has included participation in several large multi-institutional collaborative research projects that have had a significant impact on the field, including supporting efforts to identify imaging methods for the evaluation of treatments, to aid diagnosis, and to enhance prevention research for Alzheimer's disease and dementia. These projects have included the Alzheimer's Disease Neuroimaging Initiative (ADNI), for which I served as a member of the MRI and PET Cores, as well as other multi-institutional projects on APOE risk and pathology confirmed dementia. These projects focused on the use of neuroimaging methods using PET and MRI for the evaluation of brain effects in Alzheimer's disease and in those at increased genetic risk for age-related dementia. Examples of my collaborative publications are illustrated below.

1. Silverman DHS, Small GW, Chang CY, Lu CS, Kung de Aburto MA, Chen W, Czernin J, Rapoport SI, Pietrini P, Alexander GE, Schapiro MB, Jagust WJ, Hoffman JM, Welsh-Bohmer KA, Alavi A, Clark CM, Salmon E, de Leon MJ, Mielke R, Cummings JL, Kowell AP, Gambhir SS, Hoh CK, Phelps ME. (2001) Neuroimaging in evaluation of dementia: Regional brain metabolism and long-term outcome. JAMA, 286, 2120-7. (Article featured in press release)
2. Jack CR Jr, Bernstein MA, Fox NC, Thompson P, Alexander G, Harvey D, Borowski B, Britson PJ, L Whitwell J, Ward C, Dale AM, Felmlee JP, Gunter JL, Hill DL, Killiany R, Schuff N, Fox-Bosetti S, Lin C, Studholme C, DeCarli CS, Krueger G, Ward HA, Metzger GJ, Scott KT, Mallozzi R, Blezek D, Levy J, Debbins JP, Fleisher AS, Albert M, Green R, Bartzokis G, Glover G, Mugler J, Weiner MW. (2008) The Alzheimer's Disease Neuroimaging Initiative (ADNI): MRI methods. J Magn Reson Imaging, 27, 685-91.
3. Reiman EM, Chen K, Liu X, Bandy D, Yu M, Lee W, Ayutyanont N, Keppler J, Reeder SA, Langbaum JB, Alexander GE, Klunk WE, Mathis CA, Price JC, Aizenstein HJ, DeKosky ST, Caselli RJ. (2009) Fibrillar amyloid-beta burden in cognitively normal people at 3 levels of genetic risk for Alzheimer's disease. Proceedings of the National Academy of Sciences USA, 106, 6820-5.
4. Leow AD, Yanovsky I, Parikshak N, Hua X, Lee S, Toga AW, Jack CR, Bernstein MA, Britson PJ, Gunter JL, Ward CP, Borowski B, Shaw LM, Trojanowski JQ, Fleisher AS, Harvey D, Kornak J, Schuff N, Alexander GE, Weiner MW, Thompson PM; for the ADNI study. (2009) Alzheimer's Disease Neuroimaging Initiative: A one-year follow up study using tensor-based morphometry correlating degenerative rates, biomarkers and cognition. Neuroimage, 45, 645-55.

Health, Lifestyle, and Genetic Risk Factors for Pathological Aging. A major focus of my current research interests includes integrating health status, lifestyle characteristics, and genetics with brain imaging and cognitive testing to investigate healthy and pathological brain aging. For example, my work was the first to demonstrate an interaction between age and hypertension on brain volume in aging, and has contributed to our understanding of how the APOE ε4 allele impacts cognition and brain structure over the adult lifespan. I have also recently proposed a new hypothesis suggesting that demands for exercise may have interacted with APOE status to influence the evolution of the human lifespan, which was recently featured on the cover of Trends in Neurosciences.

1. Strassburger TL, Lee HC, Daly E, Szczepanik J, Krasuski JS, Mentis MJ, Salerno JA, DeCarli C, Schapiro MB, Alexander GE. (1997) Interactive effects of age and hypertension on structural brain volumes. Stroke, 28, 1410-1417. (Article featured in journal editorial & AHA press release)
2. Alexander GE, Bergfield KL, Chen K, Reiman EM, Hanson KD, Lin L, Bandy D, Caselli RJ, Moeller JR. (2012) Gray matter network associated with genetic risk for Alzheimer's disease in young to early middle-aged adults. Neurobiology of Aging, 33, 2723-32.

Biographical Sketch

Gene E. Alexander, Ph.D.

continued

3. Caselli RJ, Reiman EM, Osborne D, Hentz JG, Baxter LC, Hernandez JL, Alexander GE. (2004) Longitudinal changes in cognition and behavior in asymptomatic carriers of the APOE ε4 allele. Neurology, 62, 1990-5.
4. Raichlen DA, Alexander GE. (2014) Exercise, APOE genotype, and the evolution of the human lifespan. Trends in Neurosciences, 37, 247-55. (Article featured on journal cover)

Publications above selected from more than 143; complete list of published work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/gene.alexander.1/bibliography/41140485/public/?sort=date&direction=ascending [Google Scholar H-Index = 65]

Research Support

Ongoing

NIA R01 AG049464-01 Alexander, Barnes, Coleman (MPIs) 8/1/14 – 3/31/20
Epigenetic, Neuroimaging and Behavioral Effects of Hypertension in the Aging Brain
The goal is to determine epigenetic changes induced by hypertension in brain regions important for cognition.
Role on Project: Contact PI

McKnight Brain Research Foundation Alexander, Cohen, Levin, Wadley (MPIs) 9/1/15 – 12/31/18
McKnight Inter-Institutional Cognitive Aging Assessment Core
The goal is to provide standardized clinical and cognitive measures for multi-institutional brain aging research.
Role on Project: A PI

McKnight Brain Research Foundation Alexander, Cohen, Rundek, Visscher (MPIs) 1/1/15 – 12/31/18
McKnight Inter-Institutional Neuroimaging Core and Brain Aging Registry
The goal to establish neuroimaging acquisition and a multisite brain aging registry to study brain aging.
Role on Project: A PI

NIA R01 AG054077-01 Cohen, Marsiske, Woods (MPIs) 9/1/16 – 8/31/21
Augmenting Cognitive Training in Older Adults – The ACT Grant
This multisite RCT will evaluate cognitive training and transcranial direct current stimulation for brain aging.
Role on Project: PI of the UA Field Center and UA subcontract

State of Arizona/Banner Health Subcontract Alexander (PI) 7/1/17 – 6/30/18
Influence of Health & Lifestyle Factors on Brain Aging and the Risk for Alzheimer's Disease
The goal is to study health and lifestyle factors that alter effects of brain aging and cognitive health.
Role on Project: PI

NIA R03 AG055020-01 Su (PI) 7/15/17 – 4/30/19
Ultra-sensitive and Label-free Detection of Alzheimer's Disease Biomarkers
This goal is to evaluate a highly sensitive method to identify Alzheimer's biomarkers in fluid samples.
Role on Project: Co-Investigator

Biographical Sketch

Gene E. Alexander, Ph.D.

continued

NIA P30 AG019610-17 Reiman (PI) 7/1/16 – 6/30/21
Arizona Alzheimer's Disease Core Center
This center provides core resources to support Alzheimer's Disease research in the Arizona region.
Role on Project: Co-Investigator and member of the Data Management and Statistics Core

NIH 3 R01 AG031581 Reiman, Caselli (MPIs) 4/1/14 – 3/31/19
Brain Imaging, APOE & the Preclinical Course of Alzheimer's disease
The goal is to characterize the brain changes in those at risk for Alzheimer's disease with the APOE e4 allele.
Role on Project: Dr. Alexander is Co-Investigator and PI of the UA subcontract.

NIH R01 AG049465-01 Barnes (PI) 8/1/14 – 3/31/19
Neural System Dynamics and Gene Expression Supporting Successful Cognitive Aging
The goal is to use cognitive, neurobiological and molecular methods to test reserve in a rodent model of aging.
Role on Project: Co-Investigator

UA15-011 Alexander, Raichlen (MPIs) 2/5/15 – 12/31/17
Tech Launch Arizona Wheelhouse
Evaluation of the Aerobic Training System for Enhancing Cognitive Performance in Older Adults
The goal of this project is to evaluate the benefits of exercise on cognitive function in healthy aging
Role on Project: A PI

Selected Completed Recent Research Support

NIH 1 R01 AG025526 Alexander (PI) 4/1/07 – 7/31/14
Neuroanatomical Substrates of Aging & Cognitive Decline (w/ NCE)
The goal is to study how health status and genetic risk for AD affect the brain and cognitive changes in aging.
Role on Project: PI

NIMH/NIA 2 R01 MH57899-01A1 Reiman (PI) 7/1/98 – 6/30/13
PET, APOE, & the Preclinical Course of Alzheimer's Disease
The goal is to characterize the brain changes in individuals at risk for Alzheimer's disease with APOE e4.
Role on Project: Co-Investigator and PI of the UA subcontract

NIA 1 UO1 AG024904-01 Weiner (PI) 10/1/04 – 9/30/10
Alzheimer's Disease Neuroimaging Initiative (ADNI)
The goals are to test the ability of MRI and PET to track the brain changes in MCI and Alzheimer's dementia.
Role on Project: Co-Investigator, member of MRI and PET Cores, and PI for UA subcontract

Biographical Sketch

Carol A. Barnes, Ph.D.
Regents' Professor, Psychology, Neurology and Neuroscience

Education/Training

Institution & Location	Degree	Year(S)	Field Of Study
University of California, Riverside, CA	B.A. (Honors)	1971	Psychology
Carleton University, Ottawa, Ontario, Canada	M.A.	1972	Psychology
Carleton University, Ottawa, Ontario, Canada	Ph.D. (Cum laude)	1977	Psychology

Personal Statement

Dr. Barnes has been interested in the brain circuits responsible for memory and how these circuits change during aging for more than four decades. She has applied behavioral and electrophysiological methods to the study of plasticity and circuit properties of the medial temporal lobe over that time, including in vivo evoked field potential recordings in chronically implanted freely behaving rats, and intracellular and extracellular recordings in vitro. She was instrumental (with McNaughton) in the development of ensemble tetrode recording methods for single units in awake young and old rats. More recently she has extended these methods to young and aged nonhuman primates, with chronic implants of hyperdrive recording devices that are capable of individually lowering multiple tetrodes into the hippocampus while monkeys behave. Another approach she uses to understand behavior-driven circuits is the single cell gene expression imaging method "catFISH," which was developed in her laboratory (Guzowski et al., 1999). The immediate early gene Arc is induced in a cell-specific fashion in the brain by neural activity associated with attentive, active behavior. With this method the activity history of individual cells in a population can be determined for two different time points within the same animal (ex vivo). This method contributed to moving the field closer to the goal of behavior-driven whole brain imaging with single cell resolution. Dr. Barnes directs the Evelyn F. McKnight Brain Institute at the University of Arizona and the Division of Neural Systems, Memory and Aging. She is actively involved in collaborative projects with scientists within the state of Arizona, across the United States and the world. She has a track record of conducting difficult, systematic, and thorough studies with interdisciplinary teams, as well as with her own students and postdoctoral fellows – projects that have been followed through to publication (254 total, H index 94), a number of which are now classic references on brain aging and behavior.

Positions

1978	Research Associate, Dalhousie University, Dept. Psychology, Halifax, Canada
1979 – 1980	NRSA Postdoctoral Fellow, Institute of Neurophysiology, Oslo, Norway
1981	NATO Postdoctoral Fellow, Cerebral Functions Group, University College, London, England
1982 – 1985	Assistant Professor, Department of Psychology, University of Colorado, Boulder
1985 – 1989	Associate Professor, Department of Psychology, University of Colorado, Boulder
1989 – 1990	Professor, Department of Psychology, University of Colorado, Boulder
1990 – 2006	Professor, Psychology, Neurology, ARL NSMA, Univ. Arizona, Tucson
2006	Regents' Professor, Psychology, Neurology, Univ. of Arizona, Tucson
2006	Director, Evelyn F. McKnight Brain Institute, University of Arizona, Tucson, AZ
2006	Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging, Univ. of Arizona
2008	Director, Division of Neural Systems, Memory and Aging, University of Arizona, Tucson
2009 – 2016	Associate Director, BIO5 Institute, University of Arizona, Tucson
2009	Regents' Professor, Neuroscience, University of Arizona, Tucson

Biographical Sketch

Carol A. Barnes, Ph.D.

continued

Honors

1969	NSF Summer Research Fellowship
1971	Phi Beta Kappa
1972 – 1974	Ontario Graduate Fellowship
1979 – 1981	NRSA Individual Postdoctoral Fellowship, NIH
1981 – 1982	NATO Fellowship in Science, NSF
1984 – 1989	Research Career Development Award, NIH
1987 – 1991	Neuroscience, Behavior and Sociology of Aging Committee A, NIA
1989 – 1994	Research Scientist Development Award, Level II, NIMH
1991 – 1997	Medical and Scientific Advisory Board, Alzheimer's Association
1994 – 1999	Research Scientist Award, NIMH
1994 – 1997	National Advisory Council on Aging, NIA
1995 – 1999	National Science Advisory Council, American Federation for Aging Research
1996 – 2000	Councilor, Society for Neuroscience
1997 – 2000	Medical and Scientific Advisory Council, Alzheimer's Association
1999 – 2004	Board of Scientific Counselors, NIMH
2000 – 2002	Secretary, Society for Neuroscience
2003 – 2006	President-Elect (2003-04), President (2004-05), Past-President (2005-06), Soc for Neurosci
2004	MERIT Award, National Institute on Aging, NIH
2004	Elected Norwegian Royal Society of Sciences and Letters
2006	Regents' Professor, University of Arizona
2006	Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging, University of Arizona
2007	Fellow, American Association for the Advancement of Science
2010	Elected: Mika Salpeter Lifetime Achievement Award, Society for Neuroscience
2011	Elected: Galileo Fellow, College of Science, University of Arizona
2013	Ralph W. Gerard Prize in Neuroscience, Society for Neuroscience
2014	American Psychological Association Award for Distinguished Scientific Contributions
2017	Quad-L Award, University of New Mexico

Contribution to Science

Some of my early work was inspired by two fundamental discoveries in the early 1970s. The first was the discovery of the likely biological basis of memory formation in the brain in 1973 by Terje Lomo, Tim Bliss, and Tony Gardner-Medwin. They used patterned electrical stimulation to experimentally induce changes in synaptic strength in the hippocampus, enabling the study of the process the brain may use to lay down memory traces (long-term potentiation, or LTP). In that same time period, O'Keefe and Nadel were circulating a monograph, which eventually turned into a classic and influential book (The Hippocampus as a Cognitive Map, 1978) that suggested that hippocampal function could be evaluated in animals by assessing spatial memory. These ideas made it possible to design experiments to interrogate how the brain acquires, stores, and retrieves information across the lifespan. Using awake, freely behaving rats with chronically implanted electrodes that could monitor the induction and decay of LTP over weeks, we obtained the first concrete evidence that LTP persistence and the durability of memory

Biographical Sketch

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continued

were related, and that a decline in its persistence was associated with poorer spatial memory in old animals. This relationship held in young rats as well – the better the animal's memory, the more durable was LTP. For these experiments, I developed a novel spatial memory task ("the Barnes maze"), which was conceived of and the methods published long before the more widely used, and conceptually similar, Morris water maze. The 1979 paper referenced below introduced the Barnes maze and provided the first demonstration that LTP and memory are associated – providing the groundwork for an explosion of research on the biophysical and molecular mechanisms of memory across the lifespan.

1. Barnes, C.A. (1979) Memory deficits associated with senescence: A neurophysiological and behavioral study in the rat. Journal of Comparative and Physiological Psychology, 93:74-104.
2. Barnes, C.A., Nadel, L. and Honig, W.K. (1980) Spatial memory deficit in senescent rats. Canadian Journal of Psychology, 34:29-39.
3. Barnes, C.A. and McNaughton, B.L. (1985) An age-comparison of the rates of acquisition and forgetting of spatial information in relation to long-term enhancement of hippocampal synapses. Behavioral Neuroscience, 99:1040-1048.
4. Barnes, C.A., Rao, G. and Houston, F.P. (2000) LTP induction threshold change in old rats at the perforant path – granule cell synapse. Neurobiology of Aging, 21:613-620.

Other work that is now classic in the field of brain aging is the first detailed analysis of the biophysical characteristics of aging neural tissue in vitro. These studies provided some of the early evidence that the pattern of biophysical change in the hippocampus was not that of general deterioration, but was highly selective, and in some cases suggested adaptation of function in response to perturbation of the neural system. These studies laid the groundwork to support the contention that "aging is not a disease," but a highly selective biological process, that has a comparatively subtle impact on brain and behavior compared to pathological conditions such as Alzheimer's disease. In fact, the 1980 study referenced below was the first demonstration of biological compensation at the level of synaptic transmission in aging and suggested that these kinds of adaptive processes may play an important role in the function of the aging nervous system.

1. Barnes, C.A. and McNaughton, B.L. (1980) Physiological compensation for loss of afferent synapses in rat hippocampal granule cells during senescence. Journal of Physiology (Lond), 309:473-485.
2. Barnes, C.A., Rao, G. and McNaughton, B.L. (1987) Increased electrotonic coupling in aged rat hippocampus: A possible mechanism for cellular excitability changes. Journal of Comparative Neurology, 259:547-558.
3. Barnes, C.A., Rao, G., Foster, T.C. and McNaughton, B.L. (1992) Region-specific age effects on AMPA sensitivity: Electrophysiological evidence for loss of synaptic contacts in hippocampal field CA1. Hippocampus, 2:457-468.
4. Barnes, C.A. Rao, G. and McNaughton, B.L. (1996) Functional integrity of NMDA-dependent LTP induction mechanisms across the lifespan of F344 rats. Learning and Memory, 3:124-137.

Having established that plasticity mechanisms like LTP are altered at older ages, and that, with some important exceptions, most biophysical properties of aged hippocampal neurons are intact, I extended my work from an assessment of the impact of age on the function of artificially activated networks to those activated by behavior. These were the earliest studies to examine behavior-driven single cell firing characteristics in the aged hippocampus. We developed better recording methods over the years (the tetrode, the hyperdrive device) that enabled recording from many hippocampal cells simultaneously. This made it possible to characterize how the hippocampus constructs a "cognitive map" (as proposed by O'Keefe and Nadel in 1978) of the surrounding environment. We showed that there are distinct changes in spatial representations within the hippocampus – with the older animals appearing

Biographical Sketch

Carol A. Barnes, Ph.D.

continued

to occasionally retrieve the wrong map (in CA1) upon repeated exposures to an environment. In addition, we have shown plasticity-related defects in the construction of these maps, changes in the replay of these maps during sleep in aged rats, as well as altered network functions of other temporal and frontal lobe structures.

1. Barnes, C.A., Suster, M.S., Shen, J. and McNaughton, B.L. (1997) Multistability of cognitive maps in the hippocampus of old rats. Nature, 388:272-275.
2. Shen, J., Barnes, C.A., McNaughton, B.L., Skaggs, W.E. and Weaver, K.L. (1997) The effect of aging on experience-dependent plasticity of hippocampal place cells. Journal of Neuroscience, 17:6769-6782.
3. Gerrard, J.L., Burke, S.N., McNaughton, B.L. and Barnes, C.A. (2008) Sequence reactivation in the hippocampus during slow wave sleep is impaired in aged rats. Journal of Neuroscience, 28:7883–7890.
4. Schimanski, L.A., Lipa, P. and Barnes, C.A. (2013) Tracking the course of hippocampal representations during learning: When is the map required? Journal of Neuroscience, 33:3094-3106.

My lab has developed a behavior-driven single cell imaging method that expands on the methods developed for the conduct of high-density electrical recordings from single cells. This method uses the expression of the immediate early gene Arc that can monitor activity over hundreds of thousands of cells across the brain (the catFISH method). With this method, we have been able to identify a number of selective activity changes with age within hippocampal and other temporal lobe circuits and identify transcriptional repression mechanisms that may be responsible for the reduction in behavior-induced Arc expression. This method is now used extensively not only in applications for understanding aging circuits, but in many other areas of systems neuroscience.

1. Guzowski, J.F., McNaughton, B.L., Barnes, C.A. and Worley, P.F. (1999) Environment-specific expression of the immediate-early gene Arc in hippocampal neuronal ensembles. Nature Neuroscience, 2:1120-1124.
2. Penner, M.R., Roth, T.L., Chawla, M.K., Hoang, L.T., Roth, E.D., Lubin, F.D., Sweatt, D.J., Worley, P.F. and Barnes C.A. (2011) Age-related changes in Arc transcription and DNA methylation within the hippocampus. Neurobiology of Aging, 32:2198-2210.
3. Penner, M.R., Parrish, R.R., Hoang, L.T., Roth, T.L., Lubin, F.D. and Barnes, C.A. (2016) Age-related changes in Egr1 transcription and DNA methylation within the hippocampus. Hippocampus, 26:1008-1020.
4. Thome, A., Marrone, D.F., Ellmore T.M., Chawla, M.K., Lipa, P, Ramirez-Amaya, V., Lisanby, S.H., McNaughton, B.L. and Barnes, C.A. (2017) Evidence for an evolutionarily conserved memory coding scheme in the mammalian hippocampus. Journal of Neuroscience, 37:2795–2801.

A final area in which my work has made a large impact is the examination of cognition and brain function in the aged nonhuman primate. We have developed methods for chronic high-density electrophysiological recording for behaving monkeys, which allows assessment of whether the basic principles of age-related brain changes in rats generalize to the primate brain. This is a critical gap to bridge, as the ultimate goal is to understand the human brain and cognitive aging. Because geriatric macaques are a precious experimental resource, studies generated from these animals will become classic in the field. In addition to the high-density recordings obtained from young and aged monkeys, we have been able to relate MRI imaging variables to cognitive test batteries productively, and more recently we have developed methods for telemetered recordings in nonhuman primates who are completely unrestrained. All of these approaches have contributed to a deeper understanding of the neural basis of behavior and how this changes over the lifespan.

1. Skaggs, W.E., McNaughton, B.L., Permenter, M., Archibeque, M., Vogt, J., Amaral, D.G. and Barnes, C.A. (2007) EEG sharp waves and sparse ensemble unit activity in the macaque hippocampus. Journal of Neurophysiology, 98:898-910.

Biographical Sketch

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continued

2. Thome, A., Erickson, C.A., Lipa, P. and Barnes, C.A. (2012) Differential effects of experience on tuning properties of macaque MTL neurons in a passive viewing task. Hippocampus, 22:2000-2011.
3. Engle, J., Machado, C., Permenter, M., Vogt, J, Maurer, A, Bulleri, A. and Barnes, C.A. (2016) Network patterns associated with navigation behavior are altered in aged nonhuman primates. Journal of Neuroscience, 36:12217-12227.
4. Thome, A., Gray, D.T., Erickson, C.A., Lipa P. and Barnes, C.A. (2016) Memory impairment in aged primates is associated with region-specific network dysfunction. Molecular Psychiatry, 21:1257-1262.

