



**University of Arizona
Evelyn F. McKnight Brain Institute**

Annual Report

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

Scientific Report Period: January 1, 2016 – December 31, 2016

Financial Report Period: July 1, 2015 – June 30, 2016

Institution: University of Arizona

Submitted January 14, 2017

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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. The manuscripts reported as progress below make use of the behavioral, recording and/or imaging technologies that we have pioneered here in Tucson.

Manuscripts describing original data on topics critical to the aging brain and memory **using these and other methods that were published during 2016**, include the following:

Together with my colleague, and Tucson Evelyn F. McKnight Institute Affiliate member Lalitha Madhavan, we report in Corenblum et al. that the redox-sensitive transcription factor Nrf2 mediates the decline in neural stem cell function during a critical period in middle age. Aging is characterized by diminished brain plasticity, including the reduced functioning of neural stem cells, which possess the ability to regenerate, repair and protect cell function and homeostasis. Thus, understanding age-related deterioration of stem cell populations may hold a key to discovering approaches for promoting healthy aging. We were able to identify a key time period during which there is a precipitous reduction in the survival and regeneration of neural stem cells that is mediated by reduced expression of Nrf2. We are now working on targeted neural stem cell-based strategies that can be used to promote stem cell and cognitive health.

Together with my colleague Farah Lubin at the Alabama Evelyn F. McKnight Institute, we report in Penner et al. that in aging hippocampus, there is a CpG site-specific change in methylation in DNA associated with the promoter region of the memory-associated Egr1 gene. This immediate early gene is necessary for long term plasticity and memory consolidation, and a number of observations suggest that DNA methylation is a key epigenetic mechanism that serves to regulate gene transcription within the hippocampus in response to behavioral experience. In our experiment we demonstrate hippocampal subregion-specific transcriptional and epigenetic changes that may point to a unique compensatory mechanism used by aging hippocampal granule cells. This suggests therapeutic approaches that involve manipulation of DNA methylation in specific cell types as a strategy for promoting brain function and health.

Together with my colleague, and Tucson Evelyn F. McKnight Institute Affiliate member Stephen Cowen, we report in Wiegand et al. that the network in the CA1 region of the hippocampus in aged animals has a reduced 'vocabulary' of available representational states. The consolidation of episodic memory is believed to depend on the precise coordination of networks of neurons in the hippocampus and neocortex. The "ripple oscillation" in the

hippocampus represents a key component of the coordination between hippocampal and cortical neurons, as these cells have been shown to preferentially communicate during ripple events, and there is a strong association between these ripple events and memory consolidation. The finding that there is reduced occurrence of ripple events in old rats suggests an impact on the effectiveness of memory consolidation in older animals. This observation suggests promising new avenues for investigating how aging alters network computations.

In the Thome et al. 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.

The Witharana et al. manuscript uses the advantages of the catFISH technique to assess the distribution of activity in much larger populations of neurons in freely behaving animals than is possible with current electrophysiological recording methods. We assessed gene expression and unit recording data to examine in detail the question of how many neurons in the hippocampus are likely to be completely silent in selected behavioral tasks, and whether each cell has an equal probability of being allocated at random to fire in a given location. The data suggest a non-uniform activation probability among hippocampal cells. This skewed distribution of probability of a given cell to have a place field is reminiscent of some sensory processing systems, and may enhance coding capacity and flexibility in the hippocampus for episodic memory formation and retrieval.

In the Engle et al. manuscript we report how normal aging alters whole-brain networks involved in spatial navigation behaviors in old compared to young nonhuman primates. We used high resolution positron emission tomography (microPET) to capture the brain activity of real-world behaviors as monkeys actively or passively (were moved in a chair) traversed an environment or walked on a treadmill. The results revealed consistent networks activated by these behavior conditions that were similar across age. For the young animals, however, the coactivity patterns were distinct between conditions, whereas older animals tended to engage the same networks in each condition. The combined observations of less differentiated networks between distinct behaviors and alterations in functional connections between targeted regions in aging suggest changes in network dynamics as one source of age-related deficits in spatial cognition.

Together with my colleague Adam Gazzaley (at UCSF), we examined in Gray et al. behavioral tasks that were designed to be similar to ones that Gazzaley has used in human aging studies. One of the hallmarks of the normal cognitive aging process involves alterations in executive function. While some components of executive function (set shifting and inhibition) have been studied in aged monkeys, other components have not been assessed until now. We examined how aging impacts attentional updating and monitoring processes in monkeys using an

interference task designed after a paradigm used to examine multi-tasking in older humans, and an object reversal task. Interestingly, the levels of performance in the object reversal task were not correlated with levels of performance in the interference task, suggesting that normal aging affects distinct prefrontal networks and these two executive functions independently.

Together with my colleague, and Tucson Evelyn F. McKnight Institute Affiliate member Meredith Hay, we report in Hay et al. the development of a novel preclinical model of congestive heart failure, with the goal of preventing 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 angiotensin 1-7 for 4 weeks showed significantly less cognitive impairment than did nontreated mice, but the treatment had no effect on cardiac function. Data from inflammatory plasma biomarkers in these mice suggests that Ang-(1-7) produces significant neuroprotection resulting in memory preservation.

2. Publications in peer reviewed journals

From Barnes

- Corenblum, M.J., Ray, S., Remley, Q.W., Long, M., Harder, B., Zhang, D.D., Barnes, C.A. and Madhavan, L. (2016) Reduced NrF2 expression mediates the decline in neural stem cell function during a critical middle-age period. *Aging Cell*, 4:725-736.
- 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.
- Wiegand, J.-P., Gray, D.T., Schimanski, L.A., Lipa, P., Barnes, C.A., Cowen, S.L. (2016) Age is associated with reduced sharp-wave ripple frequency and altered patterns of neuronal variability. *The Journal of Neuroscience*, 36:5650-5660.
- 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.
- Witharana, W.K.L., Cardiff, J., Chawla, M.K., Xie, J.Y., Alme, C.B., Eckert, M., Lapointe, V., Demchuk, A., Maurer, A.P., Trivedi, V., Sutherland, R.J., Guzowski, J.F., Barnes, C.A. and McNaughton, B.L. (2016) Nonuniform allocation of hippocampal neurons to place fields across all hippocampal subfields. *Hippocampus*, 26:1328-1344.
- 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.
- Gray, D.T., Smith, A.C., Burke, S.N., Gazzaley, A. and Barnes, C.A. (2016) Attentional updating and monitoring and affective shifting are impacted independently by aging in the macaque monkeys. *Behavioral Brain Research*, in press. doi: 10.1016/j.bbr.2016.06.056.
- Hay, M., Vanderah, T.W., Samareh-Jahani, F., Constantopoulos, E., Uprety, A.R., Barnes, C.A., and Konhilas, J. (2016) Cognitive impairment in heart failure: A protective role for Angiotensin-(1-7). *Behavioral Neuroscience*, in press.

