



**Evelyn F. McKnight
Brain Institute**

Annual Report

**McKnight Brain Research Foundation
Sponsored Institutes and Research Programs**

Scientific Report Period: January 1, 2015 – December 31, 2015

Financial Report Period: July 1, 2014 – June 30, 2015

Institution: University of Arizona

Submitted January 13, 2016

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1. Summary of scientific achievements since last report

The Evelyn F. McKnight Brain Institute at the University of Arizona (EMBI) has made significant progress towards our goal of understanding how aging impacts the circuits responsible for age-related memory decline using sensitive cognitive tests and two primary neurobiological tools that have been developed in the Director's laboratory. The first method is state-of-the-art ensemble electrophysiological recording in behaving animals that can monitor changes in brain networks and cognitive decline in aged rodents and nonhuman primates, and can be combined with live imaging methodologies. The second is a molecular imaging technology (the catFISH method) that allows the examination of individual cells that participate in circuits critical for memory. Application of catFISH in conjunction with methods that can quantify transcriptional and epigenetic activity provides a powerful window into how memory circuits are modified by behavior and altered during aging.

A number of exciting papers using these methods were published during 2015. Several of these were peer-reviewed overviews of topics critical to the aging brain and memory, including the following:

Sara Burke (now a faculty member and at the University of Florida and a part of the McKnight Institute there) showed last year that aging results in a reduction of the number of neurons in the perirhinal cortex (PRC) circuit that are activated in response to 3-dimensional objects (Burke et al., 2014). We hypothesize that this weaker neural representation of objects contributes to the impairments we observe in recognition memory with age in both rat and nonhuman primate models of normal aging. In the Burke and Barnes (2015) manuscript we examine in more detail how objects are represented across brain circuits in the temporal lobe, including the hippocampus, lateral entorhinal cortex and perirhinal cortex, and in the cingulate cortex. We propose that object information is integrated with spatial input to comprise associative and episodic memories, and that a deeper understanding of age-related decline in function within and between these structures is necessary to fully understand the basis of age-related cognitive decline.

In Schimanski and Barnes (2015), we review approaches that have been taken in behavioral and systems neuroscience today that have contributed to our fundamental understanding of how the brain stores information and the ways in which circuits change as a function of age and result in memory defects. The argument made in this manuscript is that this 'brain-behavior' approach (using the aging rodent model) has allowed great insights to be made into the critical processes underlying learning and memory at all ages. In the Gray and Barnes (2015) manuscript we suggest a reformulation of how normal aging could be understood from an 'adaptive perspective'. Because some normative age-related changes may reflect dynamic adjustments that optimize circuit function, we argue that it is imperative to distinguish between those changes in the aged brain that are "adaptive" from those that are "dysfunctional". This will enable therapeutic approaches to target only the latter and not the former alterations which may be beneficial.

We also published a number of manuscripts that describe original data, as follows:

In the Samson et al. (2015) manuscript we report behavioral data on strategy selection and risk-based decision making in the aged rat that are very reminiscent of studies reported in older

humans. Namely, it appears that aged rats are more ‘risk averse’, which suggests age-related differences in emotional regulation. We are analyzing further the neural data from the amygdala-dependent behaviors that we have used during high density recordings in that structure. In fact, the Society for Neuroscience poster that won the second prize in the 2015 McKnight Brain Research Foundation’s poster competition this year was by Dr. Samson, who showed that older rat amygdala neurons show enhanced responses (compared to younger rats) when they are given large, unexpected rewards. We believe that this may be a biological basis of the “positivity effect” observed in older adults.

In a collaboration between the Miami and Tucson Institutes, we published a paper showing how cardiac arrest impacts cognition and plasticity in middle-aged rats. The Tucson component was to give the Miami group assistance with implementing the Barnes maze in their laboratory. Finally, in the Insel and Barnes (2015) manuscript we further dissected the critical cellular components that comprise the medial prefrontal cortical circuits important for guiding behavior according to an animal’s expectations. We found that the activity of the regular-firing projection neurons contain information about behavioral context, and that their firing fields tend to cluster around reward sites. The activity of the fast-spiking neurons, on the other hand, is most associated with movement and accompanying sensory stimulation. The data suggest that these networks track an animal’s behavior to emphasize high valued positions, which provides a neural framework for generating expectations from behavioral state.

Finally, in the Thome et al. (2015) manuscript we combined large-scale electrophysiological recordings with cell-type specific imaging in the medial temporal lobe of cognitively-assessed, aged nonhuman primates. We found that neuron excitability in the hippocampal region CA3 is negatively correlated with the density of somatostatin-expressing inhibitory interneurons. By contrast, no hyperexcitability or interneuron loss was observed in the perirhinal cortex of these aged, memory-impaired monkeys. These data provide a link, for the first time, between selective increases in principal cell excitability and declines in a molecularly defined population of interneurons that regulate network inhibition in a primate. These data suggest that rebalancing local network excitability in regions vulnerable to the aging process may be a productive avenue in the treatment of age-related cognitive decline.

2. Publications in peer reviewed journals

From Barnes

- Burke, S.N. and Barnes, C.A. (2015) The neural representation of 3-dimensional objects in rodent memory circuits. *Behavioral Brain Research*, 285:60-66.
- Schimanski, L.A. and Barnes, C.A. (2015) Insights into age-related cognitive decline: Coupling neurophysiological and behavioral approaches. In: H.A. Bimonte-Nelson (Ed) *The Maze Book: Your Guidebook to Theories, Practice, and Protocols for Testing Rodent Cognition*. Springer: New York, pp. 121-142.
- Samson, R.D., Venkatesh, A., Lester, A.W., Weinstein, A.T., Lipa, P., and Barnes, C.A. (2015) Age differences in strategy selection and risk preference during risk-based decision making. *Behavioral Neuroscience*, 129:138-148.
- Cohan, C.H., Neumann, J.T., Dave, K.R., Alekseyenko, A., Binkert, M., Stransky, K., Lin, H.W., Barnes, C.A., Wright, C.B., Perez-Pinzon, M.A. (2015) Effect of cardiac arrest on

cognitive impairment and hippocampal plasticity in middle-aged rats. *PLoS One*, 10:e0124918.

Insel, N. and Barnes, C.A. (2015) Differential activation of fast-spiking and regular-firing neuron populations during movement and reward in the dorsal medial frontal cortex. *Cerebral Cortex*, 25:2631-2647.

Gray, D.T. and Barnes, C.A. (2015) Distinguishing adaptive plasticity from vulnerability in the aging hippocampus. *Neuroscience*, 309:17-28.

Thome, A., Gray, D.T., Erickson, C.A., Lipa P. and Barnes, C.A. (2015) Memory impairment in aged primates is associated with region-specific network dysfunction. *Molecular Psychiatry*, in press. doi:10.1038/mp.2015.160.

Penner, M.R., Parrish, R.R., Hoang, L.T., Roth, T.L., Lubin, F.D and Barnes, C.A. (2016) Age-related changes in zif268 transcription and DNA methylation within the hippocampus. *Hippocampus*, accepted with minor revisions.

From Selected Affiliates

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., Intorcchia, 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.

Cholanian, M., Krajewski-Hall, S.J, Levine, R.B., McMullen, N.T. and Rance, N.E. (2015) 17 β -Chronie oestradiol reduces the dendritic spine density of KNDy neurons in the arcuate nucleus of ovariectomized Tac2-EGFP transgenic mice. *Journal of Neuroendocrinology*, 27:253-263.

Jones, B., Pest, S. M., Vargas, I.M., Glisky, E. L. and Fellous, J-M. (2015) Contextual reminders fail to trigger memory reconsolidation in aged humans and rats. *Neurobiology of Learning and Memory*, 7-14.

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. *Behavioral and Brain Sciences*, 38:e1.

Mittelman-Smith, M.A., Krajewski-Hall, S.J., 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.

Nguyen, L.A., Haws, K.A., Fitzhugh, M.C., Torre, G.A., Hishaw, G.A. and Alexander, G.E. (2015) Interactive effects of subjective memory complaints and hypertension on learning and memory performance in the elderly. *Aging, Neuropsychology, and Cognition*. July 17, 1-17. [Epub ahead of print]

3. Publications (other)

From Barnes

Siniard, A.L., Corneveaux, J.J., DeBoth, M., Chawla, M.K., Barnes, C.A. and Huentelman, M.J. (2015) RNA sequencing from laser capture microdissected brain tissue to study normal

aging and Alzheimer's disease. In: Applied Neurogenomics. Springer: New York, pp 111-120.

Article featuring Dr. Carol Barnes "Most of us will age normally" by Tom Beal, Arizona Daily Star, September 26, 2015.

From Selected Affiliates

Article announcing new R24 grant to Dr. Charles Witte and Dr. Stephen Cowen "UA Researchers Develop Brain Mapping Technology", UA Now, December 2015.

Article featuring Dr. Stephen Cowen and Dr. Michael Heien "In this lab, two heads are better than one", UA Now, September 2, 2015.