Dr. Barnes, full list of publications can be found at:
https://scholar.google.com/citations?hl=en&user=ujQTWgIAAAAJ&view_op=list_works

Research Support

Ongoing

NIA 1 R01 AG003376 Barnes: PI 01/01/16 – 11/30/20 (project period)
Neurobehavioral Relations in Senescent Hippocampus
This research program is directed towards an understanding of the decline in spatial cognition and memory with age. Nonhuman primates are assessed behaviorally and electrophysiologically (hippocampus, perirhinal cortex), and the ensemble activity of the entorhinal and perirhinal cortical units in young and old rats are examined.
Role on Project: PI

NIA 1 RO1 AG05058 Barnes: PI 09/1/15 – 05/31/20 (project period)
NIH/NIA
Cell Assemblies, Brain Adaptation and Cognitive Aging
The aims of this grant are to better understand the underlying causes of two hallmarks of cognitive aging – behavioral slowing and multitasking deficits. We will examine how the aging brain adapts to the changed dynamics intrinsic to both hippocampus and PFC in rats, and how these structures interact or compete during aging, as well as the cellular correlates of multitasking in an aging primate model, to assess how aging weakens the resilience of working memory circuits in the face of interference.
Role: PI

NIA 1 RO1 AG049465 Barnes: PI 08/01/14 – 03/31/19 (project period)
Neural System Dynamics & Gene Expression Supporting Successful Cognitive Aging
The major goal of this project is to understand the basis of differing cognitive trajectories that occur even over the lifespan of inbred rat strains. Methods used include cognitive assessment batteries for frontal and temporal lobe regions, 7T MRI scanning methods, transcriptional evaluation, and circuit activity pattern assessment using the Arc catFISH single cell imaging method devised in Barnes' laboratory. All methods are applied to animals of different ages and aptitudes so that the underlying basis of differential cognitive functioning across the lifespan may be identified.
Role on Project: PI

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continued

NIA 1 RO1 AG049464 Coleman/Barnes/Alexander: PI's 08/01/14 – 03/31/19 (project period)
Epigenetic, Neuroimaging & Behavioral Effects of Hypertension in the Aging Brain
The major goals of this project are to determine what hypertension-induced epigenetic changes occur in a transgenic rat model of hypertension. Blood pressure can be slowly elevated in this rat model from middle to older ages, mimicking the course of hypertension development observed in human aging. Epigenetic changes induced by hypertension that occur in temporal and frontal lobe structures will be measured and related to behavioral assays of these regions as well as with high resolution MRI scans to assess grey and white matter integrity.
Role on Project: PI (Multi-PI)

NIA 1 R01 AG048907 Huentelman/Barnes: PI's 09/30/14 – 05/31/18 (project period)
CATT: Development and Application of a Neuronal Cell Activity-Tagging Toolbox
Our overall goal of this EUREKA award is to develop methods to label cells that were active during a defined temporal period and utilize a new approach to investigate the impact of aging on the circuit elements engaged by those behaviors as well as the transcriptional function of those behavior-driven labeled cells. The "Cell Activity-Tagging Toolbox" will provide a means to "permanently mark" the specific cells that were engaged in a defined behavioral experience. This is an extension of the catFISH methodology that can only labels cells for minutes to hours after a behavior.
Role: PI (Multi-PI)

NIA 5 P30 AG019610 Reiman: PI 08/15/16 – 06/30/21 (project period)
Arizona Alzheimer's Disease Core Center
Dr. Barnes serves as director of the Ad Hoc review program for research proposals for the Arizona Alzheimer's Disease Core Center.
Role on Project: Co-Investigator

NIA 1 T32 AG044402 (Barnes) 05/01/16 – 04/30/21 (project period)
Postdoctoral Training, Neurobiology of Aging and Alzheimer's Disease
Dr. Barnes serves as program director, Dr. Paul Coleman and Eric Reiman as co-directors, and Dr. Matthew Huentelman and Health Bimonte-Nelson as associate directors of this statewide postdoctoral training grant focused on training postdoctoral fellows in the Arizona Alzheimer's Consortium, consisting of six participating institutions statewide.
Role: PI

Completed in last three years

NIA 5 R37 AG012609 Barnes: PI 07/01/09 – 06/30/15 (project period)
Cell Assemblies, Pattern Completion and the Aging Brain
This award was designed to assess whether there are age differences in the network properties of ensembles of cells recorded in hippocampus and prefrontal cortical regions that change computations in these areas to produce cognitive deficits in aged rats in vivo.
Role on Project: PI

Biographical Sketch

Roberta Diaz-Brinton

Director, Center for Innovation in Brain Science, University of Arizona Health Sciences; Professor, Pharmacology and Neurology, College of Medicine

Education/Training

Institution & Location	Degree	Year(S)	Field Of Study
University of Arizona, Tucson, AZ	B.A.	05/1979	Psychobiology
University of Arizona, Tucson, AZ	M.A.	08/1981	Neuropsychology
University of Arizona, Tucson, AZ	Ph.D.	08/1984	Psychobiology & Neuropharmacology
Rockefeller University, NY	Postdoc	07/1987	Neuropharmacology & Neuroendocrinology

Personal Statement

I am the inaugural director of the Center for Innovation in Brain Science at the University of Arizona Health Sciences and professor of Pharmacology and Neurology, College of Medicine, University of Arizona as of May 9, 2016, and, during the transition, remain professor of Pharmacology and Pharmaceutical Sciences, Biomedical Engineering and Neurology, at the University of Southern California. My research has focused broadly on the mechanisms by which the aging brain develops late onset Alzheimer's disease. I lead two large programs of research that are organized under the following main themes: 1) Female Aging Brain and Sex Differences in Transitions of Aging leading to late-onset AD, and 2) Allopregnanolone regenerative systems neurobiology and regenerative therapeutic for Alzheimer's disease. These programs of research are supported by the National Institute on Aging (R01, P01, U01, U54) and by philanthropic foundations. Our research spans discovery to IND enabling translation to clinical trials. We have advanced our basic science discoveries into two clinical trials that target different mechanisms of action and steroid systems in the brain. Fundamental insights that have emerged from our research indicate that the aging brain is dynamic and adaptive. The dynamic adaptive nature of the aging brain has led to an increasing focus on transition states of the aging brain and their plasticity and limits. Further, we have developed extensive experience in translational research to enable FDA INDs, regulatory strategy, and therapeutic development. The nature of our research requires effective and collaborative teams that are mission focused. Teams that I lead include basic, translational, and clinical scientists and technology transfer professionals. During the course of my academic career, I have mentored predoctoral and postdoctoral fellows, undergraduates and, through the Science Technology and Research Program inner city Los Angeles, high school students.

Positions and Honors

Positions

2016 – Present	Director, Center for Innovation in Brain Science, Professor of Pharmacology and Neurology, College of Medicine, University of Arizona, Tucson, Arizona
2001 – 2017	Professor, Department of Pharmacology and Pharmaceutical Sciences, School of Pharmacy, Professor, Department of Biomedical Engineering, Viterbi School of Engineering, Professor, Department of Neurology, Keck School of Medicine University of Southern California
2007 – 2014	Director of Preclinical Translation and Regulatory Support, USC Clinical and Translational Science Institute (USC and Children's Hospital Los Angeles)
2009 – Present	Professor of Neurology, Keck School of Medicine, University of Southern California
2016 – Present	Director of the Center for Innovation in Brain Science, Professor of Pharmacology, College of Medicine, University of Arizona

Biographical Sketch

Roberta Diaz-Brinton

continued

Select Professional Service

1999 – Present	Member, Scientific Review Board of Alzheimer's Drug Development Foundation, NY
2005 – 2009	External Advisory Board NIH/NIA Women's Health Initiative Memory Study
2007 – 2008	NIH Blue Ribbon Panel on NIMH Intramural Research Programs
2007 – 2013	Member, Alzforum Scientific Advisory Board
2008	NIH Blueprint Initiative on K-12 Activities
2009 – 2011	Member, Society for Neuroscience Board of Councilors
2009 – 2013	Member, NIMH IRP Board of Scientific Councilors, NIH
2013 – 2016	Member Society for Neuroscience, Committee on Committees
2013 – 2017	Member, NIH Center for Scientific Review Advisory Council
2015 – Present	Board of Governors, Alzheimer's Drug Discovery Foundation, New York, NY
2015 – Present	Chair, Medical & Scientific Advisory Council Alzheimer's Association, Los Angeles, CA

Select Honors

1999	Laboratory Named "The Norris Foundation Laboratory for Neuroscience Research"
2003	University of Southern California Remarkable Woman Award
2005	10 Best Minds, US News & World Report
2005	Woman of the Year, California State Senate
2006	Science Educator of the Year, Society for Neuroscience
2009	North American Menopause Society /Wyeth Pharmaceuticals SERM Research Award
2010	Presidential Citizens Medal, President Barack Obama
2014	Los Angeles Woman of the Year, LA Magazine
2015	Scientist of the Year Award, Alzheimer's Drug Discovery Foundation
2017	Disruptive Women to Watch in 2017, Disruptive Women in Health Care
2017	Recipient: NIH MERIT (Method to Extend Research in Time) Award; for outstanding record of scientific achievement as principal investigator on National Institute of Aging (NIA) research projects.

Complete list of published work in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/roberta.brinton.1/bibliography/40443387/public/?sort=date&direction=ascending

Contribution to Science

The focus of my research has been to discover mechanisms leading to late-onset Alzheimer's disease and to translate those insights into therapeutics to prevent, delay, and treat the disease. Results of my systems biology research programs have resulted in fundamental discoveries of steroid action in the brain that have been translated into two independent clinical trials targeting different receptor systems and mechanisms of action. Research endeavors in my laboratory are organized under three major themes: 1) Aging Female Brain and endocrine mechanisms of aging that increase risk of late onset Alzheimer's disease, 2) Sex Differences in mechanisms leading to late onset Alzheimer's disease, and 3) Allopregnanolone regenerative systems neurobiology and regenerative therapeutic for Alzheimer's disease.

Biographical Sketch

Roberta Diaz-Brinton

continued

The Aging Female Brain and endocrine mechanisms of aging that increase risk of late-onset Alzheimer's disease program of research is devoted to understanding the mechanisms underlying the increased lifetime risk of Alzheimer's in women. Outcomes of this pioneering research indicate that the female brain is highly dependent upon estrogen, which functions as a master regulator of the bioenergetic system of the brain. The perimenopausal transition, unique to the female, results in a bioenergetic shift in the brain from a glucose-dependent brain to a brain dependent on the alternative fuel ketone bodies. The adaptive bioenergetic shift to utilizing ketone bodies as an auxiliary fuel creates a risk for catabolizing brain lipids, myelin, to generate ketone bodies to fuel a starving brain. Based on our discovery science of estrogen action in brain, we developed a GMP clinical grade estrogen receptor beta selective formulation that progressed into a NIA sponsored Phase 1b/2a clinical trial of Phytoserms for Menopause Symptoms and Age-Associated Memory Decline. Results of the PhytoSERM clinical trial are currently being analyzed.

1. Brinton, R.D., Yao J, Yin F, Mack WJ, Cadenas, E. Perimenopause as a neurological transition. Nat Rev Endocrinol. 2015 Jul;11(7):393-405. doi: 10.1038/nrendo.2015.82. Epub 2015 May 26. PMID: 26007613 PMCID in Process.
2. Yin F, Yao J, Sancheti H, Feng T, Melcangi RC, Morgan TE, Finch CE, Pike CJ, Mack WJ, Cadenas E, Brinton RD. The perimenopausal aging transition in the female rat brain: decline in bioenergetic systems and synaptic plasticity. Neurobiol Aging. 2015 Apr 1. pii: S0197-4580(15)00198-0. doi: 10.1016/j.neurobiolaging.2015.03.013. PMCID: PMC4416218.
3. Yao J, Irwin RW, Zhao L, Nilsen J, Hamilton RT, Brinton RD, Mitochondrial bioenergetic deficit precedes Alzheimer's pathology in female mouse model of Alzheimer's disease. Proc Natl Acad Sci U S A. 2009 Aug 25;106(34):14670-5. Epub 2009 Aug 10. PMCID: PMC2732886.
4. Yao, J., Hamilton, RT, Cadenas, E. Brinton RD. Decline in mitochondrial bioenergetics and shift to ketogenic profile in brain during reproductive senescence, Biochim Biophys Acta. 2010 Oct:1800 (10):1121-6 Epub 2010 PMID 20538040 PMCID:PMC3200365.

Sex Differences in mechanisms leading to late onset Alzheimer's disease program investigates the underlying mechanisms for the difference between female and male risk of developing late-onset Alzheimer's disease. Outcomes of which research indicate that the female and male brain bioenergetically age quite differently in remarkable and unanticipated ways which may be beneficial to the ApoE4- male but may be deleterious to the ApoE4+male.

1. Zissimopoulos JM, Barthold D, Brinton RD, Joyce G. Sex and race differences in the association between statin use and the incidence of Alzheimer disease. JAMA Neurol. 2016 Dec 12. PMID:27942728 PMCID in Process.
2. Zhao L, Mao Z, Woody SK, Brinton RD. Sex differences in metabolic aging of the brain: Insights into female susceptibility to Alzheimer's disease. Neurobiol Aging. 2016 Jun;42:69-79. Epub 2016 Feb 18. PMCID in process.
3. Wang Y. and Brinton RD. Triad of Risk for Late Onset Alzheimer's: Mitochondrial Haplotype, APOE Genotype and Chromosomal Sex. Frontiers in Aging Neuroscience 2016 Oct 4;8:232. PMCID:PMC5047907.
4. Riedel BC, Thompson PM, Brinton RD. Age, APOE and sex: Triad of Risk of Alzheimer's disease. J Steroid Biochem Mol Biol. 2016 Jun;160:134-47. PMC 4905558.

The allopregnanolone regenerative systems neurobiology and regenerative therapeutic for Alzheimer's disease programs of research is devoted to elucidating the regenerative mechanisms of the brain and harnessing those mechanisms to both promote endogenous mechanisms of regeneration while simultaneously targeting mechanisms underlying Alzheimer's disease. Outcomes of this pioneering research indicate that the neurosteroid allopregnanolone significantly increases endogenous neural stem cell generation which restores learning and memory functions to age-associated normal in both males and females. Further allopregnanolone reduces the burden of disease by promoting mitochondrial function and beta amyloid clearance. Based on our discovery science of allopregnanolone regenerative mechanisms, we advanced allopregnanolone through IND-enabling research (PK,PD and toxicology), acquired an FDA

Biographical Sketch

Roberta Diaz-Brinton

continued

IND to conduct a NIA sponsored Phase 1b clinical trial of allopregnanolone in persons with mild cognitive impairment or early Alzheimer's disease. The NIA-sponsored clinical trial Allopregnanolone for Mild Cognitive Impairment Due to Alzheimer's Disease or Mild AD is currently ongoing.

1. Brinton RD. Neurosteroids as regenerative agents in brain: Therapeutic implications. Nature Endocrine Reviews. 2013 Feb 26. PMID:2343883 PMCID in Process.
2. Singh C, Liu L, Wang JM, Irwin RW, Yao J, Chen S, Henry S, Thompson RF, Brinton RD. Allopregnanolone restores hippocampal-dependent learning and memory and neural progenitor survival in aging 3xTgAD and nonTg mice. Neurobiol Aging. 2012 Aug;33(8):1493-506. Epub 2011 Jul 30. PMC3232295.
3. Chen S, Wang JM, Irwin RW, Yao J, Liu L, Brinton RD. Allopregnanolone promotes regeneration and reduces ß-amyloid burden in a preclinical model of Alzheimer's disease. PLoS One. 2011;6(8):e24293. Epub 2011 Aug 30. PMC3168882.
4. Wang JM, Singh C, Liu L, Irwin RW, Chen S, Chung EJ, Thompson RF, Brinton RD. Allopregnanolone reverses neurogenic and cognitive deficits in mouse model of Alzheimer's disease. Proc Natl Acad Sci U S A. 2010 Apr 6;107(14):6498-503. Epub 2010 Mar 15 -PMC2851948.

Research Support

Active

NIH / NIA R37-AG053589* (previously R01-AG053589) 03/15/2017 – 02/28/2022
Aging and Estrogenic Control of The Bioenergetic System In Brain
The proposed program of research is designed to first test estrogenic control of the bioenergetic system in the female brain requires: 1) both nuclear and mitochondrial genomes; 2) integration of gene expression across both genomic compartments, and 3) activation of rapid signaling cascades to provide real-time feedback on bioenergetic performance. Second, that loss of estrogen in the aging female brain leads to a systematic disintegration of estrogenic control of nuclear and mitochondrial genomes followed by decline in bioenergetic sensing mechanisms.
*Recipient NIH MERIT (Method to Extend Research in Time) Award, recognizing outstanding scientific contributions and allowing for up to 5 years noncompetitive extension.
Role: PI

NIH / NIA U01-AG047222 (Brinton) 06/15/2014 – 02/28/2019
Allopregnanolone a Regenerative Therapy for Alzheimer's: FDA-Required Toxicology
This project addresses the urgent need to develop therapeutics to prevent, delay, and treat Alzheimer's disease (AD). A promising regenerative medicine, Allo, is being developed. Allo activates the brain's own regenerative ability while also reducing the pathology of AD. Studies proposed here are required by the FDA to ensure that Allo is safe to use for extended period of time to generate new neurons, restore cognitive function, reduce AD pathology and to regenerate the connective tracts of the brain.
Role: PI

NIH / NIA UF1-AG046148 (Brinton) 09/20/2013 – 08/31/2017
Allopregnanolone Regenerative Therapeutic for MCI/AD: Dose Finding Phase I
This project addresses the urgent need to develop therapeutics to prevent, delay, and treat Alzheimer's disease (AD) in those at greatest risk, the aged. A promising regenerative medicine approach is to activate the brain's endogenous regenerative ability while also reducing the pathology of AD. We propose here to conduct a Phase 1 clinical study of the neurosteroid allopregnanolone (Allo), which promotes the generation of new neurons, restores cognitive function, reduces AD pathology and regenerates white matter in brain.
Role: PI

Biographical Sketch

Roberta Diaz-Brinton

continued

NIH / NIA P01 AG026572 (Brinton) 09/30/2011 – 08/31/2021
Perimenopause in Brain Aging and Alzheimer's Disease
The Perimenopause in Brain Aging and Alzheimer's Disease Program Project will determine how the brain changes during the perimenopausal transition and how these changes can lead to development of early risk factors for developing Alzheimer's disease. The goal of these studies is the early identification of those at greatest risk for developing AD and the window of opportunity for interventions to prevent Alzheimer's disease in those at greatest lifetime risk, postmenopausal women.
Role: Program PI; PL Administrative Core A, Project 1 and Project 4

Completed

NIH / NIA R34AG049652 (Brinton) 09/30/2014 – 08/31/2016
Systems Pharmacology for Predictive Alzheimer's Therapeutics: SysPharmRx-AD
Our goal is to develop therapeutics to prevent, delay, and cure Alzheimer's disease. The proposed planning grant to create an Alzheimer's Disease Translational Center for Predictive Drug Development is a critical step to realizing this goal.
Role: PI

NIH / NIA R01 AG032236 (Brinton) 07/01/2009 – 07/31/2016
Estrogen-Induced Neuroprotective Mitochondrial Mechanisms
The overall aim of this project is to determine the mechanisms and long-term consequences of estrogen on mitochondrial function in brain. Our target outcome is sustaining mitochondrial function to sustain neurological health for prevention of neurodegenerative diseases associated with mitochondrial dysfunction.
Role: PI

U01 AG031115 (Brinton) 04/15/2008 – 03/31/2014 NIH/NIA
Development of Allopregnanolone as a Neurogenic Regenerative Therapeutic Agent
The goal is to develop allopregnanolone as a safe and efficacious therapeutic to prevent or treat age-associated memory deficit. This a translational therapeutic development project to conduct preclinical analyses required for an Investigational New Drug (IND) application to the FDA to determine the efficacy of allopregnanolone as a neurogenic regenerative and disease modifying agent for Alzheimer's disease.
Role: PI

NIH / NIA R01AG033288 (Schneider) 06/01/2010 – 05/31/2015
Estrogen Receptor-Beta PhytoSERMs for Management of Menopause and Age-Associated Memory Decline: Pilot Development Trials.
Role: PI

NIH / NIA 2P50 AG005142-26A1 (Chui) 07/01/2012 – 03/31/2015
Alzheimer Disease Research Center
Project 2 – Brinton
Role: PI Project 2

Biographical Sketch

Ying-hui Chou
Assistant Professor of Psychology

Education/Training

Institution & Location	Degree	Year(S)	Field Of Study
National Taiwan University, Taipei	BS	06/1994	Occupational Therapy
Boston University, Boston, MA	MS	01/2001	Occupational Therapy
Boston University, Boston, MA	ScD	01/2005	Movement and Rehabilitation Sciences
Brigham and Women's Hospital/Harvard Medical School, Boston, MA	Postdoctoral	07/2005	Brain Imaging
Duke University Medical Center, Durham, NC	Postdoctoral	04/2012	Gerontology and Brain Imaging
Duke University Medical Center, Durham, NC	Other training	04/2012	Transcranial Magnetic Stimulation
Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA	Other training	06/2013	Transcranial Magnetic Stimulation
Duke University Medical Center, Durham, NC	Postdoctoral Fellow	08/2013	Brain Imaging
Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA	Other training	03/2015	Transcranial Direct Current Stimulation

Personal Statement

I received postdoctoral training in brain imaging and cognitive science at Surgical Planning Lab of Brigham and Women's Hospital/Harvard Medical School, Duke Brain Imaging and Analysis Center, and Duke Aging Center. In addition, I have been trained to operate non-invasive brain stimulation protocols (e.g., TMS and transcranial direct current stimulation) at the Berenson-Allen Center for Noninvasive Brain Stimulation of Harvard Medical School and Duke Psychiatry. I am currently an assistant professor of psychology at the University of Arizona (since August 2016). My laboratory focuses on applications of noninvasive brain stimulation and advanced brain imaging techniques to the development of image-guided noninvasive brain stimulation protocols for clinical populations and studying causal relations among brain networks. Over the years I have developed strong expertise in brain imaging, noninvasive brain stimulation, and cognitive science. I have produced 22 peer-reviewed journal articles and one book chapter.

1. Chou YH, Hickey PT, Sundman M, Song AW, Chen NK. Effects of Repetitive Transcranial Magnetic Stimulation on Motor Symptoms in Parkinson Disease: A Systematic Review and Meta-Analysis. JAMA Neurol. 2015 Apr 1; 72(4): 432-40. PMCID: PMC4425190.
2. Chou YH, Sundman M, Whitson HE, Gaur P, Chu ML, Weingarten CP, Madden DJ, Wang L, Kirste I, Joliot M, Diaz MT, Li YJ, Song AW, Chen NK. Maintenance and Representation of Mind Wandering during Resting-State fMRI. Sci Rep. 2017 Jan 12; 7:40722. PMCID: PMC5227708.
3. Chou YH, You H, Wang H, Zhao YP, Hou B, Chen NK, Feng F. Effect of repetitive transcranial magnetic stimulation on fMRI resting-state connectivity in Multiple System Atrophy. Brain Connect. 2015 Apr 22; 5(7): 451-9. PMCID: PMC4575511.
4. Chou YH, Chen NK, Madden DJ. Functional brain connectivity and cognition: Effects of adult age and task demands. Neurobiol Aging. 2013 Aug; 34(8): 1925-34. PMCID: PMC3674832.