From Selected Affiliates

- Filon, J.R., Intorcchia, A.J., 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., Jaconson, S., Shill, H.A., Driver-Dunckley, E., Chen, K., Reiman, E.M., Beach, T.G. and Serrano, G.E. (2016) Gender differences in Alzheimer disease: Brain atrophy, histopathology burden, and cognition. *Journal of Neuropathology & Experimental Neurology*, 75:748-754.
- Marquine, M.J., Grilli, M.D., Rapcsak, S.Z., Kaszniak, A.W., Ryan, L., Walther, K., and Glisky, E.L. (2016) Impaired personal trait knowledge, but spared other-person trait knowledge, in an individual with bilateral damage to the medial prefrontal cortex. *Neuropsychologia*, 89:245-253.
- 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.
- Mittelman-Smith, M.A., Krajewski-Hall, S.J., McMullen, N.T. and Rance, N.E. (2016) Ablation of KNDy neurons results in hypogonadotropic hypogonadism and amplifies the anterior-induced LH surge in female rats. *Endocrinology*, 157:2015-2027.
- Nguyen, L.A., Haws, K.A., Fitzhugh, M.C., Torre, G.A., Hishaw, G.A. and Alexander, G.E. (2016) Interactive effects of subjective memory complaints and hypertension on learning and memory performance in the elderly. *Neuropsychol Dev Cogn B Aging Neuropsychol Cognition*, 23:154-170.
- Okun, A., McKinzie, D.L., Witkin, J.M., Remeniuk, B., Husein, O., Gleason, S.D., Oyarzo, J., Navratilova, E., McElroy, B., Cowen, S.L., Kennedy, J.D., Porreca, F. (2016) Hedonic and motivational responses to food reward are unchanged in rats with neuropathic pain. *Pain* 157:2731–2738.
- Raichlen DA, Bharadwaj PK, Fitzhugh MC, Haws KA, Torre GA, Trouard TP, & Alexander GE. (2016) Differences in resting state functional connectivity between young adult endurance athletes and healthy controls. *Frontiers in Human Neuroscience*, 10:610.
- Sherman, S.M., Buckley, T.P., Baena, E., Ryan, L. (2016). Caffeine Enhances Memory Performance in Young Adults during Their Non-optimal Time of Day. *Front Psychol*, 14:7:1764.
- Wiegand, J-P.L., Gray, D.T., Schimanski, L.A., Lipa, P., Barnes, C.A., Cowen, S.L. (2016) Age Is Associated with Reduced Sharp-Wave Ripple Frequency and Altered Patterns of Neuronal Variability. *J Neurosci* 36:5650–5660.
- Alexander GE. (2017) An emerging role for imaging white matter in the preclinical risk for Alzheimer’s disease - Linking β -amyloid to myelin. *JAMA Neurology*, in press. (Invited Editorial)

3. Publications (other)

From Selected Affiliates

- New York Times Commentary on Raichlin, Bharadwaj, Fitzhugh, Haws, Torre, Trouard, Alexander). Running as the Thinking Person’s Sport. , December 14, 2016. <http://www.nytimes.com/2016/12/14/well/move/running-as-the-thinking-persons-sport.html>

4. Presentations at scientific meetings

From Barnes

- Barnes, C.A. Does the neural hardware in archicortex of birds, turtles, rats and monkeys perform similar computations? Neuroscience Community Data Blitz, Museum of Contemporary Art, Tucson, AZ, January 2016. (Invited)
- Corenblum, M.J., Ray, S., Long, M., Harder, B., Zhang, D.D., Barnes, C.A. and Madhavan, L. A novel role of Nrf2 in the age-related decline in neural stem cell function. Stem Cell Models of Neural Regeneration and Disease, Dresden, Germany, February 2016. (Abstract)
- Barnes, C.A. Hippocampal cell activity in unrestrained nonhuman primates, session: Place cells across animal species, Winter Conference on Neural Plasticity, Maui, HI, February 2016. (Invited)
- Barnes, C.A. Impact of normal aging on circuits critical for Memory, Neuroscience and Animal Behavior Graduate Program Lecture Series, Emory University, Atlanta, GA, February 2016. (Invited)
- Barnes, C.A. Aging is not a disease: normal lifespan changes in brain circuits critical for memory, William G. Lutte Lectureship in Neuroscience, University of Florida, Gainesville, FL, March 2016. (Invited)
- Barnes, C.A. Cognition/Perception: Primate work on normative brain and cognitive aging, International Future Primate Neuroscience Symposium, Shenzhen Institute of Advanced Technology Shenzhen, China, March 2016. (Invited)
- Nguyen, M., Chawla, M.K., Barnes, C.A. Arc fluorescence in situ hybridization in cleared whole brains utilizing hybridization chain reaction amplification. American Society for Biochemistry and Molecular Biology 2016 Annual Meeting, San Diego, CA, April 2016. (Abstract)
- Wang, C., Pacheco, S., Baggett, B., Chawla, M., Gray, D., Utzinger, U., Barnes, C.A., Liang, R., Whole brain imaging with a scalable microscope, Clinical and Translational Biophotonics Conference, Ft. Lauderdale, FL, April 2016. (Abstract)
- Comrie, A.E., Gray, D.T., Burke, S.N., Smith, A.C., Barnes, C.A. Different monkey models of human cognitive aging exhibit disparities in learning and performance of memory tasks, 20th Annual Posters on the Hill, Washington, DC, April 2016. (Abstract)
- Barnes, C.A. Impact of aging on temporal lobe circuits critical for memory, Special Seminar, Kyoto University, Kyoto Japan, April 2016. (Invited)
- Barnes, C.A. Impact of normal aging on brain circuits critical for memory function, Special Seminar, Okinawa Institute, Okinawa, Japan, April 2016. (Invited)
- Barnes, C.A. Normative brain aging: Why does it result in memory impairments? Neuroscience Research Colloquia, University of British Columbia, Vancouver, Canada, May 2016. (Invited)
- Barnes, C.A. Impact of aging on brain circuits critical for memory. Stanford Neuroscience Institute Seminar Series, Stanford University, Los Angeles, CA, May 2016. (Invited)
- Barnes, C.A. Recent progress in recording from completely unrestrained primates. 1st Interdisciplinary Navigation Symposium, Bad Gastein, Austria, June 2016. (Invited)
- Barnes, C.A. Impact of aging on circuits critical for normal memory function. John G. Nicholls Lecture, Neural Systems and Behavioral Course, Marine Biological Laboratory, Woods Hole, MA, July 2016. (Invited)