4. Presentations at scientific meetings

From Barnes

Corenblum, M.J., Ray, S., Remley, Q.W., Long, M., Harder, B., Zhang, D.D., Barnes, C.A. and Madhavan, L. A novel role for nrf2 in neural stem cell function during aging. The Keap1/Nrf2 Pathway in Health Disease Conference, Biochemical Society. Cambridge, UK. January 2015. (Abstract)

Comrie, A.E., Chawla, M.K., Gray, D.T., Baggett, B.K., Utzinger, U., and Barnes, C.A. Novel methods for behavior-driven molecular and structural investigation in rodent whole brain. Twenty-sixth Annual Undergraduate Biology Research Program, January 2015. (Abstract)

Koutia, A.J., Lester, A.W., and Barnes, C.A. Studying the effects of age on visual cue-based spatial navigation using a novel behavioral apparatus. Twenty-sixth Annual Undergraduate Biology Research Program, January 2015. (Abstract)

Takamatsu, C., Gray, D.T., Uprety, A.R., Espinoza, A.I., Koutia, A.J., Zavilla, A., Comrie, A.E., and Barnes, C.A. Understanding the role of inhibitory interneurons in cognitive aging. Twenty-sixth Annual Undergraduate Biology Research Program, January 2015. (Abstract)

Barnes, C.A. Normal brain aging: Impact of circuits and memory. Cheves Smythe Distinguished Lecture Speaker, UT Health Medical School, Houston, TX, March 2015. (Invited)

Samson, R.D., and Barnes, C.A. Age differences in strategy selection and risk preference during risk-based decision making. Decision Neuroscience and Aging Conference, Miami, FL, March 2015. (Abstract)

Barnes, C.A. Impact of aging on neural circuits critical for memory, UT Austin Conference on Learning and Memory, University of Texas at Austin, Austin, Texas, April 2015. (Invited)

Barnes, C.A. Impact of aging on brain circuits and behavior. Advances in Neural Systems Conference, Center for Learning, Memory and Emotion, New York University, New York, NY, May 2015. (Invited)

Barnes, C.A. (Session Leader) Temporal lobe contributions to representations in memory Session. Spring Hippocampal Research Conference, Taormino, Sicily, June 2015.

Barnes, C.A. Extent of remapping due to context change differs along the CA1 proximo-distal axis. Functional specialization along the transverse axis of the hippocampus session. Spring Hippocampal Research Conference, Taormino, Sicily, June 2015. (Invited)

Corenblum, M.J., Ray, S., Remley, Q.W., Long, M., Harder, B., Zhang, D.D., Barnes, C.A. and Madhavan, L. A role for Nrf2 in neural stem cell function during aging. International

- Society for Stem Cell Research 2015 Annual Meeting, Stockholm, Sweden, June 2015. (Abstract)
- Chance, F.S., Maurer, A.P., Burke, S.N., and Barnes, C.A. Different weightings of input components to hippocampal CA1 place cells in young and aged rats. 24th Annual Computational Neuroscience Meeting, Prague, Czech Republic, July 2015. (Abstract)
- Barnes, C.A. Normal brain aging: Impact on circuits critical for memory. Neuroscience Graduate Program Distinguished Speaker Series, University of Southern California, Los Angeles, CA, September 2015. (Invited)
- Barnes, C.A. Memory and the aging brain. Cognitive Sciences Working Group Meeting, Takeda Pharmaceuticals, Deerfield, IL, October 2015. (Invited)
- Liang, R., Wang, C., Pacheco, S., Baggett, B.K., Chawla, M.K., Gray, D.T., Utzinger, U., and Barnes, C.A. Understanding behavioral networks: A novel, scalable microscope designed to enable whole brain imaging of behavior-driven circuits with subcellular resolution. Program No. 179.01. 2015 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, Online, October 2015. (Abstract)
- Chawla, M.K., Gray, D.T., Huentelman, M.J. and Barnes, C.A. Is Arc mRNA expression regulated by the threshold for dendritic Ca⁺⁺ plateau potentials generated from integration of entorhinal cortical inputs to granule cells? Program No. 179.02. 2015 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, Online, October 2015. (Abstract)
- Samson, R.D., Duarte, L., and Barnes, C.A. Enhanced single unit firing to unexpected large rewards in aged amygdala neurons. Program No. 179.03. 2015 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, Online, October 2015. (Abstract)
- Duarte, L., Samson, R.D., and Barnes, C.A. Enhanced beta band activity in the aged amygdala during probabilistic decision making. Program No. 179.04. 2015 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, Online, October 2015. (Abstract)
- Lester, A.W., Koutia, A.J., and Barnes, C.A. Age-related changes in external cue-based navigation in the medial entorhinal-hippocampal network. Program No. 179.05. 2015 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, Online, October 2015. (Abstract)
- Wiegand, J.-P., Gray, D.T., Schimanski, L.A., Lipa, P., Barnes, C.A., and Cowen, S.L. Time-dependent decrease in the peak frequency and power of hippocampal sharp-wave ripples and high-gamma events during post-behavior sleep in aged and young rats. Program No. 179.06. 2015 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, Online, October 2015. (Abstract)
- Gray, D.T., Ashford, S.L., Pyon, W., Burke, S.N., Smith, A.C., and Barnes, C.A. Behavioral evidence for enhanced interference during working memory and associative learning tasks in aged macaques. Program No. 179.07. 2015 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, Online, October 2015. (Abstract)
- Comrie, A., Gray, D.T., Burke, S.N., Smith, A.C., and Barnes, C.A. Species- and aged-related differences in learning and performance on working memory tasks in two species of macaque monkeys. Program No. 179.08. 2015 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, Online, October 2015. (Abstract)
- Kyle, C., Permenter, M.R., Vogt, J.A., Barnes, C.A. Behavioral impact of long-term chronic implantation of neural recording devices in the rhesus macaque. Program No. 179.09. 2015 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, Online, October 2015. (Abstract)

- Bharadwaj, P.K., Burke, S.N., Trouard, T.P., Chen, K., Moeller, J.R., Barnes, C.A., and Alexander, G.E. Age-associated regional network pattern of MRI gray matter in the bonnet macaque. Program No. 179.10. 2015 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, Online, October 2015. (Abstract)
- Madhavan, L., Corenblum, M.J., Ray, S., Long, M., Harder, B., Zhang, D. and Barnes, C.A. A role for Nrf2 in neural stem cell function during aging. Program No. 220.25. 2015 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, Online, October 2015. (Abstract)
- Barnes, C.A. Impact of aging on brain circuits critical for normal memory function. Barrow Neurological Institute Neuroscience Conference, Phoenix, AZ, November 2015. (Invited)
- Andersh, K., Gray, D.T. and Barnes, C.A. Age-related reversal learning impairments in bonnet macaques. Annual Biomedical Research Conference for Minority Students, Seattle, WA, November 2015. (Abstract)
- Nguyen, M., Chawla, M.K. and Barnes, C.A. Visualization of neurokinin B neurons in cleared whole brains. The American Society for Cell Biology Annual Meeting, San Diego, CA December 2015 (Abstract)

From Selected Affiliates

- Cowen, S.L. Effort, reward and dopamine. Neuroscience Graduate Interdisciplinary Data Blitz, University of Arizona, Tucson, AZ, January 2015 (Invited)
- Ahern, G.L. Dementia: Diagnosis and Treatment Options. 2015 Update on Psychiatry. University of Arizona Department of Psychiatry, Starr Pass, Tucson, AZ, February 2015. (Invited)
- Woolverton, C., Crawford, M., Grilli, M. and Glisky, E.L. Self-imagining improves memory in older adults. International Neuropsychological Society, Denver, CO, February 2015. (Abstract)
- Cowen, S.L. Ripples, neurons, and aging. Quantitative Biology Colloquium, University of Arizona, Tucson, AZ, February 2015 (Invited)
- Polsinelli, A., Rentscher, K.E., Mehl, M.R. and Glisky, E.L. Evidence for emotional regulation in older adults' autobiographical memories using automatic text analysis. 25th Annual Rotman Research Institute Conference, Toronto, Canada, March 2015. (Abstract)
- Singh, P., Stickel, A., Kawa, K., Buller, A. and Ryan, L. Age related decrease in white matter and gray matter volumes related to family history of Alzheimer's disease. Cognitive Neuroscience Society Annual Meeting. San Francisco, CA, March 2015. (Abstract)
- Cowen, S.L. The circuitry of choice: roles of neural activity and neuromodulation in decision making. Undergraduate Neuroscience Association, University of Arizona, Tucson, AZ, March 2015 (Invited)
- Alexander, G.E. Research studies on healthy and pathological brain aging. Alzheimer's Disease Consortium Annual Retreat, Winslow, AZ, March 2015.
- Alexander, G.E. Influence of health factors on cognitive and brain aging. McKnight Inter-Institutional Meeting, Miami, FL, April 2015. (Invited)
- Cowen, S.L. The influence on aging on the variability of neuronal activity. McKnight Inter-Institutional Meeting, Miami, FL, May 2015. (Invited)
- Cowen, S.L. The influence of aging on the variability of neuronal activity. UC Davis Colloquium, Davis, CA, May 2015. (Invited)