Biographical Sketch

Ying-hui Chou

continued

Positions and Honors

Positions and Employment

199 – 1995	Occupational Therapist, Department of Psychiatry, Taipei Veterans General Hospital, Taiwan
1995 – 1997	Occupational Therapist, Department of Physical Medicine and Rehabilitation, National Taiwan University Hospital, Taiwan
2001 – 2003	Research Assistant, Center for Neurological Rehabilitation, Boston University, Boston, MA
2001 – 2003	Teaching Assistant of (1) Neurological Systems and (2) Scientific Inquiry, Department of Physical Therapy, Boston University, Boston, MA
2004 – 2005	Postdoctoral Fellow of Radiology, Brigham and Women's Hospital/ Harvard Medical School, Boston, MA
2005 – 2008	Chair and Assistant Professor, Department of Occupational Therapy, Fu-Jen Catholic University, Taiwan
2008 – 2011	Maternity Leave
2011 – 2013	Postdoctoral Fellow, Center for Aging and Human Development and Brain Imaging and Analysis Center, Duke University Medical Center, Durham, NC
2013 – 2016	Medical Instructor, Brain Imaging and Analysis Center, Duke University Medical Center, Durham, NC
2016	Assistant Professor of Psychology, University of Arizona, Tucson, AZ

Other Experience and Professional Memberships

1999 – 2001	Member, American Occupational Therapy Association
2005 – 2006	Member, International Society of Magnetic Resonance in Medicine
2011 – 2012	Member, Cognitive Neuroscience Society

Honors

1999	The Study Abroad Scholarship, Ministry of Education, Taiwan
2000	The Carolyn Kohn Memorial Scholarship, American Occupational Therapy Foundation, USA
2005	The Educational Stipend Award, International Society for Magnetic Resonance in Medicine, USA
2006	The E.K. Zavoisky Stipend, International Society for Magnetic Resonance in Medicine, USA
2007	The Fu-Jen University Excellence in Teaching Award, Fu-Jen Catholic University, Taiwan

Biographical Sketch

Ying-hui Chou

continued

Contribution to Science

Resting-state fMRI and its applications to cognitive science and clinical populations. Resting-state functional connectivity measured by fMRI has played an essential role in understanding brain functional networks and their relations to cognitive function and diseases. Measures of resting-state functional connectivity refer to temporal correlations of fMRI signals between spatially distinct brain regions when participants are not performing a perceptual or behavioral task. In a longitudinal study, we acquired resting-state fMRI data of healthy participants nine times during one year. Our findings indicate that the functional connectivity measures exhibit outstanding long-term reproducibility and are potentially suitable as biomarkers for monitoring disease progression and treatment effects in clinical trials and individual patients. In a series of studies, we documented age- and disease-related alterations in resting-state functional connectivity, their correlations with cognitive function and symptom severity, and treatment effects using functional connectivity as an outcome measure. This body of work has demonstrated the usefulness of resting-state functional connectivity for understanding cognitive function and for clinical applications.

1. Chou YH, Panych LP, Dickey CC, Petrella JR, Chen NK. Investigation of long-term reproducibility of intrinsic connectivity network mapping: A resting-state fMRI study. Am J Neuroradiol. 2012 May; 33(5): 833-8. PMCID: PMC3584561.
2. Chou YH, Chen NK, Madden DJ. Functional brain connectivity and cognition: Effects of adult age and task demands. Neurobiol Aging. 2013 Aug; 34(8): 1925-34 PMCID: PMC3674832.
3. Whitson HE, Chou YH, Potter GG, Diaz MT, Chen NK, Lad EM, Johnson MA, Cousins SW, Zhuang J, Madden DJ. Phonemic fluency and brain connectivity in age-related macular degeneration: A pilot study. Brain Connect. 2015 Apr; 5(2): 126-35. PMCID: PMC4361291.
4. Wang L, Chou YH, Potter GG, Steffens DC. Altered synchronization among neural networks in geriatric depression. BioMed research international. 2015 January 11. NIHMSID: NIHMS690881.

Repetitive transcranial magnetic stimulation for neurodegenerative disorders. Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive brain stimulation technique that has been closely examined as a possible treatment for Parkinson's disease (PD). However, results evaluating the effectiveness of rTMS in PD are mixed, mostly due to low statistical power or variety in individual rTMS protocols. Recently, we published a meta-analysis of 20 clinical trials in 470 patients with PDa. Pooled evidence suggests a significant medium effect size favoring active rTMS over sham rTMS for reducing motor symptoms. Findings of our meta-analysis highlight the need for multimodal studies that combine the use of rTMS and different neuroimaging techniques when developing an rTMS treatment protocol. As a first step to combine the rTMS and brain imaging techniques, we measured both motor symptoms and brain functional connectivity before and after a 10-session, 5 Hz, rTMS intervention targeting the primary motor cortex in patients with multiple system atrophyb. Our results showed significant rTMS-related changes in motor symptoms and functional connectivity. Specifically, 1) significant improvement of motor symptoms was observed in the active-rTMS group, but not in the sham-rTMS group; and 2) several functional links involving the default mode, cerebellar and limbic networks exhibited positive changes in functional connectivity in the active-rTMS group. Moreover, the positive changes in functional connectivity were associated with improvement in motor symptoms for the active-rTMS group. The present findings suggest that rTMS may improve motor symptoms by modulating functional links connecting to the default mode, cerebellar and limbic networks, inferring a future therapeutic candidate for patients with multiple system atrophy.

1. Chou YH, Hickey PT, Sundman M, Song AW, Chen NK. Effects of repetitive transcranial magnetic stimulation on motor symptoms in Parkinson's disease: A systematic review and meta-analysis. JAMA Neurol. 2015 Apr 1; 72(4): 432-40. PMCID: PMC4425190.
2. Chou YH, You H, Wang H, Zhao YP, Hou B, Chen NK, Feng F. Effect of repetitive transcranial magnetic stimulation on fMRI resting-state connectivity in multiple system atrophy. Brain Connect. 2015 Apr 22; 5(7): 451-9. PMCID: PMC4575511.

Biographical Sketch

Ying-hui Chou

continued

Virtual reality. When I was a graduate student at Boston University, my projects were to investigate how virtual reality technology could be used to investigate perception and motion interaction. We had successfully combined the virtual reality apparatus and three-dimensional motion analysis system to investigate perceptual-motor interaction. These studies demonstrate the usefulness of virtual reality in modulating locomotion and will facilitate the development of systematic approaches for effective preventive and therapeutic intervention for gait dysfunction in older adults and patients with Parkinson's disease. Virtual reality is compatible with many brain-imaging techniques and has allowed researchers to evaluate typical and atypical brain function when users are immersed in a virtual reality environment. We published a book chapter in 2012d summarizing research findings that combine both virtual reality and brain imaging technologies. This chapter has been downloaded 2,668 times from the publisher's website (http://www.intechopen.com/books/statistics/virtual-reality-in-psychological-medical-and-pedagogical-applications/applications-of-virtual-reality-technology-in-brain-imaging-studies).

1. Chou YH, Wagenaar RC, Saltzman E, Giphart JE, Young D, et al. Effects of optic flow speed and lateral flow asymmetry on locomotion in younger and older adults: a virtual reality study. J Gerontol B Psychol Sci Soc Sci. 2009 Mar;64(2):222-31. PMCID: PMC2655160.
2. Giphart JE, Chou YH, Kim DH, Bortnyk CT, Wagenaar RC. Effects of virtual reality immersion and walking speed on coordination of arm and leg movements. Presence: Teleoperators and Virtual Environments. 2007; 16(4): 399-413.
3. Young DE, Wagenaar RC, Lin CC, Chou YH, Davidsdottir S, et al. Visuospatial perception and navigation in Parkinson's disease. Vision Res. 2010 Nov 23;50(23):2495-504. PMCID: PMC3008343.
4. Chou YH, Weingarten C, Madden DJ, Song AW, Chen N. Virtual Reality. Eichenberg C, editor. Rijeka, Croatia: Intech – Open Access Publisher; 2012. Applications of virtual reality technology in brain imaging studies; p.203-228.

Complete list of published work In MyBibliography:
http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/40106197/?sort=date&direction=descending

RESEARCH SUPPORT

Current

Arizona Alzheimer's Consortium Pilot Program Chou (PI) 07/01/2017 – 06/30/2018
Use of TMS and fMRI Measures to Assess the Risk of Conversion of MCI to Dementia
In this pilot project, we propose probing cortical excitability and plasticity in individuals with MCI in order to assess the diagnostic potential of TMS-evoked responses.

Arizona Alzheimer's Consortium Pilot Program Wilson (PI) 07/01/2017 – 06/30/2018
The Neural Substrates of Explore-exploit Decisions in Old Age
The purpose of the study is to understand the neural systems underlying explore-exploit decisions and how these systems change in old age and with cognitive decline.
Role: Co-Investigator

Biographical Sketch

Ying-hui Chou

continued

Completed

R01-AG039684 Madden (PI) 04/22/2012 – 05/31/2016
NIH/NIA
Neuroimaging of Visual Attention in Aging
The major goal of this project is to investigate structural and functional connectivity of the brain in relation |to age-related differences in visual attention performance.
Role: Co-Investigator

R01-MH098301 Madden, Wang (PI) 02/01/2013 – 06/30/2016
NIH/NIMH
Dorsal Cingulate Activity and Cognitive Decline in Late-Life Depression
The long-term goals of the proposed project are to better understand the neural mechanisms linking depression and cognitive impairment, establish biomarkers for early identification of depressed individuals at risk for cognitive impairment, and understand the neural plasticity of late-life depression with and without cognitive impairment following prevention programs and clinical interventions.
Role: Co-Investigator

R21-DA033083 McClernon (PI) 10/01/2014 – 12/30/2014
NIH/NIDA
Environments as Smoking Cues: Imaging Brain Substrates, Developing New Treatments
The overarching goal of our collaborative research program is to increase the efficacy of CETs by incorporating contextual cues from the smoker's real-world smoking environment into treatment, thereby preventing renewal.
Role: Co-Investigator

K23-AG032867 Whitson (PI) 10/01/2012 – 07/13/2013
NIH/NIA
Developing Interventions to Improve Function in Seniors with Comorbid Conditions
The goal of the study is to develop interventions that improve functional outcomes in patients who suffer from particularly disabling combinations of conditions.
Role: Post-doctoral Scholar

T32-AG000029 Cohen (PI) 03/21/2011 – 04/21/2012
NIH/NIA
Behavior and Physiology in Aging
The goal of this Duke Aging Center Postdoctoral Training Program is to continue to train highly skilled research scientists who have strong backgrounds in substantive areas related to aging and who also have the potential for leadership in gerontological research.
Role: Post-doctoral Scholar

Private Foundation Chen (PI) 2006 – 2007
Changhua Christian Hospital Research Fund, Taiwan
Effect of Repetitive Transcranial Magnetic Stimulation on Cortical Excitability in Patients with Epilepsy
The purpose of the study was to investigate the effect of repetitive transcranial magnetic stimulation on cortical excitability in patients with epilepsy.
Role: Co-Investigator

Biographical Sketch

Stephen Cowen
Assistant Professor

Education/Training

Institution & Location	Degree	Year(S)	Field Of Study
University of Wisconsin, Madison, Wisconsin	BBA	05/1992	Management and Marketing
University of Arizona, Tucson, Arizona	PHD	05/2007	Psychology and Neuroscience
The Neurosciences Institute, San Diego, California	Postdoc	06/2008	Neuroscience

Personal Statement

A fundamental and unresolved question in neuroscience is how the activities of tens of billions of interconnected neurons become coordinated during learning, decision making, and sleep. Resolving this question is important as dysregulated neural coordination contributes to disorders such as Parkinson's disease (PD), epilepsy, Down syndrome, and schizophrenia, and may also contribute to cognitive deficits associated with normal aging. My research seeks to understand the mechanisms by which the timing of the activities of ensembles of neurons and dopamine release is coordinated during learning and sleep. Towards this end, my laboratory has developed novel instrumentation that allows, for the first time, the simultaneous measurement of the activities of large groups of neurons and fast changes in dopamine release (Parent et al., 2017). This instrument integrates high-density single-unit/local-field recording technologies to measure neural activity in rodents during decision making, navigation, and sleep with fast-scan cyclic voltammetry for the measurement of dopamine release. My laboratory is using this tool to investigate the role that dopamine plays in regulating neuronal coordination in behaving and resting animals, and we are working towards testing this device in animal models of PD and normal aging. Our ongoing and funded work on PD involves the investigation of sleep-associated oscillatory activity in PD. This work is supported by a grant from the Michael J. Fox Foundation. Specifically, we are exploring how cortico-striatal coordination is altered during sleep in a genetic form of PD (the LRRK2 G2019S mutation). We are testing the hypothesis that sleep spindles, corticothalamic oscillations associated with slow wave sleep and memory consolidation, are enhanced in this particular mutation.

My lab also investigates the roles that high-frequency brain oscillations play in learning, memory, and disease. For example, we have found that normal aging is associated with a significant decrease in the frequency of oscillations in the hippocampus that are associated with memory formation. With regard to disease, my laboratory is investigating how ketamine and ketamine-induced high-frequency activity in the striatum reduces dyskinesias in PD. Data collected in my laboratory now suggest that ketamine simultaneously enhances cortico-striatal coherence at high frequencies (~135 Hz) and reduces coherence at theta and beta frequencies (~8-30 Hz) – frequency ranges associated with Parkinsonian motor symptoms.

To assist other researchers studying these topics, my students and I have designed, built, and freely distributed custom microelectrode microdrives, data acquisition software, data-analysis software, inertial measurement systems, and automated mazes designed for the assessment decision making in rodents.

1. Parent KL, Hill DF, Crown LM, Wiegand J-P, Gies KF, Miller MA, Atcherley CW, Heien ML, Cowen SL (2017) Platform to enable combined measurement of dopamine and neural activity. Anal Chem:acs.analchem.6b03642.

2. Okun, A., McKinzie, D. L., Witkin, J. M., Remeniuk, B., Husein, O., Gleason, S. D., et al. (2016) Hedonic and motivational responses to food reward are unchanged in rats with neuropathic pain. Pain. doi:10.1097/j.pain.0000000000000695.

3. Wiegand J-PL, Gray DT, Schimanski LA, Lipa P, Barnes CA, Cowen SL (2016) Age is associated with reduced sharp-wave ripple frequency and altered patterns of neuronal variability. J Neurosci 36:5650–5660.

Biographical Sketch

Stephen Cowen

continued

4. Maurer AP, Cowen SL, Burke SN, Barnes CA, McNaughton BL. Phase precession in hippocampal interneurons showing strong functional coupling to individual pyramidal cells. J Neurosci. 2006 Dec 27;26(52):13485-92. PubMed PMID: 17192431.
5. Cowen SL, McNaughton BL. Selective delay activity in the medial prefrontal cortex of the rat: contribution of sensorimotor information and contingency. J Neurophysiol. 2007 Jul;98(1):303-16. PubMed PMID: 17507507.
6. Cowen SL, Davis GA, Nitz DA. Anterior cingulate neurons in the rat map anticipated effort and reward to their associated action sequences. J Neurophysiol. 2012 May;107(9):2393-407. PubMed PMID: 22323629.
7. Cowen SL, Nitz DA. Repeating firing fields of CA1 neurons shift forward in response to increasing angular velocity. J Neurosci. 2014 Jan 1;34(1):232-41. PubMed PMID: 24381284.

Positions and Honors

Positions and Employment

2007 – 2008	Postdoctoral Fellow	The Neurosciences Institute, San Diego, CA
2008 – 2010	Research Fellow	The Neurosciences Institute, San Diego, CA
2010 – 2012	Associate Fellow	The Neurosciences Institute, San Diego, CA
2012 – present	Assistant Professor	University of Arizona, Tucson, AZ Department of Psychology Graduate Interdisciplinary Program in Neuroscience Graduate Interdisciplinary Program in Cognitive Science Graduate Interdisciplinary Program in Physiology

Other Experience and Professional Memberships

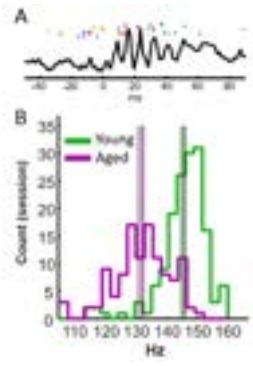
1997 – present	Member, Society For Neuroscience	The Neurosciences Institute, San Diego, CA

Honors

Recipient of a 1998-1999 National Science Foundation training grant.
Awarded the 2010 Blasker-Rose-Miah technology development grant from The San Diego Foundation.

Contribution to Science

Aging is associated with altered single-unit coordination and local-field oscillatory activity. The hippocampus is critical for the formation of episodic memories, and this capacity is reduced over the course of normal aging. Sharp-wave ripple events are high-frequency (~150 Hz) oscillations generated in the hippocampus, and these events have been implicated in the stabilization of long-term memories. Our analysis of these oscillations and of correlated single-unit activity in rats identified key changes that occur through the course of aging. Specifically, results from our analysis indicate that aging is accompanied by a decline in the oscillation frequency and rate of occurrence of these oscillations and that individual neurons fire less reliably within each ripple event. Together, these changes may contribute to age-associated memory decline.



A. Ripple oscillation during slow wave sleep and spiking activity (colored dots) of simultaneously-recorded hippocampal neurons.

B. Ripple frequency is significantly reduced in healthy aged rats.

- Wiegand J-PL, Gray DT, Schimanski LA, Lipa P, Barnes CA, Cowen SL (2016) Age is associated with reduced sharp-wave ripple frequency and altered patterns of neuronal variability. J Neurosci 36:5650–5660.

Biographical Sketch

Stephen Cowen

continued

Neural correlates of working memory can be tightly coupled with body movements. In 1971, three seminal papers were published that provided compelling evidence that the mammalian brain is capable of forming high-level and sensory-independent representations of imagined stimuli and environments. The first of these studies reported the discovery of delay cells in the prefrontal cortex (Fuster and Alexander; Kubota and Niki) and the second reported the first observation of place cells in the hippocampus (O'Keefe and Dostrovsky). A question that guides me throughout my career is how such representations are sustained through time. In one of my first investigations, I measured the activities of ensembles of neurons in the medial prefrontal cortex as rats performed memory-guided behaviors. Analysis confirmed that prefrontal neurons exhibit clear delay activity for expected cues and outcomes; however, detailed analysis of head movements determined that nearly all of these "delay neurons" were exceptionally sensitive to small changes in body posture. Indeed, the movements themselves were highly selective for the stored memories. A parsimonious explanation for this result was that animals adopted embodied solutions for solving the working-memory task where unique movements were used to help animals offload working memory demands to the body. Our results further demonstrated that higher-order regions such as the frontal cortex are exceedingly sensitive to lower-order inputs such as motor efference-copy and somatosensory information.

- Cowen SL, McNaughton BL (2007) Selective delay activity in the medial prefrontal cortex of the rat: Contribution of sensorimotor information and contingency. J Neurophysiol 98:303–316.

Anterior-cingulate neurons are involved in post-decision action maintenance and value prediction. The previously-described observation that motor activity plays a role in modulating "delay cell" activity in the prefrontal cortex motivated a search for theories of frontal function that incorporate representations of body movement. One theory proposes that the anterior cingulate cortex, a subregion of the medial prefrontal cortex, plays a critical role in the evaluation of the cost of physical effort. Evidence from rodents and primates suggests that neurons in the anterior cingulate cortex integrate information about expected effort to guide cost-benefit decision making. To identify the physiological correlates of this evaluative process, I used arrays of single-unit electrodes to record ensemble activity in the anterior cingulate cortex as animals made effort- and reward-guided evaluations. Unexpectedly, results indicated that neurons responding to the anticipated effort responded at least 100 milliseconds after animals made their decision, suggesting that these neurons do not contribute to deliberation, but, instead, may be involved in sustaining goal-directed behaviors after decisions are made. Our observations led me to the proposal that the anterior cingulate cortex facilitates "perseverance" by regulating both glutamatergic and dopaminergic transmission in the motor cortex and dorsal striatum.

- Cowen SL, Davis GA., Nitz DA. (2012) Anterior cingulate neurons in the rat map anticipated effort and reward to their associated action sequences. J Neurophysiol 107:2393–2407.
- Miller MA, Thomé A, Cowen SL (2013) Intersection of effort and risk: ethological and neurobiological perspectives. Front Neurosci 7:208.

Expanding the traditional view of the hippocampal representation of space. The discovery of the hippocampal place cell (O'Keefe and Dostrovsky, 1971) provided convincing physiological evidence that the hippocampus creates a cognitive map of the environment. With time, it was found that the response properties of these place cells were more nuanced than expected. For example, "place cells" were found to be sensitive to both location and trajectory and that these neurons coupled their activity to specific phases of the hippocampal theta (7 Hz) oscillation. My research contributed to the expansion of the traditional view of the place cell by challenging the view that spatial coding in the hippocampus is an exclusive property of principal cells. Together with Drew Maurer and Bruce McNaughton, we determined that inhibitory interneurons convey precise information about space, and that this information is only

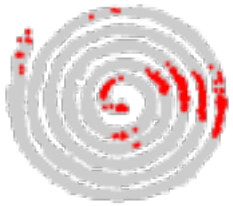
Biographical Sketch

Stephen Cowen

continued

identifiable if the phase of the theta rhythm at which interneurons fire is accounted for. We used this phase-based definition of the place field to improve upon existing measures of place-field sizes, an approach which became useful in quantifying how the spatial scale of the cognitive map changes in different regions of the hippocampus.

The second way my research extended the understanding of hippocampal function resulted from my collaboration with Dr. Douglas Nitz and our investigation of repeating place fields – a recently discovered phenomenon whereby multiple fields appear when animals visit locations with similar behavioral or visual features (Derdikman et al., 2009). Dr. Nitz and I observed that these repeating fields shift forward in space as animals run on spiral-shaped tracks. Further experiments revealed that this shift was most likely due to a buildup of inertial navigation error, suggesting that animals were actually using an inertial/vestibular strategy as opposed to a visual cue based navigation strategy – even in brightly-lit rooms. This is an interesting contribution, as one assumption in the field is that inertial navigational strategies are only employed when visual cues are unavailable.



Repeating placefields: The spiking activity (dots) of a hippocampal neuron as a rat ran on a maze in the shape of a large (10 m) spiral.

- Cowen SL, Nitz DA (2014) Repeating Firing Fields of CA1 Neurons Shift Forward in Response to Increasing Angular Velocity. J Neurosci 34:232–241.
- Maurer AP, Cowen SL, Burke SN, Barnes CA, McNaughton BL (2006a) Organization of hippocampal cell assemblies based on theta phase precession. Hippocampus 16:785–794.
- Maurer AP, Cowen SL, Burke SN, Barnes CA, McNaughton BL (2006b) Phase precession in hippocampal interneurons showing strong functional coupling to individual pyramidal cells. J Neurosci 26:13485–13492.

Development of technologies for the neuroscience community. From the onset of my scientific career, I have worked to develop software and hardware to assist the neuroscience community. Below is a list of some of these contributions and ongoing projects:

- Ultrasound measurement of electrical brain activity. I am a collaborator on Brain Initiative R24 (Lead PI: Russel Witte, UA) to develop a non-invasive ultrasound system for the measurement of electrical activity in the brain. The system capitalizes on the acoustoelectric effect, and my role is to validate the system's effectiveness by comparing in vivo measurements obtained from the ultrasound system with measurements obtained from traditional electrophysiology.
- Simultaneous dopamine and single-unit/local-field measurement. Awarded a 2014 NSF BRAIN EAGER grant to develop technologies for the simultaneous recording of the activities of ensembles of neurons and real-time measurement of dopamine release. Since receiving support, we have produced working versions of this device and successfully tested the device in anesthetized and awake and behaving rats (methods paper under review). The next stage of development will be to improve the hardware and software to improve robustness and ease of use.
    - Parent KL, Hill DF, Crown LM, Wiegand J-P, Gies KF, Miller MA, Atcherley CW, Heien ML, Cowen SL (2017) Platform to Enable Combined Measurement of Dopamine and Neural Activity. Anal Chem:acs.analchem.6b03642.
- To better characterize fine body movements in animals as they perform decision-making behaviors, I developed a novel 9-axis head-mounted inertial measurement system. Prototypes of this system are being developed for three laboratories for the investigation of brain-body interactions in the hippocampus, parietal cortex, and prefrontal cortex.