- Barnes, C.A. Impact of aging on brain circuits critical for memory (Keynote address). 6th International Conference on Memory, Budapest, Hungary, July 2016. (Invited)
- Barnes, C.A. Memory circuits in normal aging: excitability and adaptation. GRC on Mechanisms of Epilepsy and Neuronal Synchronization, Melia Golf Vichy Catalan Business and Convention Center, Girona, Spain, August 2016. (Invited)
- Corenblum, M.J., Ray, S., Zhang, D.D., Barnes, C.A., and Madhavan, L. (2016) An analysis of nrf2 expression and its effects on aging hippocampal neural stem cell function. Program No. 177.17. 2016 Neuroscience Meeting Planner. San Diego, CA: Society for Neuroscience. Online.
- Ianov, L. De Both, M.D., Chawla, M.K., Rani, A., Kennedy, A.J., Piras, I., Day, J.J., Siniard, A.L., Kumar, A., Sweatt, J.D., Barnes, C.A., Huentelman, M., and Foster, T.C. (2016) Transcriptomic profile for determining regional vulnerability to age and cognitive impairment. Program No. 182.05. 2016 Neuroscience Meeting Planner. San Diego, CA: Society for Neuroscience. Online.
- De Both, M., Ianov, L., Chawla, M.K., Rani, A., Kennedy, A.J., Piras, I., Day, J.J., Siniard, A.L., Kumar, A., Sweatt, J.D., Foster, T.C., Barnes, C.A. and Huentelman, M.J. (2016) Transcriptional differences among hippocampal subregions. Program No. 182.06. 2016 Neuroscience Meeting Planner. San Diego, CA: Society for Neuroscience. Online.
- Bleul, C., Chawla, M.K., Carey, N.J., Siniard, A.L., De Both, M.D., Barnes, C.A., and Huentelman, M.J. (2016) Activity regulated transcript identification in the hippocampus and the genetic association with AD risk. Program No. 182.07. 2016 Neuroscience Meeting Planner. San Diego, CA: Society for Neuroscience. Online.
- Chawla, M.K., Nguyen, C., Sadachar, G.S., Gray, D.T., Huentelman, M.J., and Barnes, C.A. (2016) *Arc* mRNA induction thresholds following electro-convulsive shock treatment may be regulated by dendritic Ca⁺⁺ plateau potentials. Program No. 182.08. 2016 Neuroscience Meeting Planner. San Diego, CA: Society for Neuroscience. Online.
- Comrie, A.E., Lister, J.P., Chawla, M.K., and Barnes, C.A. (2016) Activation of neuronal populations in young and aged rat Lateral Entorhinal Cortex during track-running behavior with odors. Program No. 182.09. 2016 Neuroscience Meeting Planner. San Diego, CA: Society for Neuroscience. Online.
- Lester, A.W., Kapellusch, A.J., Screen, R.T., and Barnes, C.A. (2016) Aged rats fail to integrate conflicting spatial reference frames. Program No. 182.10. 2016 Neuroscience Meeting Planner. San Diego, CA: Society for Neuroscience. Online.
- Gray, D.T., Wiegand, J.-P., Schimanski, L.A., Cowen, S.L., and Barnes, C.A. (2016) Age-related reduction in signal-to-noise ratio of sharp-wave ripple oscillations following behavior in aged rats. Program No. 182.11. 2016 Neuroscience Meeting Planner. San Diego, CA: Society for Neuroscience. Online.
- Samson, R.D., Duarte, L., and Barnes, C.A. (2016) Expectation of large rewards elicits bursts of beta-band oscillations in the aged rat amygdala. Program No. 182.12. 2016 Neuroscience Meeting Planner. San Diego, CA: Society for Neuroscience. Online.
- Umaphathy, L., Gray, D.T., Burke, S.N., Trouard, T.P. and Barnes, C.A. (2016) Uncinate fasciculus integrity assessed in young and aged bonnet macaques. Program No. 182.13. 2016 Neuroscience Meeting Planner. San Diego, CA: Society for Neuroscience. Online.
- Andersh, K.M., Gray, D.T., Smith, A.C., Burke, S.N., Gazzaley, A. and Barnes, C.A. (2016) Age-related attentional control and set shifting impairments arise independently in macaque

- monkeys. Program No. 182.14. 2016 Neuroscience Meeting Planner. San Diego, CA: Society for Neuroscience. Online.
- Pyon, W., Gray, D.T., Andersh, K.M., Permenter, M.R., Vogt, J.A., and Barnes, C.A. (2016) Cell counts of midbrain dopamine neurons in memory-impaired aged non-human primates. Program No. 182.15. 2016 Neuroscience Meeting Planner. San Diego, CA: Society for Neuroscience. Online.
- Kyle, C.T., Bennett, J.L., Stokes, J.D., Permenter, M.R., Vogt, J.A., Ekstrom, A.D., and Barnes, C.A. (2016) Histology informed probabilistic hippocampal atlases of young and old rhesus macaques. Program No. 182.16. 2016 Neuroscience Meeting Planner. San Diego, CA: Society for Neuroscience. Online.
- Madhavan, L., Corenblum, M.J., Ray, S., Long, M., Harder, B., Zhang, D.D., and Barnes, C.A. (2016) Targeting the Nrf2 pathway to improve neural stem cell function. Program No. 198.07. 2016 Neuroscience Meeting Planner. San Diego, CA: Society for Neuroscience. Online.