- Alexander, G.E. Individual differences in aerobic fitness influence the regional pattern of brain volume in healthy aging. Arizona Alzheimer's Consortium Annual Meeting, Glendale, AZ, May 2015. (Abstract)
- Ryan, L. Age differences in the interaction between perirhinal cortex and hippocampus during complex object discrimination. Spring Hippocampal Research Conference. Taormina, Sicily. June 9, 2015. (Invited)
- Cowen, S.L. Ketamine and neural oscillations. Residents Journal Club, University of Arizona Medical School, September 2015.
- Wiegand, J.-P., Gray, D.T., Schimanski, L.A., Lipa, P., Barnes, C.A., and Cowen, S.L. Time-dependent decrease in the peak frequency and power of hippocampal sharp-wave ripples and high-gamma events during post-behavior sleep in aged and young rats. Program No. 179.06. 2015 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, Online, October 2015. (Abstract)
- Heien, M.L., Parent, K.L., Hill, D.F., Wiegand, J.-P., Miller, M.A., Archerley, C.W. and Cowen, S.L. Simultaneous detection of dopamine release and neural activity. Program No. 266.08. 2015 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, Online, October 2015. (Abstract)
- Schmit, M.B., Kawa, K., Stickel, A. and Ryan, L. Fractional anisotropy in the left uncinate fasciculus and the inferior cingulum differentially predict memory and executive functions in older adults. Program No. 821.11. 2015 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, 2015. Online. (Abstract)
- Kawa, K., Schmit, M., Cardoza, J., Stickel, A., Glisky, E. and Ryan, L. Age-related differences in networks of brain activation across two executive functioning domains – updating and task-switching. Program No. 621.27. 2015 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, 2015. Online. (Abstract)
- Raichlen, D., Bharadwaj, P.K., Fitzhugh, M.C., Haws, K.A., Torre, G.A., Trouard, T.P., Alexander, G.E. Differences in resting state functional connectivity between aerobic athletes and sedentary young adults. Program No. 129.01. 2015 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, 2015. Online. (Abstract)
- Bharadwaj, P.K., Burke, S.N., Trouard, T.P., Chen, K., Moeller, J.R., Barnes, C.A. and Alexander, G.E. Age-associated regional network pattern of MRI gray matter in the bonnet macaque. Program No. 179.10. 2015 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, 2015. Online. (Abstract)
- Alexander, G.E., Bharadwaj, P.K., Haws, K.A., Nguyen, L.A., Fitzhugh, M.C., Trouard, T.P. and Hishaw, G.A. Impact of white matter hyperintensity volume on cortical brain morphology in healthy cognitive aging. Program No. 479.0.09. 2015 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, 2015. Online. (Abstract)
- Nguyen, L.A., Bharadwaj, P.K., Haws, K.A., Fitzhugh, M.C., Trouard, T.P., Hishaw, G.A and Alexander, G.E. Relation of white matter hyperintensity volume to cognitive performance in older adults. Program No. 621.16. 2015 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, 2015. Online. (Abstract)
- Kuo, P.H., Bharadwaj, P.K., Kraft, W.P., Fitzhugh, M.C., Alexander, G.E. and Zubal, G. Rapid, fully automated method for quantitative analysis of PET amyloid scans in Alzheimer's disease. Program No. 675.08. 2015 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, 2015. Online. (Abstract)

Blackmore, E.M., Krajewski-Hall, S.J. and Rance, N.E. Estradiol modulates temperature regulation in the female mouse. Program No. 77.04. 2015 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, 2015. Online. (Abstract)

Rance, N.E. Reproductive aging and the human hypothalamus: from LH pulses to hot flushes, Founder's Day Faculty science Forum, University of Arizona, Tucson, AZ, November 2015. (Invited)

Beach, T.G., Adler, C.H., Shill, H.A., Caselli, R.J., Woodruff, B.K., Ahern, G.L., Rapscak, S.Z., Reiman, E.M., Caviness, J.N., Driver-Dunckley, E., Belden, C., Serrano, G., Sue, L.I., Davis, K.J. and Sabbagh, M.N. Autopsied Dementia with Lewy Bodies Cases at the National Brain and Tissue Resource for Parkinson's Disease and Related Disorders (NBTR-PD) and Arizona Alzheimer's Disease Core Center (AZADCC). International Dementia with Lewy Bodies Conference, Ft. Lauderdale, FL, December 1-4, 2015. (Abstract)

5. Presentations at public (non-scientific) meetings or events

From Barnes

Barnes, C.A. Learning and Memory in Aging, The Yale Club of Southern Arizona, Arizona Inn, Tucson, AZ, January 2015. (Invited)

Barnes, C.A. Normal aging: what is the impact on the brain and on memory? Yuma Friends of the University of Arizona Health Sciences, Yuma, AZ, February 2015. (Invited)

Barnes, C.A. Normal aging; what is the impact on the brain and memory? Ventana Canyon Golf and Racquet Club, UA Science Lecture, April 2015. (Invited)

Barnes, C.A. Memory and the aging Brain, WiseGuise II Lunch Group, Scottsdale, AZ, October 2015. (Invited)

From Selected Affiliates

Cowen, S.L. Move it or lose it: How our bodies empower our brains, NAWBO Women's Business Wellness Workshop, Tucson, AZ, January 2015. (Invited)

Ryan, L. Eating Your Way to Healthy Aging: Enhancing Cognitive Functions Through Diet. The Core at La Encantada. Tucson, AZ, January, 2015. (Invited)

Glisky, E.L. Finding balance supports well-being. Annual Conference on Successful Aging, Tucson, AZ, February 2015. (Invited)

Alexander G.A. and Ryan, L. Staying mentally fit by being cognitively active. Annual Conference on Successful Aging. Tucson, AZ. February 20, 2015. (Invited)

Glisky, E.L. Memory changes with age: What to do about it? Voyager Resort and Hotel, Tucson, AZ, February 2015. (Invited)

Ryan, L. White matter changes in the aging brain: Factors that influence related changes in structure & functions. Neurosurgery Didactic Conference at the University of Arizona College of Medicine Arizona Health Sciences Center. Tucson, AZ, March 25, 2015. (Invited)

Ryan, L. The benefits of good nutrition and physical activity to reduce risks of health conditions that can harm brain health, e.g. heart disease, diabetes, and stroke. Pima Council on Aging Put Life Back in Your Life Series. Green Valley, AZ. April 2, 2015. (Invited)

Ryan, L. Neuroscience & Literature. Spirit of the Senses Salon. Paradise Valley, AZ. April 8, 2015. (Invited)

Ryan, L. The Psychology of Aging: Healthy Minds, Healthy Brains, Healthy Lives. Keynote presentation at the annual meeting of the Pima Council on Aging. Tucson, AZ, June 17, 2015. (Invited)

Alexander, G.E. Research Activity: Where we are now and opportunities for growth. Psychology Faculty Retreat, Department of Psychology, University of Arizona, Tucson, AZ, September 2015. (Invited)

Cowen, S.L. Memories are made of this: How our brains create the past. Arizona Integrated Wellness Cooperative, Tucson, AZ, September 2015

Alexander G.A. The brain and aging. The Spirit of Senses. Scottsdale, AZ, October 2015. (Invited)

Glisky, E.L. Hearing loss affects cognition: What to do about it? UA Living Well With Hearing Loss Community Lecture Series, Tucson, AZ, November, 2015. (Invited)

6. Awards (from McKnight affiliates)

Matthias Mehl, Appointed Fellow. Society for Personality and Social Psychology (SPSP)

Matthias Mehl, Appointed Fellow, Association for Psychological Science (APS)

Naomi Rance, Faculty Science Forum Founder's Day Award, University of Arizona College of Medicine, 2015.

7. Faculty

The structure of the Institute remains the same as last year, with Dr. Lee Ryan in the role of Associate Director of the Evelyn F. McKnight Institute in Tucson. The Strategic Advisory Board also remains the same, being comprised of Dr. Eric Reiman, Dr. Leslie Tolbert and Dr. Martha Brumfield.

The Scientific Advisory Board membership changed during this past year, with the retirement of Dr. Alfred Kaszniak. We were lucky to recruit **Dr. Stephen Cowen** to Tucson with EMBI support in 2012 (the "McNaughton" replacement). I have added Stephen to the **Scientific Advisory Committee** because of his expertise in ensemble single unit recording methods, and his collaborations with me in a number of ongoing aging experiments. Stephen has been an outstanding contributor to the McKnight Inter-Institutional group meetings over the past few years, and will be an energetic voice for the Tucson Institute within the State of Arizona and across the country.

Two new Faculty Affiliates have also joined the Institute this year. **Dr. Fabian Fernandez** joined the University of Arizona this fall as a BIO5 Fellow, and with appointments in the Departments of Psychology and Neurology. Dr. Fernandez has made critical contributions to the field of Down syndrome in his past work – having identified a key pathway disturbed in these individuals involving the signaling of the inhibitory neurotransmitter, GABA. Roche trials are currently proceeding through Phase 2 efficacy stages in young adults, and early results have been sufficiently compelling to motivate the development of further testing protocols for drug delivery in young children. His research program going forward will focus on aging, and the disruption of circadian and ultradian rhythms in the aging brain. He is currently developing a novel approach to 'light therapy' to strengthen the brain's pacemaker, and improve cognition

in the elderly. The second new Faculty Affiliate is **Dr. Matthew Grilli** who joined the Psychology Department this fall. He is interested in memory, memory disorders associated aging and brain damage, and memory rehabilitation. His research is directed towards elucidating the conditions and experiences that can improve quality of life and well-being in those with cognitive defects, and how to improve memory through self-referential encoding strategies. Both Fabian and Matt are excited to attend the McKnight Inter-Institutional meeting that will be held in Tucson April 2016.

The search for the Director of the “**Center for Innovation in Brain Science**” in the Health Sciences Center is very close to finalizing the hiring of an outstanding basic and translational scientist who conducts her research in the field of aging and neurodegenerative diseases that occur during aging. Dr. Garcia (Senior Vice President for Health Sciences) is currently exploring the final hiring agreements with this individual. He and the search committee (that both Barnes and Tolbert are on) are optimistic that the details can be worked out.