Biographical Sketch

Stephen Cowen

continued

- Designed and built numerous automated maze systems for the training and testing of decision-making and memory-driven behaviors. The design and required software is freely available. I helped set up these systems in the laboratories of three collaborators and they continue to be used.
- Produced an interactive graphical system for real-time and off-line spike sorting (Waveform Cutter, Cowen 2002). This tool became an integral part of MClust (David Redish, U. Michigan), one of the most popular open-source spike-sorting systems.

Complete list of published work on NCBI NIH Bibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/1Lk1z2JuTON/bibliography/46504043/public/?sort=date&direction=ascending.

Research Support

R44MH114776 R44 NIMH: High Density, Miniaturized, Zero Switching, Stimulation and Recording Headstage for Small Animals (Role: Co-investigator, PI: Daniel S Hedin) 8/01/17 – 1/31/18
Objective: Develop new technologies for simultaneously stimulating and recording the activities of groups of individual neurons in behaving animals.

LuMind Foundation: Brain Development, Sleep and Learning in Down Syndrome
(Role: Co-Investigator, PI: Jaime Edgin) 1/01/17 – Present
Objective: Identify neural signatures of sleep dysfunction in Down-syndrome subjects (EEG).

11014.01, Michael J Fox Foundation Cowen, Stephen Cowen (PI) 08/01/17 – 07/31/19
Identification of Network and Oscillatory Signatures Of The LRRK2 Mutation
Objective: Identify neural biomarkers that distinguish the LRRK2 genetic form of Parkinson's disease from healthy controls and idiopathic Parkinson's disease.

1R24MH109060-01, NIMH R24 Brain Initiative Grant, Russel Witte (PI) 11/01/15 – 10/31/18
My role: Co-investigator
High Resolution Electrical Brain Mapping by Real-time and Portable 4D Acoustoelectric Imaging
Objective: Develop new technologies for in vivo acoustoelectric imaging of neural activity.

DBI-1450767, NSF Stephen Cowen (PI) 09/01/14 – 08/31/17
NSF BRAIN-EAGER: Integrated Measurement of Dopamine Release and Large-Scale Ensemble Activity in Behaving Animals
Objective: Develop novel technology for the simultaneous recording of the activities of individual neurons and dopamine release in freely behaving animals.

NS084026-01A1, NIH-NINDS R01 Gene Gurkoff (PI). My role: Co-investigator 06/01/14 – 09/01/18
Restoring Functional Connectivity Following TBI
Objective: Assist investigation of functional connectivity changes associative traumatic brain injury and following deep-brain stimulation therapy. Support for travel to assist with inter-region LFP surgical procedures and recording.

Biographical Sketch

Fabian Fernandez, Ph.D.
Assistant Professor of Psychology and Neurology at the University of Arizona

Education/Training

Institution & Location	Degree	Year(S)	Field Of Study
University of Florida, Gainesville, FL	B.Sc.	2002	IDS, Neurobiology
Stanford University, Palo Alto, CA	Ph.D.	2008	Neuroscience
University of Colorado, Denver, CO	Postdoctoral	2009	Neuropharmacology
Johns Hopkins University, Baltimore, MD	Postdoctoral	2015	Translational Neurosci

Personal Statement

I see many parallels between running a laboratory and operating a technology startup. My vision is to use the lab as a vehicle to identify promising basic research that—if strategically rounded out with a little more investment—could have a disproportionate impact on the way diseases of the nervous system are conceptualized and treated. This perspective informs my current work on circadian rhythms and aging, as well as a previous project I led concerning the design of a treatment for intellectual disability in people with Down syndrome (please see Fernandez et al., Nature Neuroscience, 2007, Jamie Edgin & Fabian Fernandez, New York Times, "The Truth about Down Syndrome," and item 1 in Publications and Career Contributions).

Based in part on professor Art Winfree's conjectures on circadian singularity and other research suggesting disrupted rhythms in aging, I have recently used a photic manipulation to take away circadian function and "cognition" from a healthy animal (i.e., the Siberian hamster; Fernandez et al., Science, 2014). The central question that frames my laboratory's day-to-day activities at the University of Arizona is whether we can design a photic intervention to do the opposite: can we design short-lived light pulses with specific color temperatures, intensities, or frequency schedules that will restore disrupted rhythms and cognition back to normal in older individuals with existing memory/circadian problems? And corollary to this central question: can we do it while the person is sleeping—i.e., at a time when the circadian pacemaker, ironically enough, is most responsive to light stimulation from the retina?

To accomplish this long-term goal, my lab is in the process of developing a technology that emits a precise printed array of LED point lights with predetermined wavelength characteristics and intensity fluctuations that could be optimal for kick-starting rhythms. This device will deliver light from a long-wear contact lens in integrated bursts at times of night when the circadian system is primed to adapt in response to photic input. A natural bedfellow to these efforts is ongoing to: 1) code-break the language by which light can be used as a repetitive stimulus to shift the operation of the brain's circadian clock and rehabilitate it when it has weakened, and 2) identify individual differences in circadian profile that will increase the risk of memory impairment as a person ages. At the intersection of this data, we hope to uncover important principles for how to use naturally occurring facets of dawn- or dusk-like twilight to strengthen the pacemaker specifically in those forecast to experience circadian-linked memory troubles with normal aging (or those whose troubles might accelerate progression of Alzheimer's disease).

In my training and previous experimental work, I have demonstrated a resolve to tackle tough problems and to find elegant solutions that might find their way into everyday life. It is this tenacity that I bring to my current and future work in circadian science.

Positions and Honors

Positions and Employment

1999 – 2002	University Scholars undergraduate research fellow with Dr. Darragh P. Devine, University of Florida, Gainesville.
2002 – 2008	PhD research in neuroscience with Dr. Craig C. Garner, Stanford University, Palo Alto, CA.
2008 – 2009	Fondation Jérôme-Lejeune fellow with Dr. Alberto C.S. Costa, University of Colorado, Denver.

Biographical Sketch

Fabian Fernandez, Ph.D.

continued

2009 – 2012	Senior Scientist and Consultant, Intellimet LLC.
2012 – 2015	Research Associate with Dr. Roger H. Reeves, Johns Hopkins University, Baltimore, MD.
2015	Assistant Professor, Department of Psychology and Neurology, and BIO5 Fellow, University of Arizona, Tucson, AZ

Other Experience and Professional Memberships

2003 – 2004	Stanford University Neuroscience Program Journal Club Organizer
2003 – 2004	Stanford University Professional Development Organizer
2012	Consulting, GABA mechanisms for pharmaceutical trials of cognitive enhancement, Balance Therapeutics
2014	NIH Summit with NCATS: Next Steps for Down Syndrome Therapeutics
2014	Ad Hoc Reviewer for Proceedings of the National Academy of Sciences USA, Neurobiology of Aging, Neurobiology of Learning & Memory, and Journal of Alzheimer's Disease, among others
2015	Member, Society for Research on Biological Rhythms
2015	Member, Association for Psychological Science
2016	Elected to the Faculty Executive Advisory Committee (FEAC) of the UA Department of Psychology
2016	Arizona Alzheimer's Consortium, UA Internal Scientific Advisory Board Member
2016	Reviewer, Flanders Research Foundation (FWO), Belgium
2017	Reviewer, Medical Research Council (MRC), United Kingdom
2017	Reviewer, Velux Stiftung Foundation, Switzerland

Honors

2000	Peter J. Sones Endowed Scholarship, University of Florida, Gainesville
2001	Charles Vincent McLaughlin Endowed Scholarship, University of Florida, Gainesville
2001	Phi Beta Kappa Honor Society
2002	BSc, summa cum laude, self-tailored IDS program
2003 – 2006	NSF Predoctoral Fellowship (GRFP #2003014684)
2007 – 2008	Ruth L. Kirschstein NRSA Research Service Award (NINDS, 1F31NS056571)
2008 – 2009	La Fondation Jérôme-Lejeune Postdoctoral Fellowship
2014	U.S. Patent, 8,729,067, Pharmacological Treatment of Cognitive Impairment
2015	Fellow Award, BIO5 Institute, University of Arizona, Tucson
2016	Bisgrove Scholar Award, Science Foundation Arizona (SFAz)

Publications and Career Contributions

My early publications were concerned with therapeutics research in animal models of intellectual disability. While at Stanford University, I spearheaded efforts to "cure" memory problems in Ts65Dn mice, animals with a genetic background similar to individuals with Down syndrome (DS). For decades, it was assumed that nothing could be done to improve cognitive function in the DS population. The condition results from the over-expression of ~200 categorically-diverse genes that steer development of the brain in a completely different direction from that of the typical one.

Biographical Sketch

Fabian Fernandez, Ph.D.

continued

By 2004, it became clear, however, that the Ts65Dn DS model showed one central difference in brain signaling that could contribute to the animal's difficulties with learning and memory: an increase in the signaling of a neurotransmitter called GABA. I established that higher-than-normal GABA was a key therapeutic target—drugs that reduced this transmitter in the brain also restored the ability of these mice to remember novel objects and to navigate mazes.

These findings, published in Nature Neuroscience, were commented on in Lancet and the Journal of the American Medical Association and reported in the international press (UK Telegraph, Reuters, LA Times, Scientific American, Bloomberg, etc). They have been replicated by several laboratories around the world and are currently the basis for clinical trials by Roche and Balance Therapeutics to evaluate the ability of GABA antagonists to raise IQ in children and young adults with DS.

The last decade has seen disruptive innovation in DS research and a rethinking of treatment approaches for intellectual disability. This would not have been possible without a purpose-driven program of study and a naïve willingness to transform a new idea into value for a medically underserved area of society. Having devised a treatment approach that might be relevant for the developmental disabilities experienced by people with DS early on, I turned my attention to the fact that these individuals experience another phase of cognitive decline as they age. This process is an accelerated form of normal aging and, in some with DS, is thought to bear resemblance to Alzheimer's disease. A consensus in industry and academia suggests the memory problems accompanying normal aging and those typifying progression of dementia are coordinated by multiple factors. Over the past decade, I have explored how one of these factors—circadian arrhythmia—interferes with memory function in older animal models of DS and have focused my lab's efforts to mapping arrhythmia's effects with relevance to the older general population.

1. Fernandez F., Misilmeri M.A., Felger J.C., and Devine D.P. Nociceptin/Orphanin FQ increases anxiety-related behavior and circulating levels of corticosterone during neophobic tests of anxiety. Neuropsychopharmacology, 29: 59-71, 2004.
2. Fernandez F., Morishita W., Zuniga E., Nguyen J., Blank M., Malenka R.C., and Garner C.C. Pharmacotherapy for cognitive impairment in a mouse model of Down syndrome. Nature Neuroscience, 10: 411-413, 2007.
3. Fernandez F. and Garner C.C. Object recognition memory is conserved in Ts1Cje, a mouse model of Down syndrome. Neuroscience Letters, 421: 137-141, 2007.
4. Fernandez F. and Garner C.C. Over-inhibition: a model for developmental intellectual disability. Trends in Neurosciences, 30: 497-503, 2007.
5. Fernandez F. and Garner C.C. Episodic-like memory in Ts65Dn, a mouse model of Down syndrome. Behavioural Brain Research, 188: 233-237, 2008.
6. Fernandez F., Trinidad J.C., Blank M., Feng D.D., Burlingame A.L., and Garner C.C. Normal protein composition of synapses in Ts65Dn mice, a mouse model of Down syndrome. Journal of Neurochemistry, 110: 157-169, 2009.
7. Ruby N.F.*, Fernandez F.*, Zhang P., Klima J., Heller H.C., and Garner C.C. Circadian locomotor rhythms are normal in Ts65Dn "Down Syndrome" mice and unaffected by Pentylenetetrazole. Journal of Biological Rhythms, 25: 63-66, 2010. *Co-Primary Authors
8. Fernandez F.*, Torres V., and Zamorano P.* An evolutionarily conserved mechanism for presynaptic trapping. Cellular and Molecular Life Sciences, 67: 1751-1754, 2010. *Co-Corresponding
9. Fernandez F.* and Edgin J.O. Poor sleep as a precursor to cognitive decline in Down syndrome: A hypothesis. Journal of Alzheimer's Disease & Parkinsonism, 3:2, 2013. *Corresponding Author
10. Zampieri B.L.*, Fernandez F.*, Pearson J.N., Stasko M.R., and Costa A.C.S. Ultrasonic vocalizations during male-female interaction in the mouse model of Down syndrome Ts65Dn. Physiology & Behavior, 128: 119-125, 2014. *Co-Primary Authors

Biographical Sketch

Fabian Fernandez, Ph.D.

continued

11. Fernandez F.* and Reeves R.H. Assessing cognitive improvement in people with Down syndrome: Important considerations for drug efficacy trials. Handbook of Experimental Pharmacology, 228: 335-380, 2015. *Corresponding Author
12. Fernandez F.* and Edgin J.O. Pharmacotherapy in Down syndrome: Which way forward? Lancet Neurology, 15: 776-777, 2016. *Corresponding Author
13. Clark C.A.C., Fernandez F., et al. The medial temporal memory system in Down syndrome: Translating animal models of hippocampal compromise. Hippocampus, 27: 683-691, 2017.
14. Fernandez F.*, Nyhuis C.C., Anand P., et al. Young children with Down syndrome show normal circadian development, but poor sleep efficiency: A cross-sectional study across the first 60 months of life. Sleep Medicine, 33: 134-144, 2017. *Corresponding Author

Since 2005, my colleague, Dr. Norman Ruby, and I have explored how circadian arrhythmia impairs memory function using a novel animal model, the Siberian hamster (Phodopus sungorus) (PNAS 2008; PLoS 2013; Science, 2014). Circadian misalignment due to shift work or jet-lag is well-known to impair memory in humans. However, circadian arrhythmia in rodents induced by clock gene knockouts or surgical lesion of the suprachiasmatic nucleus (SCN), the brain's clock, is reported to have very little effect on memory. Dr. Ruby and I reasoned that this long-held disconnect occurred because the SCN remains developmentally and structurally intact in humans but not in these rodent models. What if the impairments brought on by circadian dysfunction resulted, not from the loss of a "good-functional" SCN (i.e., degeneration), but from the gain of a "bad-defective" SCN that was now sending error signals to memory systems in the medial temporal lobe? What if the proper phenotypic expression of arrhythmia in the brain – and its effects on behavior – require preservation of circuitry from "malfunctioning" SCN areas to their downstream targets? What if key aspects of this expression are lost upon severing SCN connections? We addressed these issues in the Siberian hamster, a species that can be rendered circadian arrhythmic by a simple, one-time photic treatment that does not interfere with SCN structure or development/genetics. We found that hamsters with persistent light-induced arrhythmia actually have severe deficits in spatial and object recognition memory that can be rescued by subsequent ablation of the SCN. These data suggest that chronic arrhythmia per se does not cause memory impairments in animals – or presumably humans – as has been historically believed. Rather, in line with our hypothesis, an intact, but dysrhythmic SCN is necessary to realize these deficits (Fernandez et al., Science, 2014).

15. Ruby N.F., Hwang C.E., Wessells C., Fernandez F., Zhang P., Sapolsky R., and Heller H.C. Hippocampal-dependent learning requires a functional circadian system. Proceedings of the National Academy of Sciences, 105: 15593-15598, 2008.
16. Ruby N.F., Fernandez F., Garrett A., Klima J., Zhang P., Sapolsky R., and Heller H.C. Spatial memory and long-term object recognition are impaired by circadian arrhythmia and restored by the GABAA antagonist pentylenetetrazole. PLoS ONE, 8: e72433, 2013.
17. Fernandez F., Lu D., Ha P., Costacurta P., Chavez R., Heller H.C., and Ruby N.F. Dysrhythmia in the suprachiasmatic nucleus inhibits memory processing. Science, 346: 854-857, 2014.
18. Lewis S.A., Negelspach D.C., Kaladchibachi S., Cowen S.L., and Fernandez F.* Spontaneous alternation: A potential gateway to spatial working memory in Drosophila. Neurobiology of Learning and Memory, 142: 230-235, 2017. *Corresponding Author
19. Ruby N.F., Fisher N., Patton D.F., Paul M.J., Fernandez F.*, and Heller H.C.* Scheduled feeding restores memory and modulates c-Fos expression in the suprachiasmatic nucleus and septohippocampal complex. Scientific Reports, 7: 6755, 2017. *Co-Senior Authors

Biographical Sketch

Elizabeth L. Glisky
Professor

Education/Training

Institution & Location	Degree	Year(S)	Field Of Study
University of Toronto	B.A.	05/1962	Psychology
University of Toronto	Ph.D.	06/1983	Psychology
University of Toronto	Post-Doc	06/1987	Psychology

Personal Statement

The goal of my research has been to gain an understanding of the cognitive and neural mechanisms of memory and executive function, how they change with normal aging and brain damage, and how to reduce the impact of memory disorders in everyday life. My early research focused on designing rehabilitation methods for people with severe memory disorders to help them learn new information relevant in their daily lives. For the past 20 years, I have been exploring individual differences in memory and executive function in normal aging, and how they predict performance in a variety of cognitive tasks and in the real world. To this end, we developed and normed composite measures of memory and executive function in normally aging older adults, which we have tracked longitudinally for several years, and which have yielded a rich dataset with the potential to reveal the variables most critical for successful aging. We have shown that these composite neurocognitive measures predict performance in a variety of memory and cognitive tasks, including source memory and prospective memory, in both older adults and patients. During the past 10 years, my students and I have continued to explore ways to improve memory in a variety of special populations and have shown mnemonic benefits of self-referential processing and self-imagination in older people and in young people with memory deficits. Most recently, we have become interested in the potential for social engagement to provide cognitive benefits for older people through the use of internet communication tools such as Facebook and through intergenerational interactions. We observed benefits in some aspects of executive function but not others, and are continuing work focused on the benefits of intergenerational communication for both young and older adults. We have also found a relation between executive function and hearing loss in older adults. To gain a deeper understanding of the specifics of executive function in these studies, we have constructed an executive function battery for older adults to allow us to explore specific sub-components of executive function that may work together or independently in different cognitive tasks.

1. McFarland, C., and Glisky, E. (2011) Implementation intentions and prospective memory among older adults: An investigation of the role of frontal lobe function. Aging, Neuropsychology, and Cognition, 18, 633-652.
2. Grilli, M. D., and Glisky, E. L. (2013) Imagining a better memory: Self-imagination in memory-impaired patients. Clinical Psychological Science, 1, 93-99.
3. Myhre, J. W., Mehl, M. R., and Glisky, E. L. (2016) Cognitive benefits of online social networking in healthy older adults. The Journals of Gerontology Series B: Psychological Sciences and Social Sciences. doi: 10.1093/geronb/gbw025.
4. Grilli, M. D., Woolverton, C. B., Crawford, M. S., and Glisky, E. L. (2017) Self-reference and emotional memory effects in older adults at increased genetic risk of Alzheimer's disease. Aging, Neuropsychology, and Cognition. doi:10.1080/13825585.2016.1275508.

Biographical Sketch

Elizabeth L. Glisky

continued

Positions and Honors

Positions

1987 – 1989	Visiting Assistant Professor, Department of Psychology, University of Arizona
1989 – 1995	Assistant Professor, Department of Psychology, University of Arizona
1995 – 1999	Associate Professor, Department of Psychology, University of Arizona
1999	Professor, Department of Psychology, University of Arizona
2000 – 2002	Head, Interdisciplinary Program in Gerontology, University of Arizona
2004 – 2008	Associate Head and Director of Graduate Studies, Dept. of Psychology, University of Arizona
2006	Professor, Evelyn F. McKnight Brain Institute
2008 – 2009	Acting Head, Department of Psychology, University of Arizona
2010 – 2015	Head, Department of Psychology, University of Arizona

Honors & Awards

1980 – 1981	Natural Sciences and Engineering Research Council postgraduate scholarship
1981 – 1982	University of Toronto open fellowship
1982 – 1983	Ontario Government scholarship
1983 – 1986	University of Toronto postdoctoral award to research fellow
1989 – 1990	University of Arizona, Provost's Teaching Award.
2003	Social and Behavioral Sciences Research Professorship
2006	Fellow of the Association for Psychological Science
2011	Elizabeth Hurlock Beckman Award for educational leadership and translational work in cognitive rehabilitation

Contribution to Science

In 1986, I published the first of several papers showing that severely amnesic patients could learn considerable amounts of new information. Prior to that time, there were no reports of any significant new learning capabilities in amnesic patients. The method that I developed was called the method of vanishing cues, and it was based on new empirical findings and theories by my colleague Dan Schacter, showing that people with amnesia, although severely impaired in explicit memory, could nevertheless demonstrate preserved implicit memory. My contribution was to take those findings of intact implicit memory and translate them into real world clinical outcomes for memory-impaired individuals. In several publications, we showed that these patients, using the method of vanishing cues, could learn new vocabulary, computer programming, and even a complex set of procedures for a new job. We concluded that the method was successful because it tapped into intact implicit memory allowing people to learn new things even though they had no explicit memory. The method was later explored and extended by many others in the field of neuropsychological rehabilitation and is still used clinically today.

1. Glisky, E. L., Schacter, D. L., and Tulving, E. (1986) Learning and retention of computer related vocabulary in memory impaired patients: Method of vanishing cues. Journal of Clinical and Experimental Neuropsychology, 8, 292 312.
2. Glisky, E. L., and Schacter, D. L. (1987) Acquisition of domain specific knowledge in organic amnesia: Training for computer related work. Neuropsychologia, 25, 893 906.

Biographical Sketch

Elizabeth L. Glisky

continued

3. Glisky, E. L. (1992) Acquisition and transfer of declarative and procedural knowledge by memory-impaired patients: A computer data-entry task. Neuropsychologia, 30, 899-910.
4. Glisky, E. L. (1995) Acquisition and transfer of word processing skill by an amnesic patient. Neuropsychological Rehabilitation, 5(4), 299-318.

In the early 90s, studies of source memory began to appear in the literature, with findings that source memory deficits were found in memory-impaired patients only if they had damage to frontal brain regions. In addition, some studies noted that older people performed more poorly on source memory tasks, and debate ensued about the relative contributions of frontal (FL) and medial temporal (MTL) brain regions to source memory. I became interested in the possibility that individual differences in older adults, many of whom were experiencing declining memory function, might inform this question. I decided to use neuro-psychological tests designed to measure memory function, dependent on the MTLs, and executive function, dependent on the MTLs, to look at individual differences in older adults. I normed a battery of tests on 227 older adults yielding two composite measures: one that tapped fundamental memory functions dependent on the MTLs and one that measured executive function, depending on the FLs. These composite measures were then used to predict performance on item and source memory tasks respectively, and later on other kinds of memory tasks, including prospective memory. The idea was picked up by several other researchers to explore brain-behavior relations in older adults, and the use of neuropsychological tests in older adults has now become quite commonplace.

1. Glisky, E. L., Polster, M. R., and Routhieaux, B. C. (1995) Double dissociation between item and source memory. Neuropsychology, 9, 229-235.
2. Glisky, E. L., Rubin, S. R., and Davidson, P. S. R. (2001) Source memory in older adults: An encoding or retrieval problem? Journal of Experimental Psychology: Learning, Memory, and Cognition, 27, 1131-1146.
3. Glisky, E. L., and Kong, L. L. (2008) Do young and older adults rely on different processes in source memory tasks? A neuropsychological study. Journal of Experimental Psychology: Learning, Memory, and Cognition, 34, 809-822.
4. Drag, L. L., Bieliauskas, L., Kaszniak, A. W., Bohnen, N. I., and Glisky, E. L. (2009) Source memory and frontal functioning in Parkinson's disease. Journal of the International Neuropsychological Society, 15, 399-406.