From Selected Affiliates

- Alexander, G.E. Imaging the aging brain: Implications for clinical-translational research. Arizona Research Institute for Biomedical Imaging Spring Workshop, University of Arizona, Tucson, AZ, April 2016. (Invited)
- Barney, S.P.M., Macris, D.G., Polsinelli, A.J. and Glisky, E.L. Self-compassion is associated with social connection and support in older adults. Cognitive Aging Conference, Atlanta, GA, April 2016. (Abstract)
- Woolverton, C., Breitborde, N.J.K. and Glisky, E.L. Self-imagining improves memory in individuals with first-episode psychosis. International Neuropsychological Society, Boston, MA, February 2016. (Abstract)
- Cowen, S.L. Effort-reward decision making: Neural systems and neuromodulation, Emory University. "Atlanta, GA, March 2016. (Invited)
- Cowen, S.L. Simultaneous Detection of Dopamine Release and Multiple Single-Unit Activity in Awake and Behaving Rats, Pittcon National Convention, Atlanta, GA March 2016. (Invited)
- Wiegand, J.P., Geis, K., Bartlett, M.J., Falk, T. and Cowen, S.L. Increased power of sleep spindle oscillations in the LRRK2 mouse model of Parkinson's disease. 4th World Parkinson's Congress. San Diego, CA, September 2016.
- Ye, T., Bartlett, M.J., Schmit, M., Sherman, S.J., Falk, T. and Cowen, S.L. Gamma-band oscillatory activity in the motor cortex is progressively enhanced following repeated ketamine administration in 6-OHDA-lesioned rats. 4th World Parkinson's Congress. San Diego, CA, September 2016.
- Cowen, S.L. Brains, oscillations, aging, and Parkinson's disease", Undergraduate Program in Biology, University of Arizona, May 2016. (Invited)
- Boudreau, C., Miramontes, S., Feld, S., Polsinelli, A.J. and Glisky, E.L. Dispositional mindfulness is higher among older compared to younger adults. Cognitive Aging Conference, Atlanta, GA, April 2016. (Abstract)
- Fang, X., Huynh, K., Ritchie, H., Polsinelli, A.J. and Glisky, E.L. Dispositional mindfulness is associated with better working memory in older adults. Cognitive Aging Conference, Atlanta, GA, April 2016. (Abstract).

- Marquez, J.O., Macris, D.G., Polsinelli, A.J. and Glisky, E.L. Dispositional mindfulness is associated with fewer everyday cognitive failures in older adults. Cognitive Aging Conference, Atlanta, GA, April 2016. (Abstract).
- Lawrence, A., Ryan, L. Recognition Memory Context Effects in Aging. Cognitive Neuroscience Society Annual Meeting. New York, NY, April 2016.
- Marrone, N., Moseley, S., Shehorn, J. and Glisky, E.L. (Hearing loss, cognition and healthy aging. Workshop presented at the Arizona Speech-Language-Hearing Association Convention. Tucson, AZ, April 2016. (Abstract)
- Alexander, G.E. Roadmap to healthy aging: Building connections through advancing research. Columbine Health Systems Center for Healthy Aging, Colorado State University, Fort Collins, CO, May 2016. (Invited)
- Alexander, G.E. Neuroimaging of the aging brain: Implications for clinical-translational research. Department of Psychiatry, Oregon Health & Science University, Portland, OR, May 2016. (Invited)
- Alexander, G.E. Imaging the aging brain: Implications for healthy aging and the risk for Alzheimer's disease. Human Magnetic Resonance Imaging Center, Institute for Applied Life Sciences, University of Massachusetts, Amherst, MA, May 2016. (Invited)
- Cowen, S.L. Ketamine and its impact on corticostriatal-limbic interactions, Taormina Pain Mechanisms and Therapeutics Conference, Taormina, Italy, June 2016. (Invited)
- Cowen, S.L. Identification of network and oscillatory signatures of the LRRK2 mutation, Michael J Fox Foundation Consortium Progress Update, Video Presentation, October 2016. (Invited)
- Bharadwaj, P.K., Nguyen, L.A., Haws, K.A., Hishaw, G.A., Trouard, T.P., Alexander, G.E. Differential regional alterations of white matter integrity in healthy cognitive aging. Society for Neuroscience Annual Meeting, San Diego, CA, November 2016.
- Franchetti, M., Bharadwaj, P.K., Nguyen, L.A., Haws, K.A., Fitzhugh, M.C., Hishaw, G.A., Raichlen, D.A., Alexander, G.E. Relation of physical sport activity to cognitive performance in older adults. Society for Neuroscience Annual Meeting, San Diego, CA, November 2016
- Lawrence, A., Ryan, L. Familiar context effects on pattern separation in aging. Society for Neuroscience Annual Meeting, San Diego, CA, November 2016.
- Memel, M.B., Ryan, L. An fMRI analysis of visual unitization and the age-related associative memory deficit. Society for Neuroscience Annual Meeting, San Diego, CA, November 2016.
- Nguyen, L.A., Bharadwaj, P.K., Haws, K.A., Hishaw, G.A., Trouard, T.P., Alexander, G.E. Differential effects of hypertension status and white matter hyperintensity volume on white matter integrity in older adults. Society for Neuroscience Annual Meeting, San Diego, CA, November 2016.
- Stickel, A., Walther, K., Huentelman, M., Ryan, L. FTO gene and BMI interact to predict white matter integrity in late middle age and older adults. Society for Neuroscience Annual Meeting, San Diego, CA, November 2016.
- Weigand, J.-P., Gies, K., Bartlett, M., Falk, T., Cowen, S. Stronger cortical spindles and less power variability in hippocampal ripples in a LRRK2 mouse model in Parkinson's disease. Society for Neuroscience Annual Meeting, San Diego, CA, November 2016.
- Cowen, S.L. Brains, oscillations, aging, and Parkinson's disease, University of Arizona Neural Systems and Cognitive Sciences Seminar, Tucson AZ, December 2016. (Invited)
- Cowen, S.L. Synchronous neuronal activity, Parkinson's disease, and ketamine, UA Brain Initiative Collaboration Data Blitz, Tucson, AZ, December 2016. (Invited)

Cowen, S.L. A system for the combined measurement of dopamine and neural activity (DANA), NSF/NIH Brain Initiative Investigators Meeting, Bethesda, MD, December 2016. (Invited)

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

From Barnes

Barnes, C.A. How does normal aging affect brain function and memory? Institute of Learning at Sun City Sampler Series, Catalina Visa Center in Sun City, Oro Valley, AZ, January 2016. (Invited)

Lukas, R., Bowser, R., Fulton, G.W., Wesslehoft, M., Barnes, C.A. (Panel Discussion), Beyond Alzheimer's, Cavendish Health Impact Forum sponsored by Arizona Bioscience Community, Phoenix, AZ, September 2016.

From Selected Affiliates

Glisky, E.L. (January, 2016). Memory and other changes with age: What we're trying to do about it. Voyager RV Resort and Hotel, Tucson, AZ, January 2016.

Alexander, G.E. Can technology enhance healthy lifestyles and brain fitness? Annual Conference on Successful Aging, Tucson, AZ. March 2016.

Ryan, L. Good for the heart, good for the brain: The connection between cardiovascular health and maintaining brain health as we age. Presentation for Sarver Heart Center and the Women's Heart Health Education Committee. Swede Johnson Building, Tucson, AZ. January 19, 2016.

Ryan, L. Lunch Round-Table Panel Presenter at Pain & Your Brain: Living Healthy with Arthritis Conference. Tucson, AZ. January 23, 2016.