Complete Faculty List

Director

- Carol A. Barnes, Ph.D., Regents' Professor, Departments of 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, Department of 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 of 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, Departments of Neuroscience, and Cellular and Molecular Medicine, University of Arizona

Scientific Advisory Committee (Bios included in following pages, all Scientific Advisors are also affiliated 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 of Psychology, 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

- Stephen L. Cowen, Ph.D. Assistant Professor of Psychology, Division of Neural Systems, Memory and Aging, Evelyn F. McKnight Brain Institute, University of Arizona
- Elizabeth Glisky, Ph.D., Professor, Department of Psychology, University of Arizona
- Naomi E. Rance, M.D, Ph.D., Professor, Neurology, Cell Biology and Anatomy, and Pathology; Associate Head, Department of Pathology, University of Arizona
- Lee Ryan, Ph.D., Professor, Psychology; Director, Cognition and Neuroimaging Labs, University of Arizona

Additional Affiliate Faculty:

- E. Fiona Bailey, Ph.D., Associate Professor of Physiology, University of Arizona
- Heather Bimonte-Nelson, Ph.D., Associate Professor, Honors Disciplinary Faculty. Behavioral Neuroscience Program Director, Arizona State University
- Paul Coleman, Ph.D., UA Associate, Evelyn F. McKnight Brain Institute, University of Arizona; Co-Director and Senior Scientist, J. Roberts Center for Alzheimer's Research; Professor of Neurobiology and Anatomy, University of Rochester Medical Center
- Fabian Fernandez, Ph.D., Assistant Professor, Department of Psychology, University of Arizona
- Ralph F. Fregosi, Ph.D., Professor of Physiology, University of Arizona
- Andrew J. Fuglevand, Ph.D., Associate Professor of Physiology, University of Arizona
- Katalin M. Gothard, M.D., Ph.D., Associate Professor of Physiology, University of Arizona
- Matt Grilli, Ph.D., Assistant Professor, Department of Psychology, University of Arizona
- Meredith Hay, Ph.D., Professor of Physiology, University of Arizona
- Matthew J. Huentelman, Ph.D., UA Associate, Evelyn F. McKnight Brain Institute, University of Arizona; Investigator, Neurobehavioral Research Unit, Translational Genomics Research Institute
- Anita Koshy, M.D., Assistant Professor of Neurology, University of Arizona
- Lalitha Madhavan, MBBS, Ph.D., Assistant Professor, Department of 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., Associate Professor, Department of Psychology, University of Arizona
- Lynn Nadel, Ph.D., Regents' Professor of Psychology, University of Arizona
- Janko Nikolich-Zugich, M.D., Ph.D., Professor and Chairman, Department of Immunobiology; Co-Director, Arizona Center on Aging, University of Arizona
- Mary-Frances O'Conner, Ph.D., Assistant Professor of Psychology, University of Arizona
- Mary Peterson, Ph.D., Professor of Psychology, University of Arizona

- Steve Rapcsak, M.D., Professor of 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 & Anatomy, and BIO5 Institute, University of Arizona
- David A. Sbarra, Ph.D., Associate Professor and Director of Clinical Training, Department of Psychology, University of Arizona
- Anne C. Smith, Ph.D., Neurophysiology Researcher, EMBI, University of Arizona
- Ted P. Trouard, Ph.D., Associate Professor, Biomedical Engineering
- Pixuan 'Joe' Zhou, Ph.D., Adjunct Research Professor of Optical Sciences, University of Arizona

BIOGRAPHICAL SKETCH

NAME Carol A. Barnes, Ph.D.	POSITION TITLE Regents' Professor		
EDUCATION/TRAINING			
INSTITUTION AND 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

Positions

1978	Research Associate , Dalhousie University, Department of 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 - 1996	Professor , Departments of Psychology and Neurology, University of Arizona, Tucson
2006 -	Regents' Professor , Departments of Psychology and Neurology, University of Arizona, Tucson
2006 -	Director , Evelyn F. McKnight Brain Institute, University of Arizona, Tucson
2006 -	Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging , University of Arizona, Tucson
2008 -	Director , Division of Neural Systems, Memory and Aging, University of Arizona, Tucson
2009 -	Regents' Professor , Department of Neuroscience, University of Arizona, Tucson
2009 - 2015	Associate Director , BIO5 Institute, University of Arizona, Tucson

Honors, Awards and Advisory Committees

1969	NSF Summer Research Fellowship
1971	Phi Beta Kappa
1972 – 1974	Ontario Graduate Fellowship
1979 – 1981	NRSA Individual Postdoctoral Fellowship
1981 – 1982	NATO Fellowship in Science
1984 – 1989	Research Career Development Award, N.I.H.
1987 – 1991	Neuroscience, Behavior and Sociology of Aging Committee A, N.I.A.
1989 – 1994	Research Scientist Development Award, Level II, N.I.M.H.
1991 – 1997	Medical and Scientific Advisory Board, Alzheimer's Association
1994 – 1999	Research Scientist Award, N.I.M.H.
1994 – 1997	National Advisory Council on Aging, N.I.H.
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, N.I.M.H.
2000 – 2002	Secretary, Society for Neuroscience
2003 – 2006	President-Elect (2003-04), President (2004-05), Past-President (2005-06), Society for Neuroscience
2004 – 2014	MERIT Award, National Institute on Aging, NIH
2004	Elected Norwegian Royal Society of Sciences and Letters
2007	Elected Fellow, American Association for the Advancement of Science

- 2007 Elected Executive Committee, Dana Alliance for Brain Initiatives
- 2008 – 2011 Chair, Society for Neuroscience International Affairs Committee – US National Committee (Incoming Chair 2007-2008)
- 2008 APA Division 6 D.B. Marquis Behavioral Neuroscience Award for Behavioral Neuroscience
- 2010 Mika Salpeter Lifetime Achievement Award
- 2010 Elected, Galileo Fellow, College of Science, University of Arizona
- 2010 – 2014 Elected: Chair, Gruber Foundation Neuroscience Prize Advisory Board
- 2011 APA Division 6 D.B. Marquis Behavioral Neuroscience Award for Behavioral Neuroscience
- 2013 Ralph W. Gerard Prize in Neuroscience
- 2014 American Psychological Association Award for Distinguished Scientific Contributions

2015 Publications

- Schimanski, L.A. and Barnes, C.A. (2015) Insights into age-related cognitive decline: Coupling neurophysiological and behavioral approaches. In: H.A. Bimonte-Nelson (Ed) *The Maze Book: Your Guidebook to Theories, Practice, and Protocols for Testing Rodent Cognition*. Springer: New York, pp. 121-142.
- Siniard, A.L., Corneveaux, J.J., DeBoth, M., Chawla, M.K., Barnes, C.A. and Huentelman, M.J. (2015) RNA sequencing from laser capture microdissected brain tissue to study normal aging and Alzheimer's disease. In: *Applied Neurogenomics*. Springer: New York, pp 111-120.
- Burke, S.N. and Barnes, C.A. (2015) The neural representation of 3-dimensional objects in rodent memory circuits. *Behavioral Brain Research*, 285:60-66.
- Samson, R.D., Venkatesh, A., Lester, A.W., Weinstein, A.T., Lipa, P., and Barnes, C.A. (2015) Age differences in strategy selection and risk preference during risk-based decision making. *Behavioral Neuroscience*, 129:138-148.
- Cohan, C.H., Neumann, J.T., Dave, K.R., Alekseyenko, A., Binkert, M., Stransky, K., Lin, H.W., Barnes, C.A., Wright, C.B., Perez-Pinzon, M.A. (2015) Effect of cardiac arrest on cognitive impairment and hippocampal plasticity in middle-aged rats. *PLoS One*, 10:e0124918.
- Insel, N. and Barnes, C.A. (2015) Differential activation of fast-spiking and regular-firing neuron populations during movement and reward in the dorsal medial frontal cortex. *Cerebral Cortex*, 25:2631-2647.
- Gray, D.T. and Barnes, C.A. (2015) Distinguishing adaptive plasticity from vulnerability in the aging hippocampus. *Neuroscience*, 309:17-28.
- Thome, A., Gray, D.T., Erickson, C.A., Lipa P. and Barnes, C.A. (2015) Memory impairment in aged primates is associated with region-specific network dysfunction. *Molecular Psychiatry*, in press. doi:10.1038/mp.2015.160.
- Penner, M.R., Parrish, R.R., Hoang, L.T., Roth, T.L., Lubin, F.D, and Barnes, C.A. (2016) Age-related changes in zif268 transcription and DNA methylation within the hippocampus. *Hippocampus*, accepted with minor revisions.

BIOGRAPHICAL SKETCH

NAME Geoffrey Lawrence Ahern, M.D., Ph.D.		POSITION TITLE Professor	
EDUCATION/TRAINING			
INSTITUTION AND 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 Univ 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, Univ of Arizona, Tucson
1999 - 2002	Associate Professor , Neurology, Psychology, Psychiatry, Univ 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

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, 1996-97
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 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., Intorcchia, 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. Arizona study of aging and neurodegenerative disorders and brain and body donation program. *Neuropathology*, 2015, 35:354-389.

BIOGRAPHICAL SKETCH

NAME Gene E. Alexander, Ph.D.	POSITION TITLE Professor		
EDUCATION/TRAINING			
INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
Pomona College, Claremont, CA	B.A.	1983	Psychology
Loyola University of Chicago, Chicago, IL	M.A.	1987	Clinical
Loyola University of Chicago, Chicago, IL	Ph.D.	1992	Clinical

Positions

1988-1989	Clinical Psychology Intern , Dept. of Psychiatry & Behavioral Sciences, 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 , Lab. of Neurosciences, NIA, NIH, Bethesda, MD
1993-1999	Chief Neuropsychology Unit , Lab. of Neurosciences, NIA, NIH, Bethesda, MD
1999-2003	Research Associate Professor , Dept. of Psychology, Arizona State University, Tempe
1999- date	Director , MRI Morphology Core, Arizona Alzheimer's Disease Research Ctr, Phoenix
2001-2009	Director , Data Management Program/Core, NIA AZ Alzheimer's Disease Core Center
2001- date	Member , Executive Committee, NIA Arizona Alzheimer's Disease Core Center, AZ
2003-2007	Associate Professor to Professor , Psychology Dept., Arizona State University, Tempe
2007-date	Professor , Psychology & Evelyn F. McKnight Brain Institute, Univ of Arizona, Tucson
2007-date	Director , Brain Imaging, Behavior, & Aging Lab, Univ of Arizona, Tucson, AZ