Prospective memory–remembering to do things in the future–came into the mainstream literature in the mid-90s as interest began to shift somewhat to real-world memory problems. Little research or theory existed at that time concerning how memory for future intentions differed from the more classically studied memory for past experiences, or whether it might depend on different brain regions. In 1996, I was asked to write a chapter for a book on Prospective Memory, the first of its kind, on the neuropsychology of prospective memory. The chapter was largely speculative, since little laboratory research had been done on prospective memory at all. In that chapter, I proposed that executive functions associated with frontal regions of the brain were probably implicated because of the self-initiation that was required to remember a future intention and the potential need for planning, functions that are associated with executive control. This was the beginning of a series of experiments both in my lab and in others

Biographical Sketch

Elizabeth L. Glisky

continued

looking at the differential contributions of memory and executive function to prospective memory and retrospective memory. Although prospective memory is still an area that attracts only a small number of researchers, the added insights from neuropsychology have made a significant contribution to theory development and to understanding the underlying mechanisms of prospective memory.

1. Glisky, E. L. (1996) Prospective memory and the frontal lobes. In M. Brandimonte, G. Einstein & M. McDaniel (Eds.), Prospective memory: Theory and applications (pp. 249-266). Northvale, NJ: Lawrence Erlbaum Associates.
2. McDaniel, M. A., Glisky, E. L., Rubin, S. R., Guynn, M. J., and Routhieaux, B. C. (1999) Prospective memory: A neuropsychological study. Neuropsychology, 13, 103-110.
3. McFarland, C. P., and Glisky, E. L. (2009) Frontal lobe involvement in a task of time-based prospective memory. Neuropsychologia, 47, 1660-1669.
4. McFarland, C., and Glisky, E. (2012) Implementation intentions and imagery: Individual and combined effects on prospective memory among young adults. Memory & Cognition, 40, 62-69.

In 1977, Rogers, Kuiper, and Kirker published a paper showing that processing information in relation to the self, enhanced memory more than semantic processing – what has been called the "self-reference effect." Rogers et al. interpreted this finding as evidence of special mnemonic properties of the self, while others suggested it just involved deeper processing. This debate continues. What has added to the evidence concerning the potential benefits of self-reference is more recent research in aging. Although there was one study in the 1980s, it was not until the mid-2000s where research in self-referential processing in aging again surfaced, and we were at the forefront of this renewed interest. We completed our first study in 2005 and published our first paper on aging and self-reference in 2009. One other paper preceded us in 2007. What we showed was that older adults (over the age of 75) showed a decreased benefit of semantic processing on memory, but showed the same added benefit for self-referential processing as did younger adults, suggesting again that the self had special mnemonic properties. Since then several other studies have appeared in the literature looking at the self-reference effect in older adults. In our lab, we decided to try to enhance the effect even further, combining self-referential processing with imagery – what we have called self-imagination. In a series of experiments, we have demonstrated even greater benefits in memory for self-imagination in both patient and aging populations.

1. Glisky, E. L., and Marquine, M. J. (2009) Semantic and self-referential processing of positive and negative trait adjectives in older adults. Memory, 17, 144-157.
2. Grilli, M. D., and Glisky, E. L. (2010) Self-imagining enhances recognition memory in memory-impaired individual with neurological damage. Neuropsychology, 24, 698-710.
3. Grilli, M. D., and Glisky, E. L. (2011) The self-imagination effect: Benefits of a self-referential encoding strategy on cued recall in memory-impaired individuals with neurological damage. Journal of the International Neuropsychological Society, 17, 929-933.
4. Grilli, M. D., and Glisky, E. L. (2013) Imagining a better memory: Self-imagination in memory-impaired patients. Clinical Psychological Science, 1, 93-99. doi:10.1177/2167702612456464.

Biographical Sketch

Elizabeth L. Glisky

continued

Research Support

Ongoing

Advanced Bionics Corporation 2015 – 18
Cochlear implants and cognitive impairment
Goals are to look at effects of cochlear implants on cognitive function & social engagement in adults over the age of 72.
Role: Co-PI (PI: Jacob); PI (7/17 – 7/18)

Arizona Alzheimer's Consortium 7/1/17 – 6/30/18
Memory and executive function in normally-aging older adults
The goals are to document changes over time in episodic memory and executive function in normally-aging older adults aged 65+, and to validate an executive function battery for older adults.
Role: PI

Evelyn F. McKnight Brain Research Foundation 7/1/15 – 6/30/18
Inter-Institutional cognitive aging assessment core
My responsibilities are to work with a team at the University of Arizona to develop a core assessment battery for older adults over the age of 85 to be shared across 4 sites.
Role: Co-Investigator (PI: Alexander)

Completed

2008 – 2011	National Institute on Aging, "Cognitive and neural bases of aging and memory," Subcontract.
2011	Cognitive Science Summer RA Award, "Social Networking for Older Adults," PI.
2012	Western Alliance to Expand Student Opportunities, "Self-imagination in normal aging and mild cognitive impairment," $2500 to support undergraduate Meli'sa Crawford.
2012	Evelyn F. McKnight Brain Institute, Pilot project on "Effects of Social Networking on Cognition in Socially-Isolated Older Adults," PI.
2015 – 2016	Arizona Alzheimer's Consortium, "Memory, executive function, and prospective memory training," PI.
2016 – 2017	Arizona Alzheimer's Consortium, "Interventions to improve memory and executive function in older adults in real-world settings"

Biographical Sketch

Naomi E. Rance
Professor of Pathology

Education/Training

Institution & Location	Degree	Year(S)	Field Of Study
University of Maryland, College Park	B.S.	1973	Psychology
University of Maryland, Baltimore	Ph.D.	1981	Physiology
University of Maryland, Baltimore	M.D.	1983	Medicine
The Johns Hopkins Hospital	Fellowship	1989	Neuropathology

Personal Statement

For more than 25 years, our overall goal has been to characterize and understand the physiological significance of the changes that occur in the hypothalamus secondary to menopause. We observed hypertrophy and increased gene expression in a subpopulation of estrogen receptor expressing neurons in the hypothalamic infundibular nucleus of postmenopausal women. These neurons are called KNDy neurons, based on the co-expression of kisspeptin, neurokinin B (NKB), and dynorphin. For many years, our goal was to understand the role of NKB in reproductive regulation. The significance of these studies became widely recognized with the observation that mutations in either the gene encoding NKB or its receptor (NK_3R) result in hypogonadotropic hypogonadism. In the last 10 years, we have focused on studying the role of KNDy neurons in the estrogen modulation of body temperature. The results of these studies allowed us to propose that KNDy neurons play a role in the generation of hot flushes via NK_3R signaling in the hypothalamic median preoptic nucleus. Recent clinical trials in have shown that NK_3R antagonists effectively reduce the number and severity of hot flushes, thus providing strong support for our hypothesis.

1. Rance, N.E. (2009) Menopause and the human hypothalamus: Role of kisspeptin/neurokinin B neurons in the regulation of estrogen negative feedback. Peptides, 30:111-22.
2. Rance, N.E., Krajewski, S.K., Smith, M.A., Cholanian, M. and Dacks, P.A. Neurokinin B and the hypothalamic regulation of reproduction. (2010) Brain Research, special issue entitled “New Insights into the Neurobiology of Reproduction and Puberty” 1364:116-128.
3. Mittelman-Smith, M.A., Williams, H. Krajewski-Hall. McMullen, N.T. and Rance, N.E. (2012) Role for kisspeptin/neurokinin B/dynorphin (KNDy) neurons in cutaneous vasodilatation and the estrogen modulation of body temperature. Proceedings of the National Academy of Science, USA, 109:19846-19841, PMCID: PMC3511761.
4. Rance, N.E., Dacks, P.A. Mittelman-Smith, M.A., Krajewski, S.K., Romanovsky, A. A. (2013) Modulation of body temperature and LH secretion by hypothalamic KNDy (kisspeptin, neurokinin B and dynorphin) neurons: A novel hypothesis on the mechanism of hot flushes. Frontiers in Neuroendocrinology, 34, 211-27, PMID: 23872331.

Biographical Sketch

Naomi E. Rance

continued

Positions and Honors

Positions and Employment

1976 – 1981	Predoctoral Fellow, Department of Physiology, University of Maryland
1983 – 1986	Resident, Anatomic Pathology, The Johns Hopkins Hospital
1986 – 1987	Chief Resident, Anatomic Pathology, The Johns Hopkins Hospital
1987 – 1989	Clinical and Research Fellow, Neuropathology Laboratory, The Johns Hopkins Hospital
1989 – 1995	Assistant Professor, Department of Pathology, University of Arizona College of Medicine
1989	Chief, Division of Neuropathology, University Medical Center, Tucson, Arizona
1989	Neuropathology Consultant, Forensic Science Center, Pima County, Arizona
1995 – 2000	Associate Professor, Department of Pathology, University of Arizona College of Medicine
1996	Associate Head, Department of Pathology, University of Arizona College of Medicine
2000	Professor, Department of Pathology, University of Arizona College of Medicine

Other Experience and Advisory Committees

1993	Advisory Group, Workshop on Menopause, NIH, Bethesda
1994	Ad Hoc member, Biochemical Endocrinology Study Section, NIH, Bethesda
1995, 1997	Ad Hoc Reviewer, National Science Foundation
1997	Ad Hoc member, Biochemical Endocrinology Study Section, NIH, Bethesda
1998 – 2004	Multiple Site Visit Review Committees, NIH, NIA Program Project Grants
2001	Advisory Group, NIA Workshop on Primate Models of Menopause, NIH, Bethesda
2007 – 2012	Scientific Advisory Board, Evelyn McNight Brain Institute, University of Arizona
2009	Ad Hoc Member, ICER Study Section, NIH Bethesda
2009, 2010	Ad Hoc Reviewer, Burroughs Welcome Trust
2011	Ad Hoc Member, ICER Study Section, NIH, Chicago
2014	Ad Hoc Reviewer, Burroughs Welcome Trust
2015, 2017	Ad Hoc Member, Neuroendocrinology, Neuroimmunology, Rhythms and Sleep Study Section, NIH, New Orleans, Louisiana (2015) and San Antonio, Texas (2017)

Biographical Sketch

Naomi E. Rance

continued

Invited Speaker (selected)

2004	Symposium Speaker, Annual Meeting of the Endocrine Society of Australia, Sidney, Australia
2004	Reproductive Endocrine Unit, Massachusetts General Hospital, Boston
2007	Symposium Session entitled "Lifecycle of the GnRH Neuron" Annual Meeting of the Endocrine Society, Toronto
2008	First World Conference on Kisspeptin Signaling in the Brain, Cordoba Spain
2009	Magee-Women's Research Institute and University of Pittsburgh
2010	Physiology Department, University of West Virginia
2011	Netherlands Institute of Neuroscience, Amsterdam
2011	Integrative Physiology Department, University of Colorado, Boulder
2011	Physiology Department, University of Wyoming, Laramie
2012	Symposium Speaker, Annual Meeting of the Endocrine Society, Houston Texas
2012	Barrow Neurologic Institute, Phoenix, Arizona
2012	Second World Conference on Kisspeptin Signaling in the Brain, Tokyo, Japan
2013	Endocrine Grand Rounds, Reproductive Neuroendocrine Unit, Massachusetts General Hospital, Boston
2014	Plenary Speaker, 5th International Symposium on the Physiology and Pharmacology of Temperature Regulation, South Africa
2014	Symposium entitled "The Science of Thermoregulation and Vasomotor Symptoms: New Targets for Research and Treatment," Marriot Gaylord Hotel, Washington DC.
2014	Plenary Speaker, Symposium on Hot Flashes-The North American Menopause Society 2014 Annual Meeting, Washington DC.
2017	Symposium Speaker, Plenary Symposium on Hot Flashes- 15th World Congress on Menopause, Prague, Czech Republic, September 2016

Honors

1973	Phi Beta Kappa
1983	Rudolph Virchow Prize for Research in Pathology, University of Maryland
1995	John Davis Outstanding Residency Teaching Award, Dept. of Pathology, University of Arizona
1997	Vernon and Virginia Furrow Award for Excellence in Graduate Medical Education, University of Arizona College of Medicine
1999	Basic Science Educator of the Year, University of Arizona College of Medicine
2000	Basic Science Educator of the Year, University of Arizona College of Medicine
2001	Basic Science Educator of the Year, University of Arizona College of Medicine
2002	Basic Science Educator of the Year Lifetime Award, University of Arizona College of Medicine
2007	Vernon and Virginia Furrow Award for Excellence in Innovation in Teaching, University of Arizona College of Medicine
2015	Founder's Day Speaker, University of Arizona College of Medicine

Biographical Sketch

Naomi E. Rance

continued

Contribution to Science

We have characterized changes in the morphology and neuropeptide gene expression that occur in the human hypothalamus secondary to the ovarian failure of menopause. Studies in animal models showed that the changes in neurokinin B and kisspeptin gene expression in postmenopausal women are secondary to withdrawal of ovarian estrogen and not due to age per se.

1. Rance, NE, and Young, WS III. (1991) Hypertrophy and increased gene expression of neurons containing neurokinin B and substance P messenger RNAs in the hypothalami of postmenopausal women. Endocrinology, 128:2239-2247.
2. Rance, N.E. and Bruce, T.R. (1994) Neurokinin B gene expression is increased in the arcuate nucleus of ovariectomized rats. Neuroendocrinology, 60:337-345.
3. Abel, TW, Voytko, ML, and Rance, NE. (1999) Effects of hormone replacement therapy on neuropeptide gene expression in a primate model of menopause. Journal of Clinical Endocrinology and Metabolism, 84:2111-2118.
4. Rometo, AM, Sally J. Krajewski, S.J., Voytko, M.L., Rance, N.E. (2007) Hypertrophy and increased kisspeptin gene expression in the hypothalamic infundibular nucleus of postmenopausal women and ovariectomized monkeys. Journal of Clinical Endocrinology and Metabolism, 92:2744-2750.

Based on the dramatic changes in NKB gene expression in postmenopausal women, we hypothesized that NKB neurons participate in the estrogen modulation of LH secretion. This hypothesis is supported by pharmacological and anatomic studies. Using an NK3R agonist conjugated to saporin to ablate KNDy neurons, we show that KNDy neurons are essential for the functioning of the reproductive axis.

1. Sandoval-Guzmán, T., Rance, N.E. (2004) Central injection of senktide, an NK3 receptor agonist, or neuropeptide Y inhibits LH secretion and induces different patterns of Fos expression in the rat hypothalamus. Brain Research, 1026:307-312.
2. Krajewski, SJ; Anderson, Miranda J, Iles-Shi, L; Chen, Kyung J, Urbanski, HF, Rance, NE. (2005) Morphological evidence that neurokinin B neurons modulate GnRH secretion via NK3 receptors in the rat median eminence. Journal of Comparative Neurology, 489:372-386.
3. Mittelman-Smith, M.A., Williams, H. Krajewski-Hall, S.J. Lai, J., Ciofi, P. McMullen, N.T. and Rance, N.E. (2012) Arcuate kisspeptin/neurokinin B/dynorphin (KNDy) neurons mediate the estrogen suppression of gonadotropin secretion and body weight. Endocrinology, 153:2800-2012. PMCID: PMC3359616.
4. Mittelman-Smith, M.A.,Krajewski-Hall. McMullen, N.T. and Rance, N.E. (2016) Ablation of KNDy neurons results in hypogonadotropic hypogonadism and amplifies the steroid-induced LH surge in female rats. Endocrinology, 157:2015-2027.

Neuroanatomic studies were conducted using dual labeled immunohistochemistry, anatomic tract-tracing and biocytin injections in tissue slices of EGFP-labeled transgenic mice. We described a bilateral network of KNDy neurons within the arcuate nucleus in which these neurons communicate with each other via NK3R and project to GnRH terminals in the median eminence. Connections between arcuate KNDy neurons provides an anatomic framework to explain how KNDy neurons could be coordinated to provide sex-steroid modulation of pulsatile GnRH secretion. Projections to other brain regions suggest that KNDy neurons influence a wide variety of physiologic functions including thermoregulation.

1. Krajewski, SJ; Anderson, Miranda J, Iles-Shi, L; Chen, Kyung J, Urbanski, HF, Rance, NE. (2005) Morphological evidence that neurokinin B neurons modulate GnRH secretion via NK3 receptors in the rat median eminence. Journal of Comparative Neurology, 489:372-386.

Biographical Sketch

Naomi E. Rance

continued

2. Krajewski, S. J., Burke, M. C., Anderson, M. J., McMullen, N. T., Rance, N. E. (2010) Forebrain projections of arcuate neurokinin B neurons demonstrated by anterograde tract-tracing and monosodium glutamate lesions in the rat. Neuroscience, 166:1187-1193. PMCID: PMC2823949.
3. Burke MC, Letts (Dacks) PA, Krajewski SJ and Rance, NE. (2006) Coexpression of dynorphin and neurokinin B immunoreactivity in the rat hypothalamus: Morphologic evidence of interrelated function within the arcuate nucleus. Journal of Comparative Neurology 498, 712-726.
4. Cholanian, M., Krajewski-Hall, S.J, Levine, R.B., McMullen, N.T., Rance, N.E., Chronic oestradiol reduces the dendritic spine density of KNDy (kisspeptin/neurokinin B/dynorphin) neurones in the arcuate nucleus of ovariectomised Tac2-enhanced green fluorescent protein transgenic mice. Journal of Neuroendocrinology. 27:253-263, 2015.

To determine if KNDy neurons could play a role in thermoregulation, a series of studies was performed using a rat model. Anatomical studies showed projections of KNDy neurons to the median preoptic nucleus (MnPO), an important component of the CNS pathway that regulates heat dissipation effectors. Moreover, MnPO neurons express the neurokinin 3 receptor (NK3R), the primary receptor for NKB. Further studies using a rat model strongly supported the hypothesis that KNDy neurons could influence cutaneous vasodilation (flushing) via projections to NK3R-expressing neurons in the MnPO.

1. Dacks, P.A., Krajewski, S.K and Rance, N.E. (2011) Activation of neurokinin 3 receptors in the median preoptic nucleus decreases body temperature in the rat. Endocrinology, 152:4894-4905. PMCID: PMC3230049.
2. Mittelman-Smith, M.A., Williams, H. Krajewski-Hall. McMullen, N.T. and Rance, N.E. (2012) Role for Kisspeptin/Neurokinin B/Dynorphin (KNDy) Neurons in Cutaneous Vasodilatation and the Estrogen Modulation of Body Temperature. Proceedings of the National Academy of Science, USA, 109:19846-19841, PMCID: PMC3511761.
3. Rance, N.E., Dacks, P.A. Mittelman-Smith, M.A., Krajewski, S.K., Romanovsky, A.A. (2013) Modulation of body temperature and LH secretion by hypothalamic KNDy (kisspeptin, neurokinin B and dynorphin) neurons: a novel hypothesis on the mechanism of hot flushes. Frontiers in Neuroendocrinology, 34, 211-27, PMID: 23872331.
4. Mittelman-Smith, M.A., Williams, H. Krajewski-Hall. McMullen, N.T. and Rance, N.E. (2015) Neurokinin 3 receptor-expressing neurons in the median preoptic nucleus modulate heat-dissipation effectors in the female rat. Endocrinology, 156:2552-2562.

Research Support

Ongoing

Role of Preoptic NK3R Neurons in the Estrogen Modulation of Body Temperature 8/15/2014 – 4/30/2019
Agency/number NIH NIA 1R01AG047887 $1.5 million total award
Principle Investigator: Naomi Rance

This grant explores how preoptic neurons that express the neurokinin 3 receptor participate in the neural circuits regulating body temperature. Our goal is to provide information related to mechanism of menopausal flushes.

Biographical Sketch

Lee Ryan, Ph.D.
Professor, Psychology, Neurology, Neurosciences Program, University of Arizona

Education/Training

Institution & Location	Degree	Year(S)	Field Of Study
University of Toronto, Toronto, Canada	BMus	1979	Music
University of Toronto, Toronto, Canada	MA	1981	Music
University of Toronto, Toronto, Canada	BS	1988	Psychology/Neurosicence
University of British Colombia, Vancouver, Canada	PhD	1992	Clinical/Cognitive Psych
University of California, San Diego, San Diego, CA	Post-doctoral Fellow	1993 – 1995	Neuropsychology

Personal Statement

I am a professor and the head of the Department of Psychology in the School of Mind, Brain, and Behavior at the University of Arizona, and the associate director of the Evelyn F. McKnight Brain Institute. Since 1998, I have directed the Cognition and Neuroimaging Laboratory, which provides technical and analysis support for cognitive neuroscience researchers from across the campus utilizing MRI methods. My research focuses on memory, age-related memory decline, and the neural basis of memory. I have published more than 60 scholarly articles utilizing various MRI methods, including functional MRI, ASL perfusion, voxel-based morphometry, and high-resolution diffusion tensor imaging. My research on the neural basis of memory has focused on understanding the hippocampal processes mediating autobiographical and semantic memory, how memory changes across the adult lifespan, how those changes relate to brain structure and function, and the early prediction of Alzheimer's disease. Recent studies using morphometric analyses and diffusion imaging have investigated factors that influence individual differences in age-related cognitive function, including genetic markers, obesity, hypertension, and anti-inflammatory drug use. As a clinical neuropsychologist, I work with individuals and families who are coping with chronic and progressive diseases that effect cognitive functioning, including multiple sclerosis, Parkinson's disease, and Alzheimer's disease. I teach undergraduate and graduate level courses in memory, neuropsychology, neuroanatomy, cognitive neuroscience, and MRI methods and have been very active in mentoring programs at the University of Arizona.

1. Memel, M. and Ryan, L. (2017) Visual integration enhances associative memory equally for young and older adults without reducing hippocampal encoding activation. Neuropsychologia, 100, 195-206.
2. Ryan, L., Walther, K., Bendlin, B.B., Lue L-F., Walker, D.G., and Glisky, E.L. (2011) Age-related differences in white matter integrity measured by diffusion tensor imaging and cognitive function are related to APOE status. NeuroImage, 54(2), 1565-77.
3. Alexander, G.E., Ryan, L., Bowers, D., Foster, T.C., Bizon, J.L., Geldmacher, D.S., and Glisky, E.L. (2012) Characterizing cognitive aging in humans with links to animal models. Frontiers in Aging Neuroscience, 4:21.
4. Ryan, L., Cardoza, J.A., Barense, M.D., Kawa, K.H., Wallentin-Flores, J., Arnold, W.T., and Alexander, G.E. (2012) Age-related impairment in a complex object discrimination task that engages perirhinal cortex. Hippocampus, 22(10), 1978-89.

Biographical Sketch

Lee Ryan, Ph.D.

continued

Positions and Honors

1988 – 1992	National Science & Engineering Research Council of Canada Graduate Fellowships
1993 – 1995	National Science & Engineering Research Council of Canada Postdoctoral Fellowships
1992 – 1993	Clinical internship in Neuropsychology, VAMC, La Jolla, and UCSD, San Diego, CA
1993 – 1996	Research Scientist, Department of Psychiatry, University of California, San Diego
1996 – 2003	Assistant Professor, Department of Psychology, University of Arizona
1998	Participant in Summer Institute on Aging Research, National Institute on Aging
1998 – Present	Director, Cognition & Neuroimaging Laboratories, University of Arizona
2000 – Present	Member, Memory Disorders Research Society
2003 – 2014	Associate Professor and Associate Head, Department of Psychology, University of Arizona
2013 – Present	Associate Director, Evelyn F. McKnight Brain Institute
2014 – Present	Professor, Department of Psychology, University of Arizona
2015 – Present	Head, Department of Psychology, University of Arizona

Contribution to Science

Using fMRI, I demonstrated that the hippocampus remains active during autobiographical memory retrieval, even when the memories are more than 20 years old. This finding, consistent with Multiple Trace Theory, has had a significant impact on the field's understanding of the role of medial temporal lobe structures in consolidation, storage, and retrieval of old memories. The finding helps to clarify the types of memory impairment associated with medial temporal lobe damage in patients with stroke or other pathology.