Ryan, L. Good for the heart, good for the brain: Neuroimaging studies of healthy brain aging. Presentation for Banner University Medical Center Friends. Skyline Country Club, Tucson, AZ. January 28, 2016.

Ryan, L. Good for the heart, good for the brain: The connection between cardiovascular health and maintaining brain health as we age. Heart Month Series for TMC for Seniors. Tucson, AZ. February 3, 2016.

Ryan, L. How Technology is Changing the Face of Aging. Co-director and presentation at the 4th Joan Kaye Cauthorn Annual Conference on Successful Aging. Tucson, AZ. March 1, 2016.

Alexander, G.E. Staying mentally fit by being cognitively active. Kinghorn Heritage Law Group. Tucson, AZ. April 2016.

Ryan, L. Eating Your Way to Healthy Aging: Enhancing Cognitive Function Through Food. Positive Aging for Women Conference. Tucson, AZ. October 13, 2016.

Ryan, L. and Sweitzer, N.K. Thinking from the Heart: How to protect the brain in patients with heart disease. Sarver Heart Center's 30th Anniversary Community Lecture Series. Tucson, AZ. December 14, 2016

6. Awards (from McKnight Affiliates)

Lynn Nadel, Ph.D., Lifetime Achievement Award from the Society of Experimental Psychologists (2016).

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** being comprised of Dr. Eric Reiman, Dr. Leslie Tolbert and Dr. Martha Brumfield and the **Scientific Advisory Board** being made up of Geoff Ahern, Gene Alexander, Stephen Cowen, Betty Glisky, Naomi Rance, and Lee Ryan.

The search for the Director of the “**Center for Innovation in Brain Science**” in the Health Sciences Center was finalized last year, and resulted in 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. Roberta Brinton. Her research focuses on the brain, the most energetically demanding organ of the body. Because of this energetic demand, the brain is acutely vulnerable to reduction in fuel supply, metabolic capacity and mitochondrial generation of ATP. Her research has shown that the bioenergetic aging of the brain is a potential driver of the lifetime risk for cognitive decline in normal aging, and the susceptibility with aging to neurodegenerative disease. She is a basic scientist, with a specialization in systems biology. But she is also a translational scientist, as she has taken her research findings from the bench - that demonstrated that ovarian steroids and neurosteroids are key mechanistic regulators of the bioenergetic and regenerative systems of the brain – to clinical trials that are currently underway. She will be a strong partner in the Tucson Evelyn F. McKnight Brain Institute, as she is devoted to develop personalized interventions that target stages of bioenergetic aging in both the female and male brain to optimize the aging brain, and to prevent, delay and treat Alzheimer's disease. She is now Affiliated Faculty of the Institute.

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
- Roberta Diaz Brinton, P.D., Professor, Pharmacology, Neurology and Psychology; Director, Center for Innovation in Brain Science
- 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., 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., 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., 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., Professor and Director of Clinical Training, Department of Psychology, University of Arizona
- Anne C. Smith, Ph.D., Associate Research Scientist, EMBI, University of Arizona
- Ted P. Trouard, Ph.D., 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

2016 Publications

- Wiegand, J.-P., Gray, D.T., Schimanski, L.A., Lipa, P., Barnes, C.A., Cowen, S.L. (2016) Age is associated with reduced sharp-wave ripple frequency and altered patterns of neuronal variability. *The Journal of Neuroscience*, 36:5650-5660.
- Corenblum, M.J., Ray, S., Remley, Q.W., Long, M., Harder, B., Zhang, D.D., Barnes, C.A. and Madhavan, L. (2016) Reduced NrF2 expression mediates the decline in neural stem cell function during a critical middle-age period. *Aging Cell*, 4:725-736.
- 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.
- 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.
- Witharana, W.K.L., Cardiff, J., Chawla, M.K., Xie, J.Y., Alme, C.B., Eckert, M., Lapointe, V., Demchuk, A., Maurer, A.P., Trivedi, V., Sutherland, R.J., Guzowski, J.F., Barnes, C.A. and McNaughton, B.L. (2016) Nonuniform allocation of hippocampal neurons to place fields across all hippocampal subfields. *Hippocampus*, 26:1328-1344.
- Gray, D.T., Smith, A.C., Burke, S.N., Gazzaley, A. and Barnes, C.A. (2016) Attentional updating and monitoring and affective shifting are impacted independently by aging in the macaque monkeys. *Behavioral Brain Research*, in press. doi: 10.1016/j.bbr.2016.06.056.
- 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.
- Hay, M., Vanderah, T.W., Samareh-Jahani, F., Constantopoulos, E., Uprety, A.R., Barnes, C.A., and Konhilas, J. (2016) Cognitive impairment in heart failure: A protective role for Angiotensin-(1-7). *Behavioral Neuroscience*, in press.

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	Cited in S Naifeh and GW Smith (eds.), The Best Doctors in America, 2015-2016

2016 Publications

Filon, J.R., Intorcchia, A.J., 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., Rapsack, S.Z., Ahern, G.L., Burke, A.D., Jaconson, S., Shill, H.A., Driver-Dunckley, E., Chen, K., Reiman, E.M., Beach, T.G. and Serrano, G.E. (2016) Gender differences in Alzheimer disease: Brain atrophy, histopathology burden, and cognition. *Journal of Neuropathology & Experimental Neurology*, 75:748-754

BIOGRAPHICAL SKETCH

NAME		POSITION TITLE	
Gene E. Alexander, Ph.D.		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
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
2016 Special Topic Associate Editor, Special Topic on "Neuroimaging Approaches to the Study of Cognitive Aging", *Frontiers in Aging Neuroscience*

2016 Publications

Nguyen, L.A., Haws, K.A., Fitzhugh, M.C., Torre, G.A., Hishaw, G.A. and Alexander, G.E. (2016) Interactive effects of subjective memory complaints and hypertension on learning and memory performance in the elderly. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn*, 23, 154-70.
Raichlen, D.A., Bharadwaj, P.K., Fitzhugh, M.C., Haws, K.A., Torre, G.A., Trouard, T.P. and Alexander, G.E. (2016) Differences in resting state functional connectivity between young adult endurance athletes and healthy controls. *Frontiers in Human Neuroscience*, 10, 610. (Press: article featured in New York Times story)
Alexander, G.E. (2017) An emerging role for imaging white matter in the preclinical risk for Alzheimer's disease - Linking β -amyloid to myelin. *JAMA Neurology*, in press. (Invited Editorial)

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

2016 Publications

Okun, A., McKinzie, D.L., Witkin, J.M., Remeniuk, B., Husein, O., Gleason, S.D., Oyarzo, J., Navratilova, E., McElroy, B., Cowen, S.L., Kennedy, J.D., Porreca, F. (2016) Hedonic and motivational responses to food reward are unchanged in rats with neuropathic pain. *Pain* 157:2731–2738.