Honors, Awards and Advisory Committees

1995- date	Ad Hoc Reviewer, 20 journals in Neuropsychology, Psychiatry, Neurology, & Neurosci.
1996-1999	Staff Recognition Awards (annual), Laboratory of Neurosciences, National Inst. on Aging
2000- date	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 Peer Review Comm, Psychology: Exp/Clin, Fulbright Scholar Prog
2006	Chair, Special Emphasis Panel, Clin Neurosci & 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, Special Emphasis Panel, SPRINT Ctr Review, ZHL1 CCT-B C2 1, NHLBI, NIH
2008-date	Member, Neuroimaging Workgroup, International Conf. on Alzheimer's Disease/ISTAART
2009	Reviewer, Special Emphasis Panel, 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 Opportunity Grants in Genetics, Epigenetics & Genomics, NIA
2009	Member, SEP, Program Project Review Group, Brain Dopamine, ZAG1 ZIJ-8 J3, NIA, NIH
2009	Member, SEP, Program Project Review Group, Neuroimaging & Aging, ZAG1 ZIJ-5 JF, NIA
2009-date	Member, Faculty Annual Performance Comm, Psychology Dept., Univ. of Arizona
2010	Member, Neurological Sciences & Disorders K Review Committee, NSD-K, NINDS, NIH
2010	Member, Neuroscience of Aging Review Committee, NIA-N, NIA, NIH

2010 Member, SEP, Program Project Review Group, Exercise, Motor Deficits, & Aging, ZAG1-ZIJ-9, NIA, NIH

2010 Member, SEP, Program Project Review Group, Dopaminergic Dysfunction in Aging, ZAG1 ZiJ-6 J3, NIA, NIH

2010-2013 Member, Executive Committee, Neuroscience GIDP, University of Arizona

2010 Member, Academic Program Review Faculty Committee, Psych. Dept., Univ of Arizona

2010-2013 Elected to NIH Continuous Submission Status for substantial rev. service over the past 3 years

2011 Chairperson, Member Special Emphasis Panel, ZAG1 ZIJ-7 (J1), NIA, NIH

2011 Member, Neuroscience of Aging Review Committee, NIA-N, NIA, NIH

2011-date Advisory Editor, Neurobiology of Aging, Elsevier.

2011-2012 Member, Cognitive Aging Working Group, Evelyn F. McKnight Brain Institute

2011 Member, VA MHBB Merit Review Subcommittee, Veterans Administration

2011 Member, SEP, Loan Repayment Program, ZNS1 SRB-M (76), NIA, NIH

2011 Member, SEP, Biobehav. Res. Awards for Innovative New Scientists (BRAINS), ZMH1 ERB-L-04, NIMH, NIH

2011 Reviewer, Alzheimer's Disease Pilot Grant Program, Arizona Alzheimer's Disease Center

2011-date Fellow, Association for Psychological Science

2012 Member, Neurological Sciences & Disorders K Review Committee, NSD-K, NINDS, NIH

2012 Member, Neuroscience of Aging Review Committee, ZAG1 ZIJ-4 (J1), NIA, NIH

2012-date Member, Cognitive Workgroup, Evelyn F. McKnight Brain Institute

2012-date Member, MRI Standardization Workgroup, Evelyn F. McKnight Brain Institute

2012-date 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, Development Committee, Department of Psychology, University of Arizona

2013 Member, MRI Operations Committee, University of Arizona

2013 Member, Alzheimer's Disease Research Centers Review, ZAG1ZIJ4J1, NIA, NIH

2013-2019 Member, Neuroscience of Aging Review Comte, NIA-N, NIA, NIH (elected to 6 yr term)

2014 Member and Chairperson, Biobehavioral and Behavioral Processes Review Group, ZRG1 BBBP Y 04, CSR, NIH

2015 Publications

Nguyen LA, Haws KA, Fitzhugh MC, Torre GA, Hishaw GA, Alexander GE. (2015) Interactive effects of subjective memory complaints and hypertension on learning and memory performance in the elderly. *Aging, Neuropsychology, and Cognition*. July 17, 1-17. [Epub ahead of print]

BIOGRAPHICAL SKETCH

NAME Stephen L. Cowen, Ph.D.		POSITION TITLE Assistant Professor, Psychology	
EDUCATION/			
INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
University of Wisconsin	B.S.	1992	Business Administration
University of Arizona	Ph.D.	2007	Psychology

Positions

2007 - 2008 **Postdoctoral Fellow**, The Neuroscience Institute, San Diego, CA
 2008 - 2009 **Research Fellow**, The Neuroscience Institute, San Diego, CA
 2009 - 2013 **Associate Fellow**, The Neuroscience Institute, San Diego, CA
 2013 – present **Assistant Professor**, Department of Psychology, University of Arizona, Tucson, AZ
 2013 – present **Assistant Professor**, Evelyn F. McKnight Brain Institute, University of Arizona, Tucson, AZ

Fellowships, Honors and Awards

1998 – 1999 National Science Foundation Training Grant
 2010 Blasker-Rose Miah Technology Development Grant, San Diego Foundation

2015 Publications

Wiegand, J-P, Gray, G.T., Schimanski, L.A., Lipa, P., Barnes, C.A. and Cowen, S.L. (2015) Age is associated with reduced sharp-wave ripple frequency and neuronal variability, under revision.

NAME		POSITION TITLE	
Elizabeth L. Glisky, Ph.D.		Professor	
EDUCATION/TRAINING (<i>Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.</i>)			
INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
University of Toronto, Ontario, Canada	B.A.	1958-1962	Psychology
University of Toronto, Ontario, Canada	Ph.D.	1978-1983	Psychology
University of Toronto, Ontario, Canada	Postdoc	1983-1987	Psychology

Positions

1987 - 1989	Visiting Assistant Professor , Dept of Psychology, University of Arizona, Tucson
1989 - 1995	Assistant Professor , Department of Psychology, University of Arizona, Tucson
1995 - 1999	Associate Professor , Department of Psychology, University of Arizona, Tucson
2000 - 2002	Head , Interdisciplinary Program in Gerontology, University of Arizona, Tucson
1999 -	Professor , Department of Psychology, University of Arizona, Tucson
2004 - 2008	Associate Head and Graduate Coordinator , Department of Psychology, University of Arizona, Tucson
2007 -	Professor , Evelyn F. McKnight Brain Institute, University of Arizona, Tucson
2008 – 2009	Acting Head , Department of Psychology, University of Arizona, Tucson
2010 - 2015	Head , Department of Psychology, University of Arizona, Tucson

Honors, Awards and Advisory Committees

1980 - 1981	Natural Sciences and Engineering Research Council postgraduate scholarship
1981 - 1982	University of Toronto open fellowship
1982 - 1983	Ontario Government scholarship
1983 - 1886	University of Toronto postdoctoral award to research fellow
1989 - 1990	University of Arizona, Provost's Teaching Award
2003	Social and Behavioral Sciences Research Professorship
2007	Fellow of the Association for Psychological Science
2011	Elizabeth Hurlock Beckman Award

2015 Publications

Jones, B., Pest, S. M., Vargas, I.M., Glisky, E. L. and Fellous, J-M. (2015). Contextual reminders fail to trigger memory reconsolidation in aged humans and rats. *Neurobiology of Learning and Memory*, 7-14.

BIOGRAPHICAL SKETCH

NAME Naomi E. Rance, M.D., Ph.D.		POSITION TITLE Professor of Pathology	
EDUCATION/TRAINING			
INSTITUTION AND 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

Positions

1976 -1981	Predoctoral Fellow , Department of Physiology, University of Maryland, Baltimore, MD
1983 -1986	Resident , Anatomic Pathology, The Johns Hopkins Hospital, Baltimore, MD
1986 -1987	Chief Resident , Anatomic Pathology, The Johns Hopkins Hospital, Baltimore, MD
1987 -1989	Clinical and Research Fellow , Neuropathology Lab, Johns Hopkins Hospital, Baltimore
1989 -1995	Assistant Professor , Dept of Pathology College of Medicine, Univ of Arizona, Tucson, AZ
1989 -	Chief , Division of Neuropathology, University Medical Center, Tucson, AZ
1989 -	Neuropathology Consultant , Forensic Science Center, Pima County, Tucson, AZ
1995 -	Associate Professor , Dept of Pathology College of Medicine, Univ of Arizona, Tucson, AZ
1996 -	Associate Chairperson , Dept of Pathology College of Medicine, Univ of Arizona, Tucson
2000 -	Professor , Department of Pathology, Univ of Arizona College of Medicine, Tucson, AZ
2007 -	Professor , Evelyn F. McKnight Brain Institute, University of Arizona, Tucson, AZ

Honors, Awards and Advisory Committees

1973	Phi Beta Kappa
1983	Rudolph Virchow Prize for Research in Pathology, University of Maryland
1993	Advisory Group, Workshop on Menopause, NIH, Bethesda
1994, 1997	Ad Hoc member, Biochemical Endocrinology Study Section, NIH, Bethesda
1995	John Davis Outstanding Residency Teaching Award, Dept. of Pathology, Univ of Arizona
1995, 1997	Ad Hoc Reviewer, National Science Foundation
1998 - 2004	Site Visit Review Committees, NIH, NIA Program Project Grants
1999, 2000, 2001	Basic Science Educator of the Year, University of Arizona College of Medicine
2001	Advisory Group, NIA Workshop on Primate Models of Menopause, NIH, Bethesda
2002	Basic Science Educator of the Year Lifetime Award, Univ of Arizona College of Medicine
2007	Vernon and Virginia Furrow Award for Excellence in Innovation in Teaching, Univ Arizona
2009	Ad Hoc Reviewer, ICER Study Section, NIH Bethesda
2010	Ad Hoc Reviewer, Burroughs Welcome Trust
2011	Ad Hoc Reviewer, ICER Study Section, Chicago Illinois

2015 Publication

Cholanian, M., Krajewski-Hall, S.J, Levine, R.B., McMullen, N.T. and Rance, N.E. (2015) 17 β -Chronic oestradiol reduces the dendritic spine density of KNDy neurons in the arcuate nucleus of ovariectomized Tac2-EGFP transgenic mice. *Journal of Neuroendocrinology*, 27:253-263.