1. Campbell, J., Nadel, L., Duke, D., and Ryan, L. (2011) Remembering all that and then some: recollection of autobiographical memories after a 1-year delay. Memory. 19(4), 406-15.
2. Nadel, L., Winocur, G., Ryan, L, and Moscovitch, M. (2007) Systems consolidation and hippocampus: Two views. Debates in Neuroscience, 4, 55-66.
3. Nadel, L., Ryan, L., Hayes, S., Gilboa, A., and Moscovitch, M. (2003) The role of the hippocampal complex in episodic long-term memory. In T. Ono, G. Matsumoto, R.R. Lllinas, A. Berthoz, R. Norgren, H. Nishijo and R., Tamura (Eds.), Limbic and Association Cortical Systems - Basic, Clinical and Computational Aspects, 7-12 October 2002. Excerpta Medica International Congress Series (ICS), Amsterdam, Elsevier Science.
4. Ryan, L., Nadel, L., Keil, K., Putnam, K., Schnyer, D., Trouard, T., and Moscovitch, M. (2001) Hippocampal complex and retrieval of recent and very remote autobiographical memories: Evidence from functional magnetic resonance imaging in neurologically intact people. Hippocampus, 11: 707-714.

Using fMRI, I demonstrated that the hippocampus is important for the retrieval of both episodic and semantic memory, contrary to previous views of the hippocampus as a structure that is primarily or even solely involved in episodic retrieval. These studies have highlighted the interactive nature of these two systems.

1. Ryan, L., Lin, C.Y., Ketcham, K., and Nadel, L. (2010) The role of medial temporal lobe in retrieving spatial and nonspatial relations from episodic and semantic memory. Hippocampus, 20(1),11-8.
2. Greenberg, D.L., Keane, M.M., Ryan, L., and Verfaillie, M. (2009) Impaired category fluency in medial temporal lobe amnesia: The role of episodic memory. Journal of Neuroscience, 29(35), 10900-10908. PMCID: PMC2761020.

Biographical Sketch

Lee Ryan, Ph.D.

continued

3. Ryan, L., Hoscheidt, S., and Nadel, L. (2008) Time, space, and episodic memory. In E. Dere, A. Easton, J. Huston, and L. Nadel (Eds.). Handbook of Episodic Memory Research.
4. Ryan, L., Cox, C., Hayes, S., and Nadel, L. (2008) Hippocampal activation during episodic and semantic memory retrieval: Category production and category cued recall. Neuropsychologia, 46, 2109-2121.

My laboratory has shown that cardiovascular health risk factors, including obesity, hypertension, and inflammation, have a negative impact on both the structure and function of the aging brain. These brain changes are associated with increased age-related memory and executive function impairments. These studies are important because they suggest that healthy lifestyles that prevent the occurrence of cardiovascular disease may maintain brain health as well.

1. Ryan, L. and Walther, K. (2014) White matter integrity in older females is altered by increased body fat. Obesity (Silver Spring), 22(9):2039-46.
2. Ryan, L., Walther, K., Bendlin, B.B., Lue L-F., Walker, D.G., and Glisky, E.L. (2011) Age-related differences in white matter integrity measured by diffusion tensor imaging and cognitive function are related to APOE status. NeuroImage, 54(2), 1565-77.
3. Walther, K., Bendlin, B.B., Glisky, E.L., Trouard, T.P., Lisse, J.R., Posever, J.O., and Ryan, L. (2011) Anti-inflammatory drugs reduce age-related decreases in brain volume in cognitively normal older adults. Neurobiology of Aging, 32(3), 497-505.
4. Walther, K., Birdsill, A.C., Glisky, E.L., and Ryan, L. (2010) Structural brain differences and cognitive functioning related to body mass index in older females. Human Brain Mapping, 31(7), 1052-64.

Recently, I published a theoretical article that uses neuroscientific evidence to build an integrative memory model to explain the common process of change in psychotherapy. This is the first comprehensive model of its kind, based largely on the concept of memory reconsolidation, that provides an explanatory framework for change across all modalities of psychotherapy. The model also makes predictions regarding ways to increase the efficacy of psychotherapies, as well as predictions regarding the connection between episodic memory and the "self."

1. Lane, R.D., Ryan, L., Nadel, L., and Greenberg, L. (2015) Memory reconsolidation, emotional arousal and the process of change in psychotherapy: New insights from brain science. Behav Brain Sci, 38:e1.

Complete list of published work in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/lee.ryan.1/bibliography/44215085/public/?sort=date&direction=descending

Research Support

Ongoing

U01 HL131014 Sweitzer, Hay, Ryan, Arai (MPI) 3/01/2017 – 2/28/2021
NHLBI
Evaluation of the Safety and Efficacy of Angiotensin 1-7 to Enhance Cognitive Function in Participants Undergoing Coronary Artery Bypass Graft (CABG) Surgery
This project is designed to evaluate the safety and efficacy of Ang-(1-7) to enhance cognitive function in participants undergoing CABG surgery. Further, by teaming with the unique capabilities of the NIH Clinical Center, these studies will measure, for the first time, post-CABG surgery brain inflammation and microglia activation as measured by PET

Biographical Sketch

Lee Ryan, Ph.D.

continued

imaging of [11C]PBR28 and test the hypothesis that Ang-(1-7) will result in a decrease in brain inflammation and microglia activation in CABG patients. When completed, this clinical study will have advanced development of a new therapy with potential to treat cognitive impairment in CABG patients.
Role: MPI

AAC Ryan (PI) 7/1/2017 – 6/30/2018
Department of Health Services, State of Arizona
Perirhinal Cortical Structure and Function in Older Adults and Its Role in Memory
This grant studies hippocampal and perirhinal function and how it relates to genetic risk for Alzheimer's disease in a group of older adults using functional MRI.
Role: PI

Completed

AAC Ryan (PI) 7/1/2016 – 6/30/2017
Department of Health Services, State of Arizona
Memory Functioning in Heart Failure Patients with Risk for Alzheimer's Disease
This grant studied the hippocampal and perirhinal function in a group of heart failure patients compared to age-matched controls using functional MRI.
Role: PI

AAC Ryan (PI) 7/1/2015 – 6/30/2016
Department of Health Services, State of Arizona
Angiotensin (1-7) Treatment to Improve Cognitive Functioning in Heart Failure Patients
This grant studied the safety and efficacy of Ang-(1-7) to enhance cognitive function in as well as the impact of Ang-(1-7) on inflammatory markers and neuroimaging measures in participants with heart failure.
Role: PI

AAC Ryan (PI) 7/1/2014 – 6/30/2015
Department of Health Services, State of Arizona
The Impact of Family History For Alzheimer's Disease on Cognition and Brain Function
This grant studied the neural and genetic correlates of family history for Alzheimer's while controlling for APOE e4 status, using volumetric, diffusion, and ASL perfusion MRI.
Role: PI

HB2354 Ryan (PI) 7/1/1998 – 6/30/2014
Department of Health Services, State of Arizona
Cognition & Neuroimaging Laboratories
This grant provided support for functional neuroimaging research at the University of Arizona focusing on topics relevant to aging, memory, and Alzheimer's disease, including a pilot grant program for developing new fMRI research projects.
Role: PI

Biographical Sketch

Robert C. Wilson
Assistant Professor of Psychology and Cognitive Science

Education/Training

Institution & Location	Degree	Year(S)	Field Of Study
University of Cambridge	B.A.	06/2002	Natural Sciences
University of Cambridge	M.Sci.	06/2002	Chemistry
University of Pennsylvania	M.S.E.	05/2003	Bioengineering
University of Pennsylvania	Ph.D.	05/2009	Bioengineering
Princeton University	Postdoc	12/2014	Psychology and Neuroscience

Personal Statement

I am an expert in computational neuroscience and mathematical psychology. I have modeled learning and decision making at a variety of levels – from low level neural networks to high level Bayesian inference – and have extensive experience linking theoretical models to experimental data. I have expertise in developing explore-exploit experiments (Wilson et al, JEP:General 2014), building cognitive models of complex tasks (Wilson, R. C., & Niv, Y., 2012), and linking models to behavioral and neural data (Wilson et al. Neuron 2014), and my work on the effects of TMS on explore-exploit behavior (Zajkowski, W., Kossut, M., and Wilson, R. C, in revision).

1. Wilson, R. C., Geana, A., White, J. M., Ludvig, E. A., and Cohen, J. D. (2014) Humans use directed and random exploration to solve the explore-exploit dilemma. JEP:General, 143 (6) 2074-2081.
2. Wilson, R. C., and Niv, Y. (2012) Inferring relevance in a changing world. Front Hum Neurosci, 5:189.
3. Wilson, R. C., Takahashi, Y. K., Schoenbaum, G. and Niv, Y. (2014) Orbitofrontal cortex as a cognitive map of task space. Neuron, 81(2) 267-279.
4. Zajkowski, W., Kossut, M., and Wilson, R. C. (in revision) A causal role for right frontopolar cortex in directed, but not random, exploration. eLife.

Positions and Honors

2003 – 2009	Graduate Student, Department of Bioengineering, University of Pennsylvania
2009 – 2014	Postdoctoral Research Associate, Princeton Neuroscience Institute
2015 – Present	Assistant Professor of Psychology and Cognitive Science, University of Arizona

Biographical Sketch

Robert C. Wilson

continued

Contribution to Science

How humans and animals solve the explore-exploit dilemma. Many decisions in life involve a tradeoff between exploring new options for information and exploiting known options for reliable reward. For example, when dining at a favorite restaurant, do you explore the new ravioli that is sure to be informative, or exploit the known pizza that is sure to be good? Beyond eating out, the explore-exploit dilemma occurs at all levels of decision making, from picking a TV show to watch or a person to marry, and there are real advantages to solving it well. Yet despite its importance, solving the dilemma optimally is intractable in all but the simplest settings and so the question arises as to how we balance exploration and exploitation in practice. In recent work I have shown that humans use two distinct strategies for solving the explore-exploit dilemma: a directed strategy in which information seeking drives exploration by choice, and a random strategy in which behavioral variability drives exploration by chance. In addition, initial studies from my lab and my collaborators suggest that these two strategies rely on dissociable neural networks, with directed exploration dependent of frontal pole, correlating with blink rate and developing over the course of adolescence, while random exploration appears to be tied to norepinephrine. The identification of the two strategies, in addition to experiments with which to quantify them, is already having a significant impact on the field. Versions of my task are currently being run in at least nine different labs around the world to study exploration in mental illness, across development, in animals and in response to drugs.

1. Wilson, R. C., Geana, A., White, J. M., Ludvig, E. A., and Cohen, J. D. (2014) Humans use directed and random exploration to solve the explore-exploit dilemma. JEP:General, 143 (6), 2074-2081.
2. Somerville, L. H., Sasse, S. F., Garrad, M. C., Drysdale, A. T., Abi Akar, N., Insel, C., and Wilson, R. C. (accepted). Charting the Expansion of Strategic Exploratory Behavior During Adolescence. JEP:General.
3. Krueger, P. K., Wilson, R. C., and Cohen, J. D. (accepted). Directed and random exploration in the domain of losses. Judgment and Decision Making.
4. Zajkowski, W., Kossut, M., and Wilson, R. C. (in revision). A causal role for right frontopolar cortex in directed, but not random, exploration. In revision at eLife.

Learning in the presence of abrupt change. Whether getting a new job or a new president, life is full of "change points" that cause the rules of the game to shift abruptly. Learning and making predictions in such circumstances can be challenging because change points can render much of the past irrelevant. In this work, I developed a series of computational models to look at how humans and animals learn in the face of such environmental change points. These models ranged in scale from low-level neural network models to high-level cognitive models. All of these models made detailed experimental predictions, some of which have been tested and borne out in experiments by my collaborators.

1. Wilson, R. C., and Finkel, L. H. (2009) A neural implementation of the Kalman filter. Advances in Neural Information Processing Systems 22, 2062-2070.
2. Wilson, R. C., Nassar, M. R., and Gold, J. I. (2010) Bayesian online learning of the hazard rate in change-point problems. Neural Computation, 22 (9), 2452-2476.
3. Wilson, R. C., and Niv, Y. (2012) Inferring relevance in a changing world. Front Hum Neurosci, 5:189.
4. Wilson, R. C., Nassar, M. R., and Gold, J. I. (2013) A Delta-rule approximation to Bayesian inference in change-point problems. PLoS Comp Biol, 9 (7), e1003150.

Biographical Sketch

Robert C. Wilson

continued

The role of orbitofrontal cortex in learning and decision making. Orbitofrontal cortex (OFC) has long been known to play an important role in learning and decision making. However, the exact nature of that role has remained elusive. I have recently proposed a new unifying theory of OFC function in which the OFC provides an abstraction of currently available information in the form of a labeling of the current task state. This "cognitive map" of "task space" in OFC is then used as a scaffold for learning and decision making throughout the brain. The theory accounts for many of the puzzling findings related to OFC such as its role in a number of behavioral tasks, as well as more recent findings showing the effect of OFC lesions on the firing of dopaminergic neurons in ventral tegmental area (VTA). This work has been well received by the field and has been cited more than 100 times in just over two years.

Takahashi, Y. K., Roesch, M. R., Wilson, R. C., Toreson, K., O'Donnell, P., Niv, Y., and Schoenbaum, G. (2011) Expectancy-related firing of midbrain dopamine neurons depends on orbitofrontal cortex. Nature Neuroscience, 14, 1590-1597.

Wilson, R. C., Takahashi, Y. K., Schoenbaum, G. and Niv, Y. (2014) Orbitofrontal cortex as a cognitive map of task space. Neuron, 81 (2) 267-279.

Complete list of published work in MyBibliography:

- Lab website (also includes in press articles and conference papers)
  - http://www.u.arizona.edu/~bob/publications.html
- NCBI My Bibliography (published journal papers only)
  - http://www.ncbi.nlm.nih.gov/sites/myncbi/robert.wilson.3/bibliography/48037481/public/?sort=date&direction=ascending

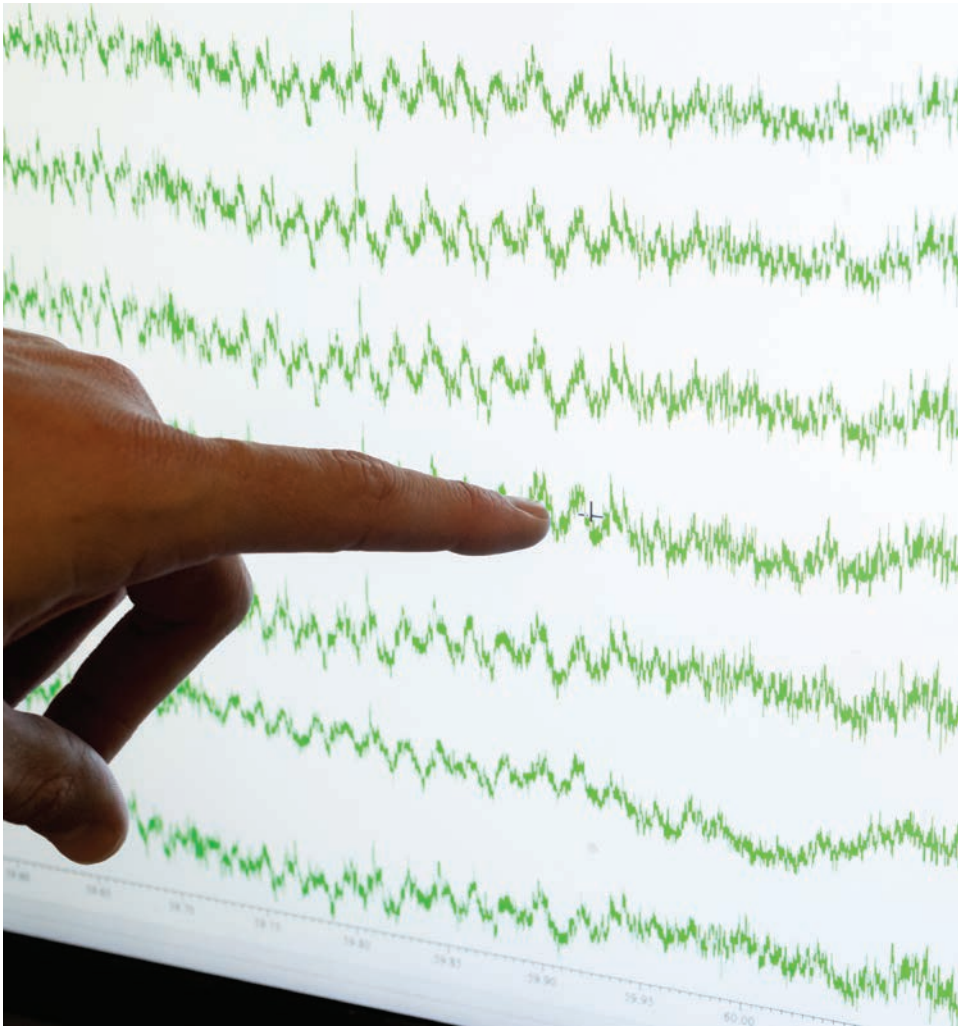
Research Support

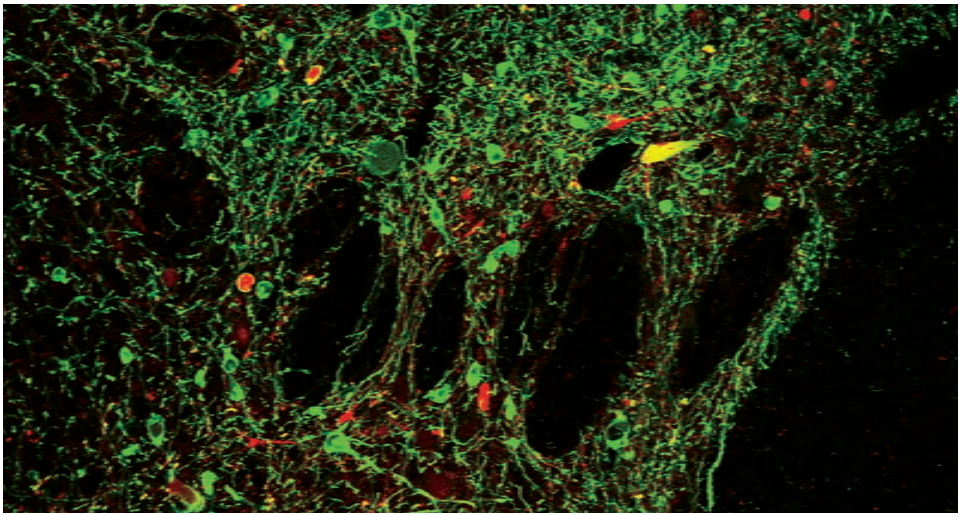
Completed

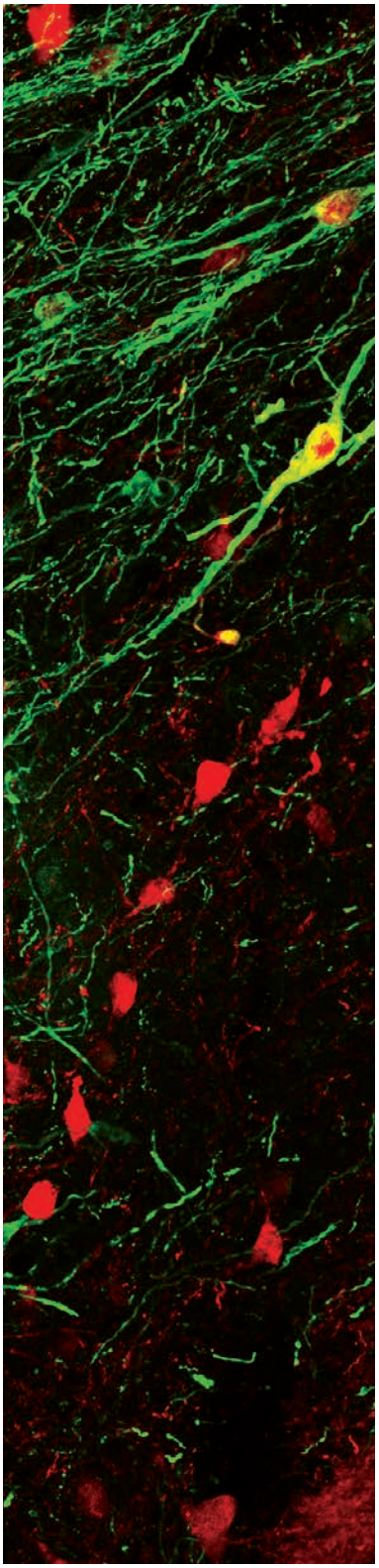
5T32 MH 65214 Cohen (PI) 04/1/12 – 9/30/13
Postdoctoral training grant

Pending

Sloan Research Fellowship
Dean's Innovation Fund







Upper left: Recordings from the hippocampus to student brain oscillations in aging. Lower left: Tissue section from an old monkey showing the medial ventral tegmental area (VTA). Green label is for cells containing dopamine; red label is for cells containing the calcium binding protein calbindin; yellow indicates that the cell contains both. Right: Tissue section from an old monkey, showing the lateral VTA (colors are same as from lower left example).