Wiegand, J-P.L., Gray, D.T., Schimanski, L.A., Lipa, P., Barnes, C.A., Cowen, S.L. (2016) Age Is Associated with Reduced Sharp-Wave Ripple Frequency and Altered Patterns of Neuronal Variability. *J Neurosci* 36:5650–5660.

NAME Elizabeth L. Glisky, Ph.D.		POSITION TITLE 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

2016 Publications

- 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
- Marquine, M. J., Grilli, M. D., Rapcsak, S. Z., Kaszniak, A. W., Ryan, L., Walther, K. and Glisky, E. L. (2016) Impaired personal trait knowledge, but spared other-person trait knowledge, in an individual with bilateral damage to the medial prefrontal cortex. *Neuropsychologia*, 89, 245-253.

BIOGRAPHICAL SKETCH

NAME		POSITION TITLE	
Naomi E. Rance, M.D., Ph.D.		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

2016 Publication

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

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 - present	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

2016 Publications

- Sherman, S.M., Buckley, T.P., Baena, E., Ryan, L. (2016). Caffeine Enhances Memory Performance in Young Adults during Their Non-optimal Time of Day. *Front Psychol*, 14;7:1764.
- Marquine, M.J., Grilli, M.D., Rapcsak, S.Z., Kaszniak, A.W., Ryan, L., Walther, K., & Glisky, E.L. (2016). Impaired personal trait knowledge, but spared other-person trait knowledge, in an individual with bilateral damage to the medial prefrontal cortex. *Neuropsychologia*, 89:245-253.

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.

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

Kous Kondapalli (Barnes)

Area of Interest: Age related changes and cognitive performance levels in working memory across the entire life-span of rats

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

Stephanie Matijevic (Ryan)

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

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.

Minhkhoei Nguyen (Barnes)

Area of Interest: Whole brain clearing and using branched DNA labelling technique to map IEG expression in the cleared rat brain

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 cognition in socially isolated older adults

Ariana Stickel (Ryan)

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

Jean Paul (Cowen)

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

Cindy Woolverton (Glisky)

Area of Interest: Self-referential processing and emotional memory in normal aging and in older adults at genetic risk for Alzheimer's disease

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 Brewster (Koutia)

Alison Comrie (Gray/Lister)

Harshaan Dhaliwal (Carey)

Leroy Duarte (Samson)

Ali Gilliland (Chawla)

Koustubh Kondapalli (Chawla)

Kaitline Martin (Carey)

Christie Nguyen (Chawla)

Minhkhoei Nguyen (Chawla)

Revathi Pillai (Carey)

Surbhi Patel (Lester/Chawla)

Olivia Pietz (Carey)

Reena Puri (Chawla)

Wonn Pyon (Gray)

Walid Raslan (Carey)

Donna Sayegh (Carey)

Gayatri Sadachar (Chawla)

Udai Singh (Chawla)

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-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

Same as previous years – nothing new to report.

(c) Extramural funding - 2016

Grants Received – from Barnes (McKnight affiliate faculty underlined)

5 R01 AG003376-32 (PI: Barnes)

Title: Neurobehavioral Relations in Senescent Hippocampus

Dates: 12/08/16 – 11/30/17 (01/17 – 11/20 project period)

Amount: \$705,228/year total costs (\$618,272/year direct)

5 R01 AG012609-02 (PI: Barnes)

Title: Cell Assemblies, Brain Adaptation and Cognitive Aging

Dates: 06/01/16 – 05/31/17 (09/15 – 05/20 project period)

Amount: \$458,772/year total costs (\$307,382/year direct)

1 R01 AG049465-03 (PI: Barnes; co-I's: Alexander, Billheimer, Huentelman, Trouard)

Title: Neural System Dynamics & Gene Expression Supporting Successful Cognitive Aging

Dates: 08/01/16 – 03/31/17 (08/14 – 03/19 project period)

Amount: \$772,234/year total costs (\$581,747/year direct)

5 R01 AG049464-03 (PI's: Coleman, Barnes, Alexander; co-I's: Billheimer, Huentelman, Trouard)

Title: Epigenetic, Neuroimaging & Behavioral Effects of Hypertension in the Aging Brain

Dates: 09/30/16 – 05/31/17 (08/14 – 05/19 project period)

Amount: \$507,744/year total costs (\$447,322/year direct)

1 R01 AG048907-03 (PI's: Huentelman, Barnes, co-PI: Okuno)

Title: CATT: Development and Application of a Neuronal Cell Activity-Tagging Toolbox

Dates: 06/15/16 – 05/31/17 (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)
\$345,473/year total costs (\$261,045/year direct)

2 P30 AG019610-17 (PI: Reiman; co-I: Barnes, Director, Ad Hoc Review Program)

Title: Arizona Alzheimer's Disease Core Center Ad Hoc Review

Dates: 08/15/16 – 06/30/17 (9/16 – 6/21 project period)

Amount: \$24,476/year total costs (\$15,945/year direct) / UA Subcontract

State of Arizona, DHS Grant (PI: Barnes; co-I's: Konhilas, Ryan, Glisky, Watts, Lussier)

Title: Arizona Alzheimer's Consortium – Exploring the microbiome-gut brain axis: impact of microbial communities and their genes in aging

Date: 07/01/16 – 06/30/17

Amount: \$95,000/year direct costs

1 T32 AG044402-01A1 (PI: Barnes; co-I: Reiman, Coleman, Bimonte-Nelson, Huentelman)
Title: Postdoctoral Training, Neurobiology of Aging and Alzheimer's Disease
Dates: 05/15/16 – 04/30/17 (5/15 – 4/21 project period)
Amount: \$241,186/year total costs (\$223,320/year direct)

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

1 R01 AG049465-03 (PI: Barnes; co-I's: Alexander, Billheimer, Huentelman, Trouard)
As listed above.

1 R01 AG049464-03 (PI's: Coleman, Barnes, Alexander; co-I's: Billheimer, Huentelman,
Trouard)
As listed above.

2 P30 AG019610-17 (PI: Reiman; co-PI: Ahern)
Title: Arizona Alzheimer's disease Core Center (UA Clinical Core)
Dates: 08/15/16 – 06/30/17 (9/16 – 6/21 project period)
Amount: \$43,084/year total costs (\$31,358 direct)