BIOGRAPHICAL SKETCH

NAME		POSITION TITLE	
Lee Ryan, Ph.D.		Professor, Psychology, Neurology, and Neurosciences Program	
EDUCATION/TRAINING			
INSTITUTION AND 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/Neuroscience
University of British Columbia, Vancouver, Canada	Ph.D.	1992	Clinical/Cognitive Psychology
University of California, San Diego, CA	Postdoctoral	93-95	Neuropsychology

Positions

1992 - 1993	Clinical Internship , Department of in Neuropsychology, VA Medical Center, La Jolla, and University of California at San Diego, San Diego, CA
1993 - 1996	Research Scientist , Department of Psychiatry, University of California, San Diego, CA
1998	Participant , Summer Institute on Aging Research, National Institute on Aging
1996 - 2003	Assistant Professor , Departments of Psychology and Neurology, University of Arizona, Tucson, AZ
1996 - present	Director , Cognition & Neuroimaging Laboratories, University of Arizona, Tucson, AZ
2003 - 2014	Associate Professor , Departments of Psychology and Neurology, University of Arizona, Tucson, AZ
2007 - 2014	Associate Professor , Evelyn F. McKnight Brain Institute, University of Arizona, Tucson, AZ
2008 - present	Associate Head , Department of Psychology, University of Arizona, Tucson, AZ
2014 - present	Professor , Departments of Psychology and Neurology, Evelyn F. McKnight Brain Institute, University of Arizona, Tucson, AZ
2015 -	Head , Department of Psychology, University of Arizona, Tucson

Honors

1988 - 1992	National Science & Engineering Research Council of Canada Graduate Fellowships
1993 - 1995	National Science & Engineering Research Council of Canada Postdoctoral Fellowships
2000	Member, Memory Disorders Society

2015 Publications

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. Behavioral and Brain Sciences, 38:e1

8. Trainees (faculty advisor in brackets)

Postdoctoral

Monica Chawla, Ph.D. (Barnes)

Area of Interest: Immediate early gene expression in aging in the rat.

Rachel Samson, Ph.D. (Barnes)

Area of Interest: Age-related changes in the amygdala and emotional perception in the rat.

Marina Cholanian (Rance)

Area of Interest: Morphology and electrophysiology of Neurokinin B neurons in the hypothalamic arcuate nucleus.

Predoctoral

Elsa Baena (Ryan)

Area of Interest: fMRI studies of memory function in normal older adults.

Lindsey Crown (Cowen)

Area of Interest: Investigating how ketamine alters dopamine levels in the brain.

Daniel Gray (Barnes)

Area of Interest: Circuits involved in working memory and their decline with age in a non-human primate model of aging.

Mary Katherine Franchetti (Alexander)

Area of Interest: Effects of sleep and physical activity on aging.

Kari Haws (Alexander)

Area of Interest: Cognition and neuroimaging in cognitive aging.

Dan Hill (Cowen)

Area of Interest: How the frontal cortex alters dopamine release in aging

Mingzhu Hou (Glisky)

Area of Interest: Source memory and aging.

Kevin Kawa (Ryan)

Area of Interest: Brain imaging, genetics, and cognitive changes in normal older adults.

Colin Kyle (Barnes)

Area of Interest: Brain aging and hippocampal ensembles recorded in the unrestrained young and old non-human primate.

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.

Molly Memel (Ryan)

Area of Interest: The underlying mechanisms of memory impairment in older adults.

Suzanne Moseley (Glisky)

Area of Interest: Hearing loss, cognition, and aging.

Laura Nguyen (Alexander)

Area of Interest: Relation of cognitive complaints in relation to cognition and aging in the elderly.

Stacey Pest (Nadel/Glisky)

Area of Interest: Reconsolidation in normal aging

Angelina Polsinelli (Glisky)

Area of Interest: Meditation, cognition, and emotion in normal aging.

Ruth Robbins (Glisky)

Area of Interest: Social networking and cognitive in normal aging.

Ariana Stickel (Ryan)

Area of Interest: Brain imaging, genetics, and cognitive changes in normal older adults.

Jean Paul Wiegand (Cowen)

Area of Interest: Oscillatory activity related to memory formation in aging.

Janelle Wohltmann (Glisky)

Area of Interest: Social networking in normal aging; memory and executive function; source memory.

Cindy Woolverton (Glisky)

Area of Interest: Self-referential processing in normal aging and schizophrenia.

Tony Ye (Cowen)

Area of Interest: Effect of Parkinson's disease and ketamine on oscillatory activity in the aging brain

Undergraduate Students (from Barnes' lab with graduate student / postdoctoral mentor in brackets)

Eze Ahanonu (Samson/Insel)

Katherine Andersh (Gray)

Jessica Burkhart (Gray/Lester)

Alison Comrie (Gray/Chawla)

Harshaan Dhaliwal (Chawla)

Leroy Duarte (Samson)

Ali Gilliland (Chawla)

Koustubh Kondapalli (Chawla)

Adele Koutia (Lester)

Christie Nguyen (Chawla)

Minhkhoy Nguyen (Chawla)

Surbhi Patel (Chawla)

Reena Puri (Chawla)

Wonn Pyon (Gray)

Gayatri Sadachar (Chawla)

Chelsea Takamatsu (Gray)

9. Clinical/translational programs

2012-2017 Alzheimer's Disease Core Center – UAHSC Clinical Core. Protocol # P30 AG19610-01, National Institute on Aging. Total grant: \$51,686 / year;

- Ahern - \$15,755 / year; 10% salary support, 10% effort. (Overall PI: E. Reiman, MD).
- 2013-present A Placebo-controlled, Double-blind, Parallel-group, Bayesian Adaptive Randomization Design and Dose Regimen-finding Study to Evaluate Safety, Tolerability and Efficacy of BAN2401 in Subjects With Early Alzheimer's Disease. Protocol # BAN2401-G000-201. Eisai. Total grant: \$107,194/patient. 2% salary support, 2% effort.
- 2013-present Effect of Passive Immunization on the Progression of Mild Alzheimer's disease: Solanezumab (LY2062430) versus Placebo. Protocol # H8A-MC-LZAX. Lilly Pharmaceuticals. Total grant: \$32,863/patient. 2% salary support, 2% effort.
- 2013-2015 A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, 26-Week, Phase 3 Study of Two Doses of EVP-6124 or Placebo in Subjects with Mild to Moderate Alzheimer's Disease Currently or Previously Receiving an Acetylcholinesterase Inhibitor Medication. Protocol # EVP-6124-025. EnVivo Pharmaceuticals. Total grant: \$27,944/patient. 2% salary support, 2% effort.
- 2013-present A Phase III, Randomized, Placebo-Controlled, Parallel-Group, Double-Blind Clinical Trial to Study the Efficacy and Safety of MK-8931 (SCH 900931) in Subjects with Amnesic Mild Cognitive Impairment Due to Alzheimer's Disease (Prodromal AD). Protocol # 019-00. Merck Sharp & Dohme. Total grant: \$37,069/patient. 2% salary support, 2% effort.

10. Technology transfer

Provisional patent application: Drs. Meredith Hay (McKnight affiliate), John Konhilas and Carol Barnes. U.S. Patent Application #14/801,557, "Ang-(1-7) Derivative Oligopeptides and Methods for Using and Producing the Same," July 16, 2015.

International patent application: Drs. Yitshak Zohar, Linda Restifo (McKnight affiliate), and Linan Jiang. PCT/US15/63978 "Systems for dissociation of biological tissue, filed December 4, 2015.

11. Budget update

(c) Extramural funding (covering period July 1, 2014 to June 30, 2015)

Grants Received – from Barnes

5 RO1 AG003376-30 (PI: Barnes)

Title: Neurobehavioral Relations in Senescent Hippocampus
 Dates: 05/01/14 – 4/30/16 (w/ one year – no cost extension)
 Amount: \$674,882/year total costs (\$594,557/year direct)

5 R37 AG012609-20 (PI: Barnes)

Title: Cell Assemblies, Pattern Completion and the Aging Brain
 Dates: 07/01/14 – 06/30/15 (w/ one year – no cost extension)

Amount: \$276,854/year total costs (\$184,347/year direct)

1 R01 AG049465-01 (PI: Barnes; co-I's: Alexander, Billheimer, Huentelman, Trouard)
Title: Neural System Dynamics & Gene Expression Supporting Successful Cognitive Aging
Dates: 08/01/14 – 03/31/15 (08/14 – 03/19 project period)
Amount: \$691,127/year total costs (\$545,494/year direct)

1 R01 AG049464-01 (PI's: Coleman, Barnes, Alexander; co-I's: Billheimer, Huentelman, Trouard)
Title: Epigenetic, Neuroimaging & Behavioral Effects of Hypertension in the Aging Brain
Dates: 08/01/14 – 03/31/15 (08/14 – 03/19 project period)
Amount: \$517,448/year total costs (\$412,301/year direct)

1 R01 AG048907-01 (PI's: Huentelman, Barnes, co-PI: Okuno)
Title: CATT: Development and Application of a Neuronal Cell Activity-Tagging Toolbox
Dates: 09/30/14 – 05/31/15 (09/14 – 05/18 project period)
Amount: \$1,056,635 (\$815,334 direct)
Status: Awarded 9/30/2014 (\$1,056,635 total costs, \$815,334 direct) (UA subcontract)
\$328,198/year total costs (\$245,145/year direct costs)

5 P30 AG019610-15 (PI: Reiman; co-I: Barnes, Director, Ad Hoc Review Program)
Title: Arizona Alzheimer's Disease Core Center Ad Hoc Review
Dates: 07/01/14 – 06/30/15 (7/11 – 6/16 project period)
Amount: \$20,332/year total costs (\$13,420/year direct) / UA Subcontract

McKnight Brain Research Foundation (UA PI: Barnes; UA co-I: Huentelman)
Title: Evelyn F. McKnight Inter-Institutional Bio-Informatics Core
Date: 12/1/14 – 12/1/15 (12/1/15 – 6/30/16 project period w/ extension)
Amount: \$150,000 direct costs / \$300,000 over 2 years