Trainees

Postdoctoral

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

Sevag Kaladchibachi, Ph.D. (Fernandez)
Area of Interest: Age-related changes in circadian responses to light and their effort on memory

Koeun Lim, Ph.D. (Chou)
Area of Interest: Development of image-guided rTMS protocols

Rachel Samson, Ph.D. (Barnes)
Area of Interest: Age-related changes in the amygdala and emotional perception in the rat

Waitsang Keung, Ph.D. (Wilson)
Area of Interest: Age-related changes in exploration and exploitation

Darya Zabelina, Ph.D. (Andrews-Hanna)
Area of Interest: Cognitive neuroscience of attention and creativity

Predoctoral

Elize Bason (Brinton)
Area of Interest: Epigenetic regulation of endocrine aging: Transitions of the perimenopausal and menopausal brain

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

Sarah Cook (Wilson)
Area of Interest: The effect of top-down processing on perceptual decision making

Lindsey Crown (Cowen)
Area of Interest: Investigating how ketamine alters dopamine levels in the brain

Hannah Doolish (Fernandez)
Area of Interest: Effects of frequent long-haul travel on circadian system aging and health

Maunil (Neal) Desai (Brinton)
Area of Interest: Cognitive benefits of allopregnanolone in ApoE 4 to limit progression of Alzheimer's disease

Daniel Gray (Barnes)
Area of Interest: Circuits involved in working memory and their decline with age in a nonhuman primate model of aging

Mary Katherine Franchetti (Alexander)
Area of Interest: Effects of physical activity and sleep on cognitive and brain aging

Dan Hill (Cowen)
Area of Interest: How the frontal cortex alters dopamine release in aging

Trainees

continued

Mingzhu Hou (Glisky)
Area of Interest: Source memory and aging

Kous Kondapalli (Barnes)
Area of Interest: Age-related changes and cognitive performance levels in working memory across the entire life span of rats (Master's degree received 2017)

Bryan Kromenacker (Wilson)
Area of Interest: The interaction between mental effort and mental representations

Colin Kyle (Barnes)
Area of Interest: Brain aging and hippocampal ensembles recorded in the unrestrained young and old nonhuman primate (Master's received degree 2017)

Ashley Lawrence (Ryan)
Area of Interest: Cardiovascular risk factors and glucose metabolism and the impact on aging

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

Stephanie Matijevic (Ryan)
Area of Interest: Brain imaging and cognitive changes in normal older adults

Andrew McKinnon (Ryan)
Area of Interest: Brain imaging, cognitive aging, and lifestyle factors

Molly Memel (Ryan)
Area of Interest: The underlying mechanisms of memory impairment in older adults

Aarti Mishra (Brinton)
Area of Interest: Mechanistic role of ApoE4 and inflammation in the development of at-risk aging phenotype in females and its implication on Alzheimer's disease

Jack-Morgan Mizell (Wilson)
Area of Interest: Age-related changes in exploration and exploitation

Suzanne Moseley (Glisky)
Area of Interest: Hearing loss, cognition, and aging (Doctoral degree 2017)

Laura Nguyen (Alexander)
Area of Interest: Relation of vascular factors to cognition and brain white matter in healthy aging

Minhkhoi Nguyen (Barnes)
Area of Interest: Whole brain clearing and using branched DNA labelli technique to map IEG expression in the cleared rat brain (Master's degree 2017)

Stacey Pest (Nadel/Glisky)
Area of Interest: Reconsolidation in normal aging (Doctoral degree 2017)

Angelina Polsinelli (Glisky)
Area of Interest: Meditation, cognition, and emotion in normal aging (Doctoral degree 2017)

Trainees

continued

Quentin Raffaelli (Andrews-Hanna)
Area of Interest: Cognitive neuroscience of spontaneous cognition

Ruth Robbins (Glisky)
Area of Interest: Social networking and cognition in socially isolated older adults

Hashem Sadegiyeh (Wilson)
Area of Interest: Cognitive correlates of exploration and exploitation

Christine Solinsky (Brinton)
Area of Interest: Development of iPSC-based biomarker strategy to identify neuroregenerative responders to allopregnanolone

Ariana Stickel (Ryan)
Area of Interest: Brain imaging, genetics, and cognitive changes in normal older adults

Mark Sundman (Chou)
Area of Interest: Cortical excitability and plasticity of individuals with MCI

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

Siyu Wang (Wilson)
Area of Interest: The neural correlates of exploration and exploitation

Yvette (Yiwei) Wang (Brinton)
Area of Interest: Estrogen regulation of mitochondrial genome and implication of mitochondrial genetic variances in therapeutics for Alzheimer's disease

Jean Paul Wiegand(Cowen)
Area of Interest: Oscillatory activity related to memory formation in aging

Cindy Woolverton (Glisky)
Area of Interest: Effects of intergenerational interactions in young and older adults

Tony Ye (Cowen)
Area of Interest: Effect of Parkinson's disease and ketamine on oscillatory activity in the aging brain

Clinical / translational programs

Drs. Meredith Hay and Lee Ryan (both EMBI affiliate faculty) are conducting a study to evaluate the safety and efficacy of angiotensin 1-7 to enhance cognitive function in participants undergoing coronary artery bypass graft surgery. Many older individuals undergo this surgical procedure and report negative effects on their cognition as a result. The hypothesis is that this drug will result in a decrease in brain inflammation and microglia activation in these individuals, which was predicted on the basis of preclinical animal experiments conducted at the UA. If the hypothesis is supported in this trial, the researchers will apply to conduct further tests.

Dr. Roberta Brinton (EMBI affiliate faculty) is conducting a study to evaluate allopregnanolone as a therapeutic agent to treat age-associated memory deficits. She is conducting a translational therapeutic development project, required for an Investigational New Drug application to the FDA, to determine the efficacy of allopregnanolone as a neurogenic regenerative and disease modifying agent, first for Alzheimer's disease, and then potentially for normal aging brain health.

Dr. Gene Alexander (EMBI affiliate faculty), together with Cohen (McKnight, UF), Marsiske (McKnight, UF), and Woods (McKnight, UF), are participating in a multi-site evaluation of cognitive training along with transcranial direct current stimulation for its impact on cognitive aging. Dr. Alexander also is engaged in a project, along with Raichlen (UA), on the effects of an aerobic training system for enhancing cognitive performance in healthy older adults.

Dr. Geoff Ahern (EMBI affiliate faculty) is engaged in the following clinical trials:

2015 – 2019	Randomized, Double-Blind, Placebo Controlled, Multi-Center Registration Trial To Evaluate The Efficacy And Safety Of Ttp488 In Patients With Mild Alzheimer's Disease Receiving Acetylcholinesterase Inh. Sponsored by V5V Therapeutics, LLC.
2015 – 2019	Effect of Passive Immunization on the Progression of Mild Alzheimer's Disease: Solanezumab (LY2062430) Versus Placebo to Add Extension Study Entitled Effect of Passive Immunization on Progression of. Sponsored by Quintiles, Incorporated.
2017	A 24-Month, Phase 3, Multicenter, Placebo-Controlled Study of Efficacy and Safety of Solanezumab versus Placebo in Prodromal Alzheimer's Disease. Sponsored by Eli Lilly and Company.
2017 – 2021	Open Label Extension Study for Continued Safety and Efficacy Evaluation of Azeliragon in Patients With Mild Alzheimer's Disease. Sponsored by V5V Therapeutics, LLC.

Extramural Funding

July 1, 2016 to June 30, 2017

Subcontract PI's:	**Ahern, Geoffrey L.; Rapcsak, Steven Z.** (PI: **Reiman**)
Project:	Arizona Alzheimer's Disease Core Center Clinical Core (P30 AG019610)
Sponsor:	National Institute on Aging
Project Dates:	July 2016 – June 2021
Subaward Amount:	$132,268 (current year)

Subcontact PI:	**Alexander, Gene E.** (PI's: **Reiman,** Caselli)
Project:	Brain Imaging, APOE & the Preclinical Course of Alzheimer's Disease (RO1 AG031581)
Sponsor:	National Institute on Aging
Project Dates:	May 2014 – March 2019
Subaward Amount:	$14,761 (current year)

PI:	**Alexander, Gene E.** (Multi-PI: Cohen, Woods, Marsaki, Alexander)
Project:	Augmenting Cognitive Training in Older Adults – The ACT Grant (RO1 AG054077)
Sponsor:	National Institute on Aging
Project Dates:	July 2016 – June 2021
Subaward Amount:	$292,517 (current year)

Subcontract PI:	**Alexander, Gene E.** (PI: **Reiman**)
Project:	Arizona Alzheimer's Disease Core Center Educational Core (P30 AG019610)
Sponsor:	National Institute on Aging
Project Dates:	July 2017 – June 2021
Subaward Amount:	$18,950 (current year)

Extramural Funding

July 1, 2016 to June 30, 2017

Continued

Co-Investigator	**Alexander, Gene E.** (PI: Su)
Project:	Ultra-sensitive and Label-free Detection of Alzheimer's Disease Biomarkers (R03 AG055020)
Sponsor:	National Institute on Aging
Project Dates:	August 2017 – July 2019
Award Amount:	$85,653 (current year)

Univ Arizona PI:	**Alexander, Gene E.** (Multi-PI: Cohen, Rundek, Visscher)
Project:	Neuroimaging Core and Brain Imaging Registry
Sponsor:	McKnight Brain Research Foundation
Project Dates:	January 2015 – December 2018
Subaward Amount:	$228,730 (project period)

Univ Arizona PI:	**Alexander, Gene E.** (Multi-PI: Cohen, Levin, Wadeley, Alexander); UA co-I's: **Glisky, Ryan**
Project:	Cognitive Aging Assessment Core
Sponsor:	McKnight Brain Research Foundation
Project Dates:	September 2015 – December 2018
Subaward Amount:	$200,000 (project period)

Co-Investigator:	**Andrews-Hanna, Jessica** (PI: Edgin)
Project:	Brain Development, Sleep, and Learning in Down Syndrome
Sponsor:	LuMind Foundation
Project Dates:	July 2017 – June 2018
Award Amount:	$193,500 (current year)

Univ. Arizona PI:	**Andrews-Hanna, Jessica**
Project:	Enhancing Function in Later Life: Exercise and Function Network Connectivity
Sponsor:	National Institutes of Health
Project Dates:	July 2017 – February 2019
Subaward Amount:	$12,533 (current year)

PI:	**Barnes, Carol A.**
Project:	Neurobehavioral Relations in Senescent Hippocampus (R01 AG003376)
Sponsor:	National Institute on Aging
Project Dates:	January 2016 – November 2020
Award Amount:	$661,687 (current year)

PI:	**Barnes, Carol A.**
Project:	Cell Assemblies, Brain Adaptation and Cognitive Aging (R01 AG050548)
Sponsor:	National Institute on Aging
Project Dates:	September 2015 – May 2020
Award Amount:	$492,593 (current year)

Extramural Funding

July 1, 2016 to June 30, 2017

Continued

PI:	**Barnes, Carol A.** (co-I's: **Alexander**, Billheimer, **Huentelman, Trouard**)
Project:	Neural System Dynamics & Gene Expression Supporting Successful Cognitive Aging (RO1 AG049465)
Sponsor:	National Institute on Aging
Project Dates:	August 2014 – March 2019
Award Amount:	$660,748 (current year)

PI's:	**Barnes, Carol A.**, and **Huentelman, Matt J.** (co-I: Okuno)
Project:	CATT: Development and Application of a Neuronal Cell Activity-Tagging Toolbox (RO1 AG049464)
Sponsor:	National Institute on Aging
Project Dates:	September 2014 – May 2018
Award Amount:	$300,969 (current year)

Subcontract PI:	**Barnes, Carol A.** (PI: **Reiman**)
Project:	Arizona Alzheimer's Disease Core Center Ad Hoc Review (P30 AG019610)
Sponsor:	National Institute on Aging
Project Dates:	July 2016 – June 2021
Subaward Amount:	$24,476 (current year)

PI:	**Barnes, Carol A.** (co-I's: **Bimonte-Nelson, Coleman, Huentelman, Reiman**)
Project:	Postdoctoral Training, Neurobiology of Aging and Alzheimers Disease (T32 AG044402)
Sponsor:	National Institute on Aging
Project Dates:	May 2016 – April 2021
Award Amount:	$251,424 (current year)

PI:	**Barnes, Carol A.** (Mentor on Pre-Doctoral Training Grant for Daniel Gray)
Project:	Neurobiological Basis of Age-related Deficits in Attentional Shirting and Monitoring (F31 AG055263)
Sponsor:	National Institute on Aging
Project Dates:	January 2017 – December 2019
Award Amount:	$35,014 (current year)

PI:	**Brinton, Roberta**
Project:	Aging and Estrogenic Control of the Bioenergetic System in Brain (R01 AG053589)
Sponsor:	National Institute on Aging
Project Dates:	March 2017 – February 2022
Award Amount:	$309,686 (current year)

Extramural Funding

July 1, 2016 to June 30, 2017

Continued

PI:	**Brinton, Roberta**
Project:	Perimenopause in Brain Aging and Alzheimer's Disease (R01 AG026572)
Sponsor:	National Institute on Aging
Project Dates:	September 2016 – May 2021
Award Amount:	$2,403,900 (current year)

PI:	**Brinton, Roberta**
Project:	Manufacturing of Allopregnanolone for Phase 2 Clinical Trial
Sponsor:	Alzheimer's Drug Discovery Foundation
Project Dates:	June 2017 – May 2020
Award Amount:	$450,000 (project period)

PI:	**Brinton, Roberta**
Project:	Perimenopause in APoE4 Brain: Accelerated Myelin Catabolism for Fuel
Sponsor:	Alzheimer's Association
Project Dates:	May 2017 – April 2020
Award Amount:	$249,280 (current year)

PI:	**Brinton, Roberta**
Project:	Bioinformctic Analyses to Find Current Drug Therapies that Can Prevent or Delay Alzheimer's Disease
Sponsor:	The Women's Alzheimer's Movement
Project Dates:	November 2016 – November 2017
Award Amount:	$60,000 (project period)

PI's:	**Coleman, Paul D., Barnes, Carol A.,** and **Alexander G.E.** (co-I's: Billheimer, **Huentelman, Trouard**)
Project:	Epigenetic, Neuroimaging & Behavioral Effects of Hypertension in the Aging Brain (RO1 AG049464)
Sponsor:	National Institute on Aging
Project Dates:	August 2014 – March 2019
Award Amount:	$458,236 (current year)

Subcontract PI:	**Cowen, Stephen, L.**
Project:	Restoring Functional Connectivity Following TBI
Sponsor:	National Institute of Neurological Disorders and Stroke
Project Dates:	February 2014 – January 2019
Award Amount:	$20,413 (current year)

Extramural Funding

July 1, 2016 to June 30, 2017

Continued

Co-I:	**Cowen, Stephen, L.** (PI: Witte)
Project:	High Resolution Electrical Brain Mapping by Real-Time and Portable 4D Acoustoelectric Imaging
Sponsor:	National Institute of Mental Health
Project Dates:	September 2015 – June 2018
Award Amount:	$31,175 (current year)

PI:	**Cowen, Stephen, L.**
Project:	Identification of Network, Oscillatory and Behavioral Signatures of LRRK2 Expression
Sponsor:	Michael J. Fox Foundation for Parkinson's Research
Project Dates:	May 2017 – May 2019
Award Amount:	$199,386 (project period)

Co-I:	**Cowen, Stephen, L.** (PI: Edgin)
Project:	Brain Development, Sleep and Learning in Down Syndrome
Sponsor:	LuMind Foundation
Project Dates:	July 2017 – June 2018
Award Amount:	$10,750 (project period)

PI:	**Cowen, Stephen, L.**
Project:	High Density, Miniaturized, Zero Switching, Stimulation and Recording Headstage for Small Animals
Sponsor:	Advanced Medical Electronics Corp.
Project Dates:	August 2017 – January 2019
Award Amount:	$28,750 (project period)

PI:	**Fernandez, Fabian**
Project:	2016 Bisgove Scholar Program
Sponsor:	Science Foundation Arizona
Project Dates:	August 2016 – July 2018
Award Amount:	$200,000 (project period)

PI:	**Rance, Naomi E.**
Project:	Role of Preoptic NK3R Neurons in the Estrogen Modulation of Body Temperature
Sponsor:	National Institute on Aging
Project Dates:	August 2014 – April 2019
Award Amount:	$302,094 (current year)

Extramural Funding

July 1, 2016 to June 30, 2017

Continued

Co-I:	**Rance, Naomi E.** (PI: Teske)
Project:	Pre-Clinical Model for Sleep Deprivation-Induced Obesity and Hedonic Intake Due to Noise Exposure
Sponsor:	National Institute of Neurological Disorders and Stroke
Project Dates:	July 2017 – June 2019
Award Amount:	$227,208 (current year)

PI:	**Ryan, Lee** (co-I's: **Alexander, Ahern, Andrews-Hanna, Barnes, Brinton, Edgin, Fernandez, Glisky, Grilli, Mehl, Rapcsak,** Saranathan, Su, **Trouard,** Yin)
Project:	Arizona Alzheimer's Consortium State-Funded Projects
Sponsor:	State of Arizona, DHS
Date:	July 2017 – June 2018
Amount:	$439,868 (current year)

Co-I:	**Ryan, Lee** (PI: Sweitzer)
Project:	Evaluation of the Safety and Efficacy of Angiotensin 1-7 to Enhance Cognitive Function in Participants Undergoing Coronary Artery Bypass Graft (CABG) Surgery
Sponsor:	National Heart, Lung, and Blood Institute
Project Dates:	March 2017 – February 2021
Award Amount:	$745,065 (current year)

Educational programs focusing on age-related memory loss

Event:	The Joan Kaye Cauthorn Annual Conference on Successful Aging: Decisions, Decisions, Decisions: Making Positive Choices As We Age
Date:	February, 2017
Organizers:	Lee Ryan, Ph.D., and Gene Alexander, Ph.D. (both EMBI affiliate faculty)
Venue:	University of Arizona North Ballroom, Tucson, AZ
Summary:	This one-day conference was attended by 250 members of the Tucson community and health care workers.

Other educational programs for scientists on normative aging

Event:	U13 Bedside-to-Bench Conference Series on Sensory Impairment and Cognitive Decline
Date:	October 2-3, 2017
Organizers:	Drs. Heather Whitson and Frank Lin
Venue:	Bethesda North Marriott Hotel and Conference Center, Baltimore, MD
Summary:	This was supported by NIA and by the American Geriatrics Society to heighten research attention on emerging geriatric clinical issues that have the potential to greatly improve clinical care or prevention for older adults. This workshop brought together scientist experts on auditory sensory loss in aging with those with expertise in cognition. Dr. Barnes was asked to speak on "Animal models of cognition and cognitive assessment." A white paper summarizing the talks and identifying knowledge gaps and potential research priorities in this area is being drafted.

Event:	Cognitive Aging Summit III. Cognitive Aging: Resilience and Reserve
Date:	April 6-7, 2017
Venue:	Bethesda North Marriott Hotel and Conference Center, Baltimore, MD
Summary:	This event was sponsored by the Foundation for the National Institutes of Health, the McKnight Brain Research Foundation, and the National Institute on Aging. The goal of this summit was to gather expertise on topics relevant to cognitive aging so that a white paper could be drafted with recommendations on knowledge gaps and research efforts that might be supported to fill those gaps. Dr. Barnes was asked to speak on "Animal models of brain adaptation and compensation in aging" in the session on "How Do We Operationalize Brain Reserve, Cognitive Reserve, Cognitive Resilience and Compensation?"

Collaborative programs

with McKnight institutions and research programs and non-McKnight institutions and research programs

The director, associate director, and affiliate faculty of the Evelyn F. McKnight Brain Institute at the University of Arizona have many collaborative interactions among themselves and other Institute faculty in Tucson and with other McKnight Brain Institutes. In addition, we have extensive collaborations with faculty inside the University of Arizona, across the state, across the country, and around the world. Discussion **of publications this year that have relevance to the aging brain and memory** and document these interactions include the following, which have already been highlighted on **page 8**:

Gray, D.T., Smith, A.C., Burke, S.N., Gazzaley, A. and Barnes, C.A. (2017) Attentional updating and monitoring and affective shifting are impacted independently by aging in the macaque monkeys. Behavioral Brain Research, 322:329-338.

Hay, M., Vanderah, T.W., Samareh-Jahani, F., Constantopoulos, E., Uprety, A.R., Barnes, C.A., and Konhilas, J. (2017) Cognitive impairment in heart failure: A protective role for Angiotensin-(1-7). Behavioral Neuroscience, 131:99-114.

Lester, A.W., Moffat, S.D., Wiener, J.M., Barnes, C.A. and Wolbers, T. (2017) The aging navigational system. Neuron, 9:1019-1035.

Han, P., Nielsen, M., Song, M., Yin, J., Permenter, M.R., Vogt, J.A., Engle, J.R., Dugger, B.N., Beach, T.G., Barnes, C.A., and Shi, J. (2017) The impact of aging on brain pituitary adenylate cyclase activing polypeptide pathology and cognition in mice and rhesus macaque. Frontiers in Aging Neuroscience, 9:180.

Maurer, A.P., Burke, S.N., Diba, K. and Barnes, C.A. (2017) Attenuated activity across multiple cell types and reduced monosynaptic connectivity in the aged perirhinal cortex. Journal of Neuroscience, 37(37):8965-8974.

Ianov, L., De Both, M., Chawla, M.K., Rani, A., Kennedy, A.J., Piras, I., Day, J.J., Siniard, A., Kumar, A., Sweatt, J.D., Barnes, C.A., Huentelman, M. and Foster, T.C. (2017) Hippocampal transcriptomic profiles: Subregional vulnerability to age and cognitive impairment. Frontiers in Aging Neuroscience, 9:383, doi.org/10.3389/fnagi.2017.00383

Samson, R.D., Lester, A.W., Duarte, L, Venkatesh, A. and Barnes, C.A. (2017) Emergence of beta band oscillations in the aged rat amygdala during discrimination learning and decision making tasks. ENeuro, 0245-17.

Memel, M., and Ryan, L. (2017) Visual integration enhances associative memory equally for young and older adults without reducing hippocampal encoding activation. Neuropsychologia, 100:195-206.

Kern, C., Wright, C.B., Bergfield, K.L., Fitzhugh, M., Chen, K., Moeller, J.R., Nabizadeh, N., Elkind, M.S., Sacco, R.L., Stern, Y., DeCarli, C.S., and Alexander, G.E. (2017) Blood pressure control in aging predicts cerebral atrophy related to small-vessel white matter lesions. Frontiers in Aging Neuroscience, 9:132.

Collaborative programs

with McKnight institutions and research programs and non-McKnight institutions and research programs

Continued

Raichlen, D.A., and Alexander, G.E. (2017) Adaptive Capacity: An evolutionary-neuroscience model linking exercise, cognition, and brain health. Trends in Neurosciences, 40:408-421.

Hernandez, G., Zhao, L., Franke, A.A., Chen, Y.L., Mack, W.J., Brinton, R.D., and Schneider, L.S.. (2017) Pharmacokinetics and safety profile of single-dose administration of an estrogen receptor β selective phytoestrogenic (phytoSERM) formulation in perimenopausal and postmenopausal women. Menopause. doi: 10.1097/GME.0000000000000984. [Epub ahead of print].

Yin, F., Yao, J., Brinton, R.D., and Cadenas, E. (2017) Editorial: The Metabolic-Inflammatory Axis in Brain Aging and Neurodegeneration. Frontiers in Aging Neuroscience, 9:209.

Madden, D. J., Parks, E. L., Hoagey, D. A., Cocjin, S. B., Johnson, M. A., Chou, Y.-H., Potter, G. G., Chen, N.-K., Cabeza, R., and Diaz, M. T. (2017) Sources of disconnection in neurocognitive aging: Cerebral white matter integrity, resting-state functional connectivity, and white matter hyperintensity volume. Neurobiology of Aging, 54:199-213.

Madden, D. J., Parks, E. L., Tallman, C., Boylan, M., Hoagey, D. A., Cocjin, S. B., Johnson, M. A., Chou, Y.-H., Potter, G. G., Chen, N.-K., Packard, L., Siciliano, R. Monge, Z., and Diaz, M. T. (2017) Frontoparietal activation during visual conjunction search: Effects of bottom-up guidance and adult age. Human Brain Mapping, 38(4):2128-2149.

Pacheco, S., Wang, C., Chawla, M.K., Nguyen, M., Baggett, B.K., Utzinger, U., Barnes, C.A. and Liang, R. (2017) High resolution, high speed, long working distance, large field of view confocal fluorescence microscope. Scientific Reports, 7:13349.

Plans for future research

The director of the Evelyn F. McKnight Brain Institute at the University of Arizona is in a strong position in the coming year to conduct significant research on memory in the aging brain. In addition to support from the McKnight Brain Research Foundation, her work is supported through five RO1 grants and one postdoctoral training grant. And while we were not chosen to be one of the four finalists for the $100 million MacArthur 100 & Change grant (the final winner is not yet known, but the MacArthur Foundation has supported each of these to develop their plans for the final competition, which took place at the end of 2017.), we have made progress on our ideas for a "Precision Aging" approach to the problem of cognitive decline during aging.

Dr. Barnes initially met with Dr. Masliah, the head of the Neuroscience of Aging Program at the National Institute on Aging, in a visit set up in August by Dr. Kimberly Andrews Espy, senior vice president for research at the UA. In this meeting, Drs. Barnes and Espy indicated that EMBI affiliate faculty were working on creating a white paper that would more fully outline our ideas for the creation of a National Precision Aging® Center at the UA. Dr. Masliah was definitely interested and indicated that we should also contact Molly Wagster to get her input on this project. During a retreat in October, Drs. Barnes, Ryan, Hay, and Brinton completed the white paper and sent it to Drs. Masliah and Wagster.