State of Arizona, DHS Grant (PI: Ahern)
Title: Arizona Alzheimer's Consortium – Patient Recruitment and Outreach for
Alzheimer's disease and Related Disorders
Dates: 07/01/16 – 06/30/17
Amount: \$7,500/year direct costs)

State of Arizona, DHS Grant (PI: Alexander)
Title: Arizona Alzheimer's Consortium – Risk Factors for Brain Aging & Preclinical
Alzheimer's Disease
Dates: 07/01/16 – 06/30/17
Amount: \$69,000/year direct costs

2 R01 AG031581 (PI's: Reiman, Caselli; UA co-I: Alexander)
Title: Brain Imaging, 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 (\$9,531/direct costs - UA Subcontract)

McKnight Brain Research Foundation (UA PI: Alexander; UA Co-I's: Glisky, Ryan)
Title: McKnight Inter-institutional Cognitive Aging Assessment Core
Dates: 12/17/15 – 10/17/18
Amount: \$200,000 total

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 – 12/31/18
Amount: \$228,730 total 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

1 RO1 NS08026-03 (UC Davis Subcontract; UA PI: Cowen)

Title: Restoring Functional Connectivity following TBI

Dates: 02/15/16 – 01/31/17 (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)

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

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

Dates: 07/10/15 – 07/19/16

Amount: \$124,446.35 total costs (\$99,944 direct)

5 R32 MH109060-02 (PI: Witte; co-I: Cowen, Dunninghoff, Falk, Furenlid, Krupinski, Kunyansky, Weinand)

Title: High Resolution Electrical Brain Mapping by Real-Time and Portable 4D Acoustoelectric Imaging

Dates: 09/25/15 – 06/30/17

Amount: \$31,298.16 total annual costs

LuMind Foundation (PI: Edgin co-I: Cowen, Clark)

Title: Brain Development, Sleep and Learning in Down Syndrome

Dates: 07/01/16 – 06/30/17

Amount: \$12,500 total costs

State of Arizona, DHS Grant (PI: Glisky)

Title: Arizona Alzheimer's Consortium – Interventions to Improve Memory and Executive Function in Older Adults in Real-World Settings

Dates: 07/01/16 – 06/30/17

Amount: \$32,000/year direct costs

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

State of Arizona, DHS Grant (PI: Ryan)

Title: Arizona Alzheimer's Consortium – Memory Functioning in Heart Failure Patients with Risk for Alzheimer's Disease
Dates: 07/01/16 – 06/30/17
Amount: \$69,500/year direct costs

1 R01 AG047887-01 (PI: Rance)

Title: Role of preoptic NK3R neurons in the estrogen modulation of body temperature
Dates: 05/01/16 - 40/30/2017 (8/14 – 4/19 project period)
Amount: \$302,751/year total costs (\$197,877 direct)

Grants Submitted – from Barnes (McKnight affiliate faculty underlined)

1 F31 AG055263-01 (PI: Gray; Mentor: Barnes)

Title: Neurobiological Basis of Age-Related Deficits in Attentional Shifting and Monitoring
Dates: 01/01/17 – 12/31/19 (requested dates of project)
Amount: \$105,708 Total Direct Costs
Status: Awarded 1/1/17

2 P30 AG019610-17 (PI: Reiman; co-I: Barnes, Director, Ad Hoc Review Program)

Title: Arizona Alzheimer's Disease Core Center Ad Hoc Review
Dates: 08/15/16 – 06/30/21
Amount: \$24,476/year total costs (\$15,945/year direct) / UA Subcontract
Status: Awarded 8/15/16 (5-year competitive renewal)

2 P30 AG019610 Supplement (PI: Reiman; co-I's Alexander, Barnes, Ryan)

Title: Gore G: Brain Imaging and Fluid Biomarkers Core
Dates: 07/01/17 – 06/30/21 (requested dates of project)
Amount: \$77,549 Total Costs (59,232 Direct Costs) (Requested)
Status: Under Review

State of Arizona, DHS Grant (PI: Barnes; co-I's: Konhilas, Ryan, Glisky, Watts, Lussier)

Title: Arizona Alzheimer's Consortium – Exploring the microbiome-gut brain axis: impact of microbial communities and their genes in aging
Date: 07/01/16 – 06/30/17
Amount: \$69,000/year direct costs
Status: Awarded 7/1/16

Alzheimer's Association (PI: Ryan, co-I's Barnes, Coull, Grilli, Hay, Konhilas)

Title: Angiotensin (1-7) Treatment to Improve Cognitive Functioning in MCI
Dates: 05/01/16 – 4/30/18 (requested dates of project)
Amount: \$999,996 Requested Total Costs (\$920,384 Direct)
Status: Not Awarded

NIH R21 (PI: Oddo; co-I: Barnes)

Title: Chemogenetic Tools to Remotely Stimulate Neuronal Networks in Alzheimer's disease
Dates: 08/01/16 – 07/31/18 (requested dates of project)
Amount: \$38,270 Requested Total Cost (\$24,932 direct)
Status: Not Awarded

John D. and Catherine T. MacArthur Foundation (PI: Barnes; co-I's: Brinton, Lussier;
Collaborators: DeKosky, Huentelman, Freshwater, Sacco, Standaert)

Title: Precision Aging
Date: 07/01/2017 - 06/30/2020 (requested dates of project)
Amount: \$100,000,000 Total Costs (\$90,106,521 Direct)
Status: Under Review

1 R01 MH114231 (PI's: Ekstrom, Barnes)

Title: Hippocampal low-frequency oscillations across different scales and species
Dates: 09/01/17 – 08/31/21 (requested project dates)
Amount: \$550,757 total costs; \$367,091 direct (requested budget)
Status: Under review

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

2 P30 AG019610 Supplement (PI: Reiman; co-I Alexander, Barnes, Ryan)
As listed above

State of Arizona, DHS Grant (PI: Ahern)

Title: Arizona Alzheimer's Consortium – Patient Recruitment and Outreach for Alzheimer's disease and Related Disorders
Dates: 07/01/16 – 06/30/17 (requested)
Amount: \$7,500/year direct costs (requested)
Status: Awarded 7/1/16

State of Arizona, DHS Grant (PI: Alexander)

Title: Arizona Alzheimer's Consortium – Risk Factors for Brain Aging & Preclinical Alzheimer's Disease
Dates: 07/01/16 – 06/30/17 (requested dates of project)
Amount: \$69,000/year direct costs (requested budget)
Status: Awarded 7/1/16

Univ of Florida NIH sub (PI: Woods; UA PI: Alexander; UA co-I: Allen, Hishaw, Trouard)