State of Arizona, DHS Grant (PI: Barnes)
Title: Arizona Alzheimer's Consortium – Animal Models of Normative Human Aging: From Rodents to Nonhuman Primates
Date: 07/01/14 – 06/30/15
Amount: \$60,063/year direct costs

State of Arizona, DHS Grant (PI: Barnes; co-I's: Huentelman, Liang)
Title: Arizona Alzheimer's Consortium – Technologies to Visualize Cells, Pathways and Molecular Circuits in Intact Brains; Interrogating Networks in Normal and Pathological Brains
Date: 07/01/14 – 06/30/15
Amount: \$95,000/year direct costs

State of Arizona, DHS Grant (PI: Barnes)

Title: Arizona Alzheimer's Consortium – Internal Scientific Advisory Committee

Dates: 07/01/14 – 06/30/15

Amount: \$10,000/year direct costs

UA Office of Research & Discovery Institutional Award (PI: Liang; co-PI's: Barnes,
Utzinger)

Title: Development of the H2L2-CFM System for Whole Brain Imaging

Dates: 12/1/14 – 06/30/16

Amount: \$165,000

Sarver Heart Center (PI: Hay; co-PI's: Konhilas, Huentelman, Barnes)

Title: Heart Failure and Cognitive Impairment: Ang-(1-7) Cognitive Protective
Therapy

Dates: 01/01/14 – 12/31/15

Amount: \$120,000 direct costs (total project period ending 12/2017)

Grants Received - From Selected Affiliates (McKnight affiliate faculty underlined)

1 R01 AG049465-01 (PI: Barnes; co-I's: Alexander, Billheimer, Huentelman, Trouard)
As listed above.

1 R01 AG049464-01 (PI's: Coleman, Barnes, Alexander; co-I's: Billheimer, Huentelman,
Trouard)
As listed above.

1 R01 AG047887-01 (PI: Rance)

Title: Role of preoptic NK3R neurons in the estrogen modulation of body temperature

Dates: 8/15/14 - 4/30/2015 (8/14 – 4/19 project period)

Amount: \$301,074/year total costs (\$205,000 direct)

2 R01 AG031581 (PI's: Reiman, Caselli; UA co-I: Alexander)

Title: PET, APOE & The Preclinical Course of Alzheimer Disease

Dates: 04/01/15 - 3/31/16 (5/14 – 3/19 project period)

Amount: \$14,630/year total costs (UA Subcontract)

1 R01 NS08026-01A1 (UC Davis Subcontract; UA PI: Cowen)

Title: Restoring Functional Connectivity following TBI

Dates: 02/15/14 – 01/31/15 (2/14 – 1/19 project period)

Amount: \$22,680/year total costs (\$14,970 direct) (UA Subcontract)

National Science Foundation DBI-1450767 (PI: Cowen; co-I: Heien)

Title: BRAIN EAGER: Integrated Measurement of Dopamine Release and Large-Scale
Ensemble Activity in Behaving Animals

Dates: 09/01/14 – 03/31/16 (project period)

Amount: \$300,000 total costs (\$205,350 direct)

State of Arizona, DHS Grant (PI: Ryan)

Title: Arizona Alzheimer's Consortium – The Impact of Family History for Alzheimer's disease on Cognition and Brain Function

Dates: 07/01/14 – 06/30/15

Amount: \$67,562/year direct costs

State of Arizona, DHS Grant (PI: Alexander; co-PI: Raichlen)

Title: Arizona Alzheimer's Consortium - Risk Factors for Brain Aging and preclinical Alzheimer's disease

Dates: 07/01/14 – 06/30/15

Amount: \$67,562/year direct costs

State of Arizona, DHS Grant (PI: Ahern)

Title: Arizona Alzheimer's Consortium – Patient Recruitment and Outreach for Alzheimer's disease and Related Disorders

Dates: 07/01/14 – 06/30/15

Amount: \$6,500/year direct costs

State of Arizona, DHS Grant (PI: Alexander)

Title: Arizona Alzheimer's Consortium - Arizona Traumatic Brain Injury Research Planning Workgroup

Dates: 07/01/14 – 06/30/15

Amount: \$15,000/year direct costs

McKnight Brain Research Foundation (UA PI: Alexander; UA Co-I's: Hishaw, Trouard)

Title: McKnight Inter-institutional Neuroimaging Core and Brain Aging

Dates: 01/01/15 – 12/31/17

Amount: \$228,730 total costs

2 P30 AG019610-13 (PI: Reiman; co-PI: Ahern)

Title: Arizona Alzheimer's disease Core Center (UA Clinical Core)

Dates: 07/01/14 – 06/30/15 (7/11 – 7/16 project period)

Amount: \$67,605/year total costs (\$44,187 direct costs) / UA Subcontract

Mind and Life Institute (Mentor: Glisky – training award to Polsinelli, GRA)

Title: Developing an Objective Measure of Mindfulness in Daily Life

Dates: 06/01/2015 – 05/31/2017

Amount: \$14,760.27 direct costs

UA BIO5 Fellowship FLW2014-03 (PI's: Alexander; Raichlen)

Title: Aerobic and Cognitive Training to Enhance Brain Aging

Dates: 11/1/14 – 5/31/16

Amount: \$30,000 total costs

Grants Submitted – from Barnes

1 R01 AG050548-01 (PI: Barnes; co-I: Smith)

Title: Cell Assemblies, Brain Adaptation and Cognitive Aging
Dates: 07/01/15 – 06/30/20 (requested dates of project)
Amount: \$2,993,719 total costs; \$1,978,563 direct (requested budget)
Status: Awarded 9/1/15 (\$2,376,828 total costs, \$1,570,999 direct)

2 RO1 AG003376-31 (PI: Barnes; co-I's: Bales, Ekstrom)

Title: Neurobehavioral Relations in Senescent Hippocampus
Dates: 09/01/15 – 08/31/20 (requested dates of project)
Amount: \$4,886,500 total costs; \$4,288,667 direct (requested budget)
Status: Awarded 1/1/16 (\$3,803,576 total costs, 3,295,644 direct)

State of Arizona, DHS Grant (PI: Barnes; co-I's: Hay, Konhilas, Doyle)

Title: Arizona Alzheimer's Consortium – Role of Brain Inflammation in Angiotensin (1-7) Protection from Heart Failure Induced Cognitive Impairment
Date: 07/01/14 – 06/30/15
Amount: \$16,000/year direct costs
Status: Awarded 7/1/15

NIH (PI: Madhavan, co-I: Barnes)

Title: Nrf2 as a Regulator of Neural Stem Cell Function During Aging
Dates: 07/01/15 – 06/30/20 (requested project dates)
Amount: \$2,115,379 total costs; \$1,429,316 direct (requested budget)
Status: Not funded – resubmitted July 5, 2015

Grants Submitted - From Selected Affiliates (McKnight affiliate faculty underlined)

State of Arizona, DHS Grant (PI: Alexander)

Title: Arizona Alzheimer's Consortium – Risk Factors for Brain Aging and Preclinical Alzheimer's Disease
Dates: 07/01/15 – 06/30/16
Amount: \$62,000/year (direct costs)
Status: Awarded 07/01/15

State of Arizona, DHS Grant (PI: Ryan; co-I's: Hay, Glisky, Sweitzer, Konhilas)

Title: Arizona Alzheimer's Consortium – Angiotensin (1-7) Treatment to Improve Cognitive Functioning in Heart Failure Patients)
Dates: 07/01/15 – 06/30/16
Amount: \$98,505/year (direct costs)
Status: Awarded 07/01/15

State of Arizona, DHS Grant (PI: Glisky)

Title: Arizona Alzheimer's Consortium – Memory, Executive Function, and Prospective Memory Training

Dates: 07/01/15 – 06/30/16
Amount: \$32,000/year (direct costs)
Status: Awarded 07/01/15

State of Arizona, DHS Grant (PI: Ahern)

Title: Arizona Alzheimer's Consortium – Patient Recruitment and Outreach for Alzheimer's disease and Related Disorders

Dates: 07/01/15 – 06/30/16
Amount: \$6,500/year (direct costs)
Status: Awarded 07/01/15

McKnight Brain Research Foundation (UA PI: Alexander; UA Co-I's: Ryan, Glisky)

Title: McKnight Inter-institutional Cognitive Aging and Assessment Core

Dates: 09/01/15 – 08/31/17
Amount: \$200,000 total costs (\$200,000 direct)
Status: Awarded 11/1/15

#11014 Michael J. Fox Foundation for Parkinson's Research (PI: Cowen; co-I's: Bao, Falk)

Title: Identification of Network and Oscillatory Signatures of the LRRK2 Mutation

Dates: 07/09/15 – 07/09/16 (requested dates of project)
Amount: \$124,929.44 (requested budget)
Status: Awarded 07/09/15 (\$124,929.44 total costs; \$99,943.55 direct)

1 R24 MH109060-02 (PI: Witte; co-I's: Bernas, Cowen, Denninghoff, Falk, Furenlid, Krupinski, Kunyansky, Weinand)

Title: Identification of Network and Oscillatory Signatures of the LRRK2 Mutation

Dates: 09/25/15 – 06/30/16 (requested dates of project)
Amount: \$997,720 (requested budget)
Status: Awarded 07/25/15 (\$997,720 total costs; \$972,502.5 direct)

Whitehall Foundation (PI: Cowen)

Title: Neural Basis for the Control of Physical Effort

Dates: 01/01/15 – 12/31/15 (requested dates of project)
Amount: \$30,000 (requested budget)
Status: Not funded

NIH (PI: Falk; co-I's: Cowen, Heien, Sherman)

Title: Benefits and Mechanisms of Low-Dose Ketamine Treatment for Parkinson's Disease

Dates: 07/01/15 – 06/30/20 (requested dates of project)
Amount: \$1,843,835 total costs; \$1,250,000 direct costs (requested budget)
Status: Not funded

NIH (PI: Falk; co-I's: Cowen, Heien, Sherman)