We then met with Drs. Masliah and Wagster at the Society for Neuroscience meeting in Washington, DC, in November. The white paper outlines our vision for the development of a U19 grant, and they gave us advice on the kind of preliminary data that would be required to make the proposal strongest. Dr. Wagster suggested that we contact leaders of several longitudinal cognitive aging studies to determine whether these individuals were interested in data sharing and collaboration with our group. Subsequently, Dr. Barnes contacted Drs. Marilyn Albert and Sue Resnick, both of whom have longitudinal study cohorts (BIOCARD and the Baltimore Longitudinal Study of Aging, respectively) that would be extremely useful for the development of our algorithms to customize therapeutic interventions. We have identified February 18 as a date when we can meet with Albert, Resnick, and Wagster in Baltimore, MD, to explore ideas for data sharing.

This coming year, 2018, promises to be very busy, as our target for submitting this $25 million grant to create a National Precision Aging® Center is mid-September. Drs. Barnes and Brinton trademarked the name "Precision Aging®" this year. The white paper follows on pages 88–90.

National *Precision Aging*® Center
NPAC

National Precision Aging® Center at the University of Arizona

I. Requested Action:

Given the national crisis of older individuals living with significant cognitive impairment, The University of Arizona requests support to establish the National Precision Aging® Center. The Center will create a Precision Aging® Cognitive Enhancement (PACE) system tailored to the individual to improve the cognitive health of older Americans.

II. Identified Need:

Cognitive health does not currently match lifespan. Sixteen million people in the USA are living with cognitive impairment (Hurd et al., 2013). Age-related cognitive impairment results in:

- three times more hospitalizations: a $110 billion economic burden to the healthcare system
- loss of independent living: costing $160 billion in informal care yearly
- loss of productivity: worldwide costs in 2018 are expected to exceed 1 trillion US dollars (Wimo et al., 2017)
- increased risk for Alzheimer's disease: more than1.6 million develop AD annually (Ward et al., 2013).

The current one-size-fits-all approach to our cognitive aging population is not adequate to close the gap between cognitive healthspan and lifespan.

III. Specific Requested Action:

Because of the national crisis of older individuals living with significant cognitive impairment, we request $25M to establish the **National Precision Aging® Center** at the University of Arizona.

The National Precision Aging® Center will leverage expertise and create novel advances in cognitive aging, big data and machine learning, and meta-omics to achieve the Center's goal: to develop and commercialize a novel diagnostic tool that will match an individual's risk profile with a customized therapeutic plan.

The **Precision Aging® Cognitive Enhancement System** will enable primary health care providers to identify and implement precision solutions for sustaining cognitive health.

We envision five phases of this project:

Phase I: Interrogate large scale longitudinal datasets from across the country to create profiles of risk. Factors considered will include:

- **demographic factors:** sex, age, race, geographic context, education
- **cognition:** memory, executive function, processing speed
- **vascular factors:** blood pressure, lipid profiles, glucose metabolism, obesity
- **medical disorders:** hypertension, cardiac disease, diabetes, stroke, hypercholesterolemia, metabolic syndrome
- **social support:** social engagement/isolation, married/cohabiting status, family support, financial health, mental health
- **lifestyle factors:** physical exercise, smoking, alcohol, diet
- **genetic profile:** known risk factors for each of the above categories

National *Precision Aging*® Center
NPAC

Phase II: Undertake a gap analysis to establish the mismatch between identified risk profiles in Phase 1 and current interventions for cognitive impairment. We will:

- identify the missing information in intervention studies that may be important for understanding non-responder outcomes, based on our risk profile analysis
- match these profiles to our identified risk profiles
- examine existing cognitive intervention studies to evaluate characteristics of responders and non-responders

Phase III: Develop and test customized therapeutic interventions that integrate pharmacological and nonpharmacological approaches for specific risk profiles. We will:

- develop and test customized therapeutic interventions in three pilot geographical test regions of the United states – including the southwest, the deep south, and the southeast
- augment the Phase I risk profile with in depth measurements of:
    - **meta-omics:** transcriptomics, proteomics, metabolomics, epigenomics, microbiomics
    - **inflammatory profiles:** cytokines, chemokines, T-cell and oxidative markers
    - **neuroimaging:** structure, function and potential biomarkers
    - **cognitive assessment:** validated neuropsychological instruments plus novel tests informed by human and animal research

Phase IV: Refine the match between therapeutic interventions tested in Phase III with individual cognitive outcomes. To do this we will:

- evaluate the more detailed information on responders and non-responders collected in Phase III
- adjust the treatments to improve the probability of a positive therapeutic outcome for the non-responders
- evaluate the refined interventions

Phase V: We will work with the private sector to commercialize the Precision Aging® Cognitive Enhancement (PACE) system to optimize cognitive aging for use by healthcare providers. We will:

- develop mobile software to be used in the clinic for customized diagnostics and treatment
- educate health care providers on use of the software
- create cloud-based therapy management and iterative treatment adjustment tools
- establish cloud based therapy management and treatment adjustment tools
- continue to generate and refine outcome-specific therapies through cloud-based data collection
- work towards Medicaid and Medicare reimbursement for the PACE system

National *Precision Aging*® Center
NPAC

IV. Institutional Uniqueness

The University of Arizona: The University of Arizona is ranked as one of the top 20 public research universities nationwide. The university encourages multidisciplinary research through its extensive system of shared research resources, many of which will be utilized for this project.

The University of Arizona was one of the founding members of the National Institutes of Health Precision Medicine Initiative (PMI) cohort program. The NIH PMI cohort will enroll 1 million or more U.S. participants to improve preventions and treatment of disease, based on individual differences in lifestyle, environment and genetics. The **National Precision Aging® Center** will leverage this cohort to deploy novel technologies to improve cognitive health in aging. Because of our geographic location, we are ideally situated to address cognitive health in people who are medically underserved and historically underrepresented in cognitive aging research.

University Partners: The University of Arizona is internationally known as a leader in the cognitive neuroscience of aging and the basic neural mechanisms of the aging brain. Within the university we have built several strong Institutes and Centers of Excellence that contribute to the cognitive aging research enterprise. These include:

- The University of Arizona Health Sciences and Banner Health
- The Precision Medicine Initiative Center
- The Center for Biomedical Informatics and Biostatistics
- The Center for Innovation in Brain Science
- The Center for Applied Genetics and Genomic Medicine
- The Evelyn F. McKnight Brain Institute
- The BIO5 Institute

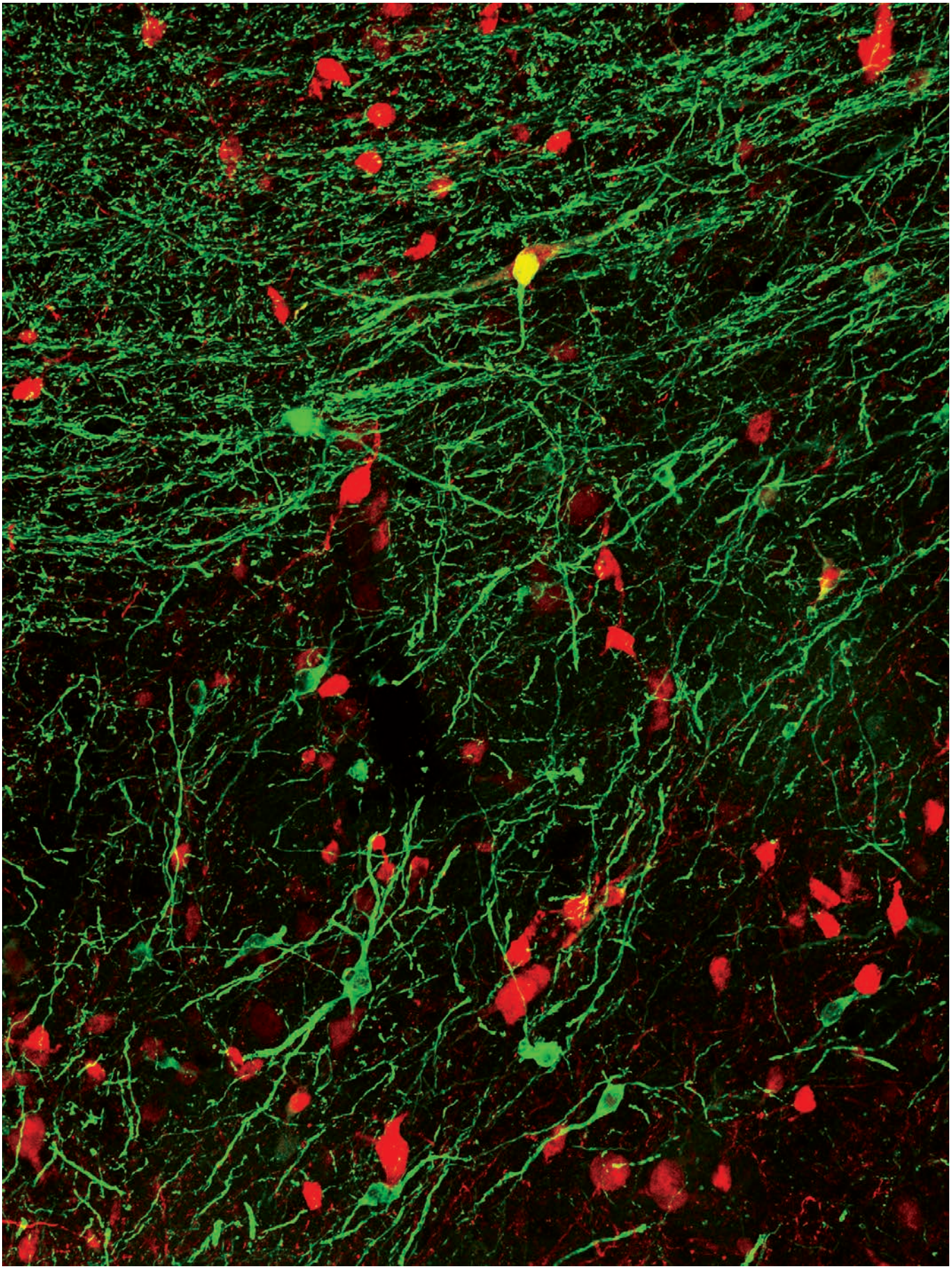
Beyond the University of Arizona: We have a wealth of resources across the State of Arizona including:

- The Arizona Alzheimer's Consortium
    - Banner Sun Health Research Institute
    - The Mayo Clinic Scottsdale
    - Barrow Neurological Institute
    - Arizona State University
    - Banner Alzheimer's Institute
- The Translational Genomics Institute

V. Summary

The establishment of the National Precision Aging® Center at the University of Arizona will create a novel system tailored to the individual to improve the cognitive health of older Americans. By working to match cognitive health with lifespan, we will decrease hospitalization time, extend independent living, improve productivity and decrease the risk for Alzheimer's disease.

The University of Arizona is uniquely positioned to lead this national effort and leverage ongoing investments in precision medicine because of our international leadership in cognitive aging and brain health.



Tissue section showing cells in the brain of an old nonhuman primate

Investment report

July 1, 2016 – June 30, 2017

Endowed Chair

Summary for 12 months ending June 30, 2017

Account Name: Evelyn F. McKnight Chair for Learning and Memory in Aging

A. Beginning Balance on July 1, 2016	$ 844,111
B. Investment Growth	$ 70,891
C. Distributions (to Endowed Chair Expendible)	$ (35,563)
D. Additional Contributions	$ –
E. Ending Balance on June 30, 2017	$ 879,439

Institute - Quasi Endowment

Summary for 12 months ending June 30, 2017

Account Name: Evelyn F. McKnight Brain Institute

A. Beginning Balance on July 1, 2016	$ 1,765,466
B. Investment Growth	$ 73,639
C. Distributions (to Institute expendable account)	$ –
D. Additional Contributions	$ –
E. Ending Balance on June 30, 2017	$ 1,839,105

Institute - Permanent Endowment

Summary for 12 months ending June 30, 2017

Account Name: Evelyn F. McKnight Brain Institute

A. Beginning Balance on July 1, 2016	$ 1,017,662
B. Investment Growth	$ 142,343
C. Distributions - UAF Development Fee	$ (60,000)
Distributions - To Expendable Account	$ (67,911)
D. Additional Contributions	$ 1,002,500
E. Ending Balance on June 30, 2017	$ 2,034,594

Additional notes

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

No

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

No

Did all activities during the report period further the Purpose?

Yes

Negative Events

N/A

Technology transfer

Nothing to report.

Additional comments

The fundraising efforts continue for the Evelyn F. McKnight Brain Institute at the University of Arizona to meet the challenge of raising private philanthropic funds to match the gift from the McKnight Brain Research Foundation to establish a permanent endowment.

Elaine Cunningham, BSN, RN, MBA, began her tenure as director of development with Research, Discovery & Innovation for Life Sciences in February 2017. Her specific focus is centered on basic science research, incorporating interdisciplinary, collaborative efforts to support the philanthropic goals of the Evelyn F. McKnight Brain Institute and the BIO5 Institute. As an accomplished fundraising professional with 20 years of experience, her successful tenures have included development positions at the University of Florida Foundation and the University of Connecticut Foundation. At both universities, her charge was to establish philanthropic programs where none had existed before – one for cancer research within the UF College of Medicine and the other within the UConn School of Nursing. Both incorporated her skill set in cultivating and soliciting major and principal gifts and developing a donor continuum focused around donor-centric interests, as well as expertise in corporate and foundation relations, project management, and operational excellence. Elaine's reputation of guiding a prospect through the donor continuum has resulted in six- and seven-figure gifts as well as other significant philanthropic commitments.

She also had a successful nursing career with areas of specialty including critical care, cardiology, bone marrow transplant, and home health care and hospice administration. Her expertise extends to marketing for high-end CCRCs and other health care organizations. Throughout her career, she has worked effectively and in partnership with physicians, faculty researchers, administration, central development, boards, colleagues, and volunteers to strategically further institutional objectives and goals.

Since arriving at UA Foundation, Elaine has accomplished the following:

- Collaborated with UAF Prospect Development team to create a viable portfolio of major and principle gift prospects. This is a work in progress, but so far we have defined 50 strong prospects. BWF RDI data analytics* were used to locate constituents with a demonstrated interest in brain topics.
- Worked with UA development colleagues, marketing and communications, RDI, and BIO5 to update the EMBI case statement and begin a website revision to be completed in the first quarter of 2018.
- Collaborated with UAF Annual Giving, which is currently creating collateral pieces for our first direct mail outreach effort, to be sent in the first quarter of 2018.
- In December 2017, solicited donors for $600K on behalf of EMBI Endowment. We expect to know results from these solicitations in the first quarter 2018.
- Traveled to eight states to meet (qualify and cultivate) with 100 prospects and donors.

*The Office of Research, Discovery & Innovation hired Bentz Whaley Flessner (BWF) to conduct a predictive modeling project of the nearly one million households in our donor database. The initial results were delivered in early summer 2017. BWF's goal is to work collaboratively with us to identify and develop prospect pools for interdisciplinary fundraising initiatives for the Office of Research, Discovery & Innovation. In doing so, they will also identify ways to grow the effectiveness and scope of prospect research services using increasingly powerful analytics tools. Their first project was to develop a prospect pool for the Evelyn F. McKnight Brain Institute.

Additional comments

In addition to the support provided through the Office of Research, Discovery & Innovation to assist with fundraising for the EMBI, Dr. Espy has been extremely proactive in approving recruitments across the University for faculty who have a focus on aging as one dimension of their research. For example, just in the Department of Psychology, we have recruited several assistant professors whose research domain involves cognitive and brain aging, including Drs. Matthew Grilli, Ying-hui Chou, and Jessica Andrews-Hanna. All of these new faculty have become affiliate faculty of the EMBI. Dr. Grilli's interest is in the clinical and cognitive neuroscience of memory and how memory changes with age. He also heads our neuropsychology efforts at the Watermark Communities facility, "Hacienda at the River" Evelyn F. McKnight Brain Institute Satellite Clinic. Dr. Chou is interested in human brain connectivity and its relation to behavior. She is conducting experiments using MRI image-guided transcranial magnetic stimulation protocols to individually optimize protocols to improve daily function in aging and in clinical populations (i.e., Parkinson's disease). Dr. Andrews-Hanna is interested in understanding internally guided cognition, with the goal of helping people live happier, healthier lives. She is currently studying how internally guided processes develop across the lifespan and change in old age.

Additionally, the Department of Psychology has successfully recruited Dr. Arne Ekstrom from the Center for Neuroscience at the University of California Davis, and he will be joining the Psychology Department next summer. His research interests are in the neurophysiological basis of human memory, and he uses intracranial EEG, fMRI, and scalp EEG methods to examine this question. He also is interested in collaborating with Dr. Barnes to develop tasks for humans and nonhuman primates with the goal of better understanding the neural basis of age-related memory changes.

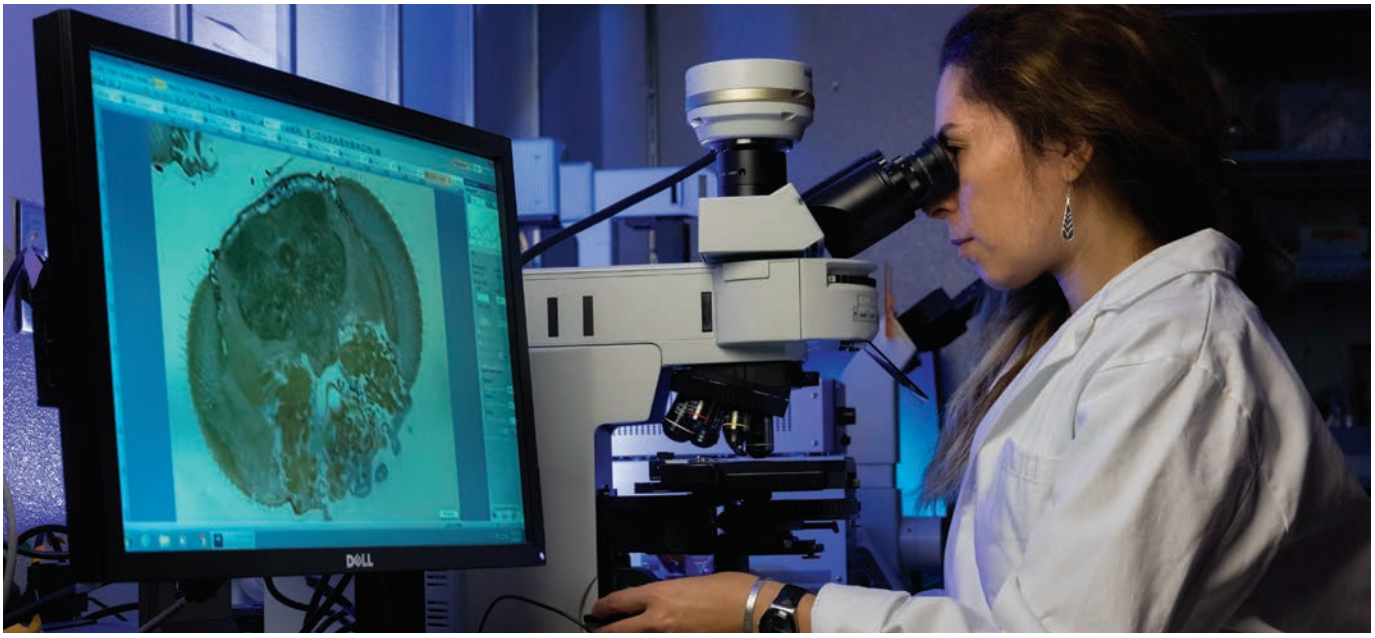
Dr. Lee Ryan, head of psychology, has also just been given permission to hire, at a senior level, a faculty member whose field of study is neuroimaging and neuropsychology of aging and dementias. Because of space constraints in the Psychology Building, this person will be given space in a building very close to Life Sciences North that houses the Evelyn F. McKnight Brain Institute (in the BIO5 building or the new building next to it, which will be completed next spring). Dr. Barnes is chair of this committee, and the job and advertisement have now been posted.

Another significant example of the University being committed to "building expertise in aging, neuroscience, and clinical trial conduct" is the establishment of the Center for Innovation in Brain Science in the College of Medicine. Dr. Roberta Brinton was recruited from USC to direct and build this center, and she is hiring people now to build basic, clinical, and translational programs in aging and neurodegenerative disease.

Finally, the Department of Molecular and Cellular Biology was given the opportunity to recruit a faculty member whose research included some aspect of understanding the aging process. Dr. Barnes was on the search committee, and the department successfully recruited Dr. George Sutphin, whose research focuses on defining the molecular pathways of aging so that therapeutic targets for clinical interventions can be developed to mitigate the deleterious effects of age. His research utilizes worms, mice, and humans, and he is likely to provide a key bridge across campus in multiple domains of aging work.

In conclusion, the University of Arizona has expended significant resources to grow the already strong community of scientists here whose research is directed at understanding the aging process at many different levels, and to mount a significant fundraising campaign for the McKnight Brain Research Foundation gift to the EMBI.

Most important scientific achievements this year



There were many significant findings published this year, each of which contributes to our understanding of the aging brain and memory loss that occurs during the aging process. I will summarize some of these from the Barnes laboratory.

- Consistent with data from older humans, older monkeys also show deficits in multi-tasking that implicate dysfunction of prefrontal cortical circuits. This is an important observation, as one limitation of a previous human study was that older adults are never matched to younger participants in computer use, and all tests have been conducted on computers. The observations in the aging animal model suggests that the age differences in behavior are due to neural changes in prefrontal cortex and not an artifact of differential computer experience in older individuals. [Gray et al., 2017]

- We showed that one month treatment with angiotensin 1-7 (a powerful anti-inflammatory agent) prevented cognitive decline in a mouse model of congestive heart failure. These preclinical data formed the basis for a successful grant for a clinical trial in bypass patients, using this drug, submitted by EMBI affiliate faculty Meredith Hay and Lee Ryan. [Hay et al., 2017]

- We were given the opportunity by a high-impact journal to synthesize the human, nonhuman primate, and rodent literature on cognitive aging of navigational systems. We discuss the current evidence on how aging affects the brain's navigational circuits and suggest promising behavioral and neural biomarkers of spatial navigation as potential therapeutic targets aimed at optimizing cognition. [Lester et al., 2017]

- We obtained data that suggest an association between levels of the mitochondrial enzyme PACAP, aging, cognitive function, and amyloid load in nonhuman primates. We noted both similarities, but also important differences, in normal aging monkeys compared to human brains with AD, which show dramatic increases in amyloid load accompanied by striking reductions in PACAP levels. [Han et al., 2017]

Most important scientific achievements this year

- We report on a prototype of a novel high-resolution, high-speed, long working distance, and large field of view confocal fluorescence microscope that may revolutionize our ability to image wide regions of whole brains that have been rendered optically transparent and macro-molecule permeable (this development is reported in Pacheco et al., 2017). We hope to use this new microscope to examine changes in circuit connectivity in normal aging brains.
- We have found one mechanism that may contribute to the hyperexcitability that we have reported in hippocampal cells in monkeys and others have reported in the hippocampus of rats and humans. Namely, we discovered reduced inhibition in the perirhinal cortex of old rats that could contribute to the circuit imbalance in aging and may be an effective therapeutic target for restoring network function. [Maurer et al., 2017]
- We were able to show that two next-generation sequencing platforms were able to validate variability in gene expression associated with hippocampal subfields, age, and cognitive status. In particular, our results confirm that cognitive decline in aging is associated with differential expression in hippocampal region CA1, particularly with respect to genes linked to calcium homeostatsis and synaptic plasticity. [Ianov et al., 2017]
- We were able to show that aging impacts network synchrony and activity of neurons in the basal lateral nucleus of the amygdala during discrimination learning and decision making. Specifically, older rats show increased power of beta frequency oscillations in the amygdala during behavior, which younger animals do not show. It is possible that these oscillations engage a network of structures that reflect a restructuring of reward circuits during aging. [Samson et al., 2017]

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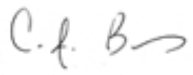

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