Title: Mechanisms Underlying the Effective Treatment of L-DOPA-induced Dyskinesia with Low-Dose Ketamine

Dates: 09/01/15 – 08/31/19 (requested dates of project)
Amount: \$1,462,306 total costs; \$1,000,000 direct costs (requested budget)
Status: Not funded

NIH (PI: Witte; co-I: Cowen; Denninghoff, Falk, Furenlid, Kunyansky, Weinand)
Title: Acoustoelectric Brain Imaging: The Next Frontier for Mapping Current Densities in the Brain
Dates: 09/30/14 – 09/29/17 (requested dates of project)
Amount: \$1,292,984 total costs; \$900,000 direct costs (requested budget)
Status: Not funded

NIH (PI: Ryan)
Title: The Impact of Significant Weight Loss on Cognition and MRI Measures of Brain Structure/Function in Obese Individuals Undergoing Bariatric Surgery
Dates: 07/01/15 – 06/30/17 (requested dates of project)
Amount: \$316,125 (requested)
Status: Not Funded

American Health Association (PI: Ryan)
Title: The Impact of Significant Weight Loss in Obese Individuals on Cognition and MRI Measures of Brain Structure/Function
Dates: 01/01/15 – 12/31/16 (requested dates of project)
Amount: \$132,549 (requested)
Status: Not Funded

12. Educational programs focusing on age related memory loss (January 1, 2015 – December 31, 2015)

Event: Annual Conference on Successful Aging: Finding Balance: Enhancing Physical, Emotional, and Social Well-Being
Date: February 20, 2015
Organizers: Lee Ryan, Ph.D. and Gene Alexander, Ph.D.
Venue: Double Tree Hotel, Tucson, AZ
Summary: This one day conference was attended by 280 members of the Tucson community and health-care workers.

13. Collaborative programs with McKnight institutions and research programs

Huentelman/Coleman/Barnes/Alexander/Trouard

With funds from the first McKnight gift, we developed techniques and collected preliminary data to use to write 3 RO1 grants that are now funded, as reported in the grant section (RO1 AG048907 [PI's: Barnes/Huentelman], RO1 AG049464 [PI's: Coleman/Barnes/Alexander]), RO1 AG049465 [PI: Barnes]).

Sweatt/Foster/Barnes/Huentelman

We created a new Inter-Institutional Epigenetics Core, which has made good progress towards a collaborative and comprehensive program to coordinate genetic and epigenetic assessment of brain tissue from cognitively-characterized young and old rats. This effort is coordinated through the Alabama Institute, as this is Dr. Sweatt's primary area of expertise. We presented the status of our current efforts towards a comparison of sequencing platforms (UF versus UA), and cognitive test sites (UA, UF) at the 2015 McKnight Poster Session at the Society for Neuroscience in Chicago. There were two conference calls after the SfN annual meeting (one in November, one in December 2015) to discuss new findings, and to discuss next steps towards publishing the data, and communicating our findings to the scientific community. In the final year of the Core, we have been making plans to expand the tests in rodents to humans in collaboration with the Miami and Arizona Institutes. Our next scheduled conference call is January 15, 2016.

Engle/Burke/Barnes

With funds from the first McKnight gift, we conducted experiments to examine auditory evoked potential and visual evoked response tests to our young and old bonnet macaques. These electrophysiological methods are well-studied clinical measures of auditory and visual function, and Dr. James Engle when he was a postdoctoral fellow in the Barnes lab, obtained these data. Additionally, when Dr. Sara Burke was a postdoctoral fellow in the Barnes lab, she and Dr. Engle also conducted preliminary analyses taken from the structural MRI scans obtained from these experiments to measure volumes of primary auditory and visual cortex of these animals to relate to the sensory physiology measures. The schedules of both Drs. Engle and Burke have been extremely busy over the past year, and Barnes hopes to re-engage implementing the completion of this study in the next year.

Cowen/Barnes/Wiegand/Gray

We have examined, with novel analytic approaches, whether the structure of ripple oscillations and ripple-triggered patterns of single-unit activity in the hippocampus is altered in aged rats, following the performance of a place-dependent eyeblink-conditioning task. We found that neural responses in aged rats differed from responses in young rats in several ways: the CA1 region of the old rats shows **1)** reduced occurrence of ripple events (ripple density), **2)** a 14 Hz reduction in the frequency of the ripple oscillation itself, and **3)** a reduced number of visited population states. Taken together, these results suggest that the CA1 network is more rigid in aged animals, and it may have a more limited "vocabulary" of available representational states. It is also conceivable that the increase in the precision of neuronal responses in aged animals is a compensatory effect to counteract the many physiological changes that accompany aging such as reduced neuronal efficiency or synaptic density. One consequence of these changes could be to impact the effectiveness of memory consolidation. We have submitted this manuscript, have received feedback from reviewers, and we are currently working on revisions.

14. Collaborative programs with non-McKnight institutions and research programs:

Gazzaley/Burke/Barnes/Erickson/Gray/Smith

With funds from the first McKnight gift, we collaborated in the design and conduct of a series of behavioral studies that were designed and completed in our young and old bonnet macaques

that examined the effects of distraction and interruption forms of interference on delay non-matching to sample task performance. These tests were all designed to be conceptually comparable to those that Dr. Adam Gazzaley had conducted in older humans, and for which he found that older individuals are disproportionately affected by distractors in a variety of tasks. The tasks developed for the bonnet macaques were all conducted using the manual version of the Wisconsin General Testing Apparatus for the interference tasks (Burke/Plange). We have adapted these behavioral tasks using a computer-controlled apparatus, with responses made using a joy stick (Gray/Erickson) to begin to prepare for the next stage of our experiments that will simultaneously record electrophysiological signals from the prefrontal cortex while the monkeys are performing the memory tests. A new addition to the collaborators involved in these experiments is Dr. Anne Smith, who has applied her state space model algorithms to these behavior data, and used these analyses for preliminary data for the submission of a grant to support the continuation of this work, which was funded last fall (AG050548). This work was also presented in abstract form at the Society for Neuroscience meeting (Gray et al., 2015). We have a target to complete a manuscript with these finding early next year.

Beach/Barnes/Engle/Dugger

Although it appears that no other animal other than humans develop the hallmark neuropathological markers of Alzheimer's disease (amyloid plaques and neurofibrillary tangles), a variety of animals have been found to have some amyloid accumulation, and others scattered intraneuronal tangles. Because of Barnes' tissue bank of behaviorally-characterized rhesus macaques, a systematic analysis can be done in these animals of the distribution and extent of the appearance of these markers in the monkey brain in relation to memory. Barnes has now identified tissue samples from 29 young and aged monkeys that have been sent to Tom Beach for staining of amyloid and tau distribution in these brains. With funds from the first McKnight gift, the last of the tissue sections were stained, and Dr. Beach (lead Neuropathologist for the Alzheimer's Core Center in Arizona) has completed the neuropathological assessments. The present data constitute the only thorough cognitive/tau and amyloid deposition analysis in the primate that exists, and thus provides the materials to prepare a landmark manuscript. Barnes is currently working to write this manuscript up – Engle and Dugger now have positions elsewhere, but we hope we will be able to finish a first draft, and discuss it with Beach by next spring.

Konhilas/Barnes/Glisky/Ryan

Dr. John Konhilas is a Professor in the Physiology Department at the University of Arizona. He is interested in the microbiome of the gastrointestinal system, and its effect on the immune system, and recovery from myocardial infarction in a mouse model of heart failure. After the grant (RO1AG049465) was awarded to me to understand factors that contribute to different levels of cognitive competency, we began to discuss whether the microbiome may influence individual differences in cognitive function in aging rodents who have been identified as “low, average, or high” performers for their age (this is done in young, middle-aged and old rats). Each of these rats goes through a cognitive test battery, is given structural and diffusion tensor MRI scans, is given an exploration behavior treatment before sacrifice so that catFISH analysis of behavior-activated circuits can be assessed in one hemisphere, and the other hemisphere undergoes region-targeted laser capture microdissection and deep sequencing to assess genetic differences in these animals. Konhilas' lab has tutored us in gut dissection that we have added

to this complex, but thorough analysis of cognitive aging. We are now expert in collecting contents and epithelial cells at 7 levels of the gastrointestinal tract at the time of sacrifice. This will be the most thorough examination to date of brain-gut interactions, specifically with a focus on cognition. Drs. Glisky and Ryan are also interested in collecting fecal samples from their high and low performing older individuals to determine if this ‘coarser analysis’ will reveal biota that tend to be correlated with successful cognitive aging. We will pursue these questions in the next year.

15. Plans for future research

We are in a strong position for the coming year to conduct significant research, as I was awarded three new ROIs in 2014, a fourth ROI was awarded in the fall 2015 and a fifth was awarded in January 2016. This should allow the lab to build on the strong foundation that was built by the investment that the McKnight Brain Research Foundation provided when it began the Evelyn F. McKnight Brain Institute in Tucson. The experiments proposed in these five grants all extend both the electrophysiological and single cell imaging molecular work in aging rats and nonhuman primates (the work the Institute was originally funded to do) and should allow us to make significant progress on both fronts. The experiments in which I am embarking, however, are not ‘quick tests, which give partial answers’. Rather, they are lengthy, complex and difficult to execute and to organize. One thing that my laboratory is known for is its ‘thorough work’ and experiments that use the most powerful tools available to answer questions about the aging brain and cognition. These studies take time, persistence and coordination. While I wish we could provide ‘answers by tomorrow’, it will take some time to be sure of ‘the right answers’ – although there may be things that “pop out” quickly and can be tested on a fast track for treatment purposes. My collaborators at UA and across the Institutes continue to build the collaborative atmosphere that make all of our Institutes stronger and better able to gain the tools needed to optimize our cognitive healthspan as we age.

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

No

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


No

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

Yes

20. Negative Events

No



Carol A. Barnes, Ph.D.
Director, Evelyn F. McKnight Brain Institute