Title: Augmenting Cognitive Training in Older Adults - The ACT Grant
Dates: 04/01/17 – 03/31/22 (requested dates of project)
Amount: \$1,474,341 total costs; \$960,483 direct (requested budget)
Status: Awarded FY 2016-2017

NIH (PI: Su; Co-I: Alexander)

Title: Ultra-sensitive and label-free detection of Alzheimer's disease biomarkers

Dates: 09/01/16 – 08/31/18 (requested dates of project)
Amount: \$164,056 total costs; \$109,177 direct (requested budget)
Status: Under review

UC California, Riverside (NIH Subcontract) (UA PI: Cowen)

Title: Electrical Modulation of Oscillations to Reduce Seizures and Improve Cognitive Function
Dates: 04/01/17 – 03/31/22 (requested dates)
Amount: \$125,309 total costs; \$81,635 direct (requested Budget)
Status: Under review

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

Title: Mechanisms of Low Dose Ketamine Treatment for Parkinson's Disease
Dates: 06/01/17 – 05/31/22 (requested dates)
Amount: \$1,845,582 total costs; \$1,348,521 direct (requested budget)
Status: Under review

NIH (PI: Miller; co-I: Cowen)

Title: Alpha-Synuclein Function in Neural Pathways for Vocal Communication
Dates: 07/01/17 – 06/30/19 (requested dates)
Amount: \$422,125 total costs; \$275,000 direct (requested budget)
Status: Under review

NIH (PI: Cowen; co-I: Falk)

Title: Identification of Network, Oscillatory, and Behavioral Signatures of LRRK2 Expression
Dates: 08/01/17 – 08/30/19 (requested dates)
Amount: \$249,999 total costs; \$199,999 direct (requested budget)
Status: Under review

State of Arizona, DHS Grant (PI: Glisky)

Title: Arizona Alzheimer's Consortium – Interventions to Improve Memory and Executive Function in Older Adults in Real-World Settings
Dates: 07/01/16 – 06/30/17 (requested)
Amount: \$32,000/year direct costs (requested)
Status: Awarded 7/1/16

NIH (PI: Glisky; co-I's Grilli, Sweitzer)

Title: Improving Medication Adherence in Heart Failure Patients: A prospective Memory Intervention
Dates: 09/01/16 – 08/31/18 (requested dates)
Amount: \$418,808 total costs; \$275,000 direct (requested budget)
Status: Not awarded

State of Arizona, DHS Grant (PI: Ryan)

Title: Arizona Alzheimer's Consortium – Memory Functioning in Heart Failure Patients with Risk for Alzheimer's Disease
Dates: 07/01/16 – 06/30/17 (requested)
Amount: \$69,500/year direct costs (requested)
Status: Awarded 7/1/16

NIH (PI: Sweitzer; co-I's: Bedrick, Hay, Khalpey, Konhilas, Ryan)

Title: Evaluation of the Safety and Efficacy of Angiotensin 1-7 to Enhance Cognitive Function in Participants Undergoing Coronary Artery Bypass (CABG) surgery
Dates: 12/01/16 – 11/30/20 (requested dates)
Amount: \$2,615,685 total costs; \$2,003,195 direct (requested budget)
Status: Award Pending – anticipated start date January 2017

NIH (PI: Grilli; co-I: Ryan)

Title: Autobiographical Memory Specificity Training: A Novel Cognitive Intervention for Older Adults
Dates: 04/01/17 – 03/31/19 (requested dates)
Amount: \$409,470 total costs; \$275,000 direct (requested budget)
Status: Under review

Alzheimer's Association (PI: Ryan, co-I's Barnes, Coull, Grilli, Hay, Konhilas)

Title: Angiotensin (1-7) Treatment to Improve Cognitive Functioning in MCI
Dates: 05/01/16 – 4/30/18 (requested dates of project)
Amount: \$999,996 Requested Total Costs (\$920,384 Direct)
Status: Not Awarded

12. Educational programs focusing on age related memory loss (2016)

Event: The Joan Kaye Cauthorn Annual Conference on Successful Aging:
How Technology is Changing the Face of Aging
Date: March 1, 2016
Organizers: Lee Ryan, Ph.D. and Gene Alexander, Ph.D.
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.

Event: Ninth Annual McKnight Inter-Institutional Meeting
Date: April 27 – 29, 2016
Organizer: Carol A. Barnes, Ph.D.
Venue: JW Marriott Tucson Starr Pass
Summary: This two day conference brought together over 90 scientists from the Tucson, Birmingham, Miami and Gainesville Evelyn F. McKnight Brain Institutes. Eighteen faculty drawn from each of the four McKnight Institutes were among the speakers at the meeting, and we were also joined by experts on memory and the aging brain from other institutions, who delivered 3 keynote addresses:

Claudia Kawas, M.D.
Professor of Neurology, School of Medicine University of California, Irvine
Successful aging: lessons from the oldest old

Scott A. Small, M.D.
Boris and Rose Katz Professor of Neurology, Columbia University
Regional vulnerability as a key to cognitive aging

Marilyn S. Albert, Ph.D.
Professor of Neurology, Director of Cognitive Neuroscience, The Johns Hopkins Hospital
Separating the earliest phase of Alzheimer's disease from age-related cognitive decline: the BIOCARD study



13. Collaborative programs with McKnight institutions and research programs

Sweatt, Day, Foster, Kumar, Huentelman, De Both, Barnes

The Inter-Institutional Epigenetics Core is close to finishing the first manuscript reporting the results of our collaborative experiments to characterize the transcription profiles across different subregions of the hippocampus that may help explain differential susceptibility to impairment in specific cognitive domains over the lifespan of the rat. The title is: "Transcriptomic analysis of the hippocampus during aging and differential cognitive performance." In our collaborative effort, we have taken advantage of two different next-generation sequencing technology platforms (Illumina HiSeq2500 and Ion Proton) to confirm differential expression that is associated with age and with cognition. The Illumina was used to generate seed lists of genes that were differentially expressed across age or cognitive function in each hippocampal

subregions (CA1, CA3, DG). The gene lists were then retested using the Ion Proton platform for validation of the results. The DG region showed the highest number of gene changes related to the age of the animal, including the greatest number of distinct genes, while region CA1 was most sensitive to changes in cognition. The second manuscript will describe in detail the performance of the Illumina and Ion Proton platforms, what questions these two technologies can be best targeted to, the advantages of using multiple sequencing platforms to validate findings, and will focus on subregion-specific expression differences independent of age or cognition. The final manuscript will examine whether changes in DNA methylation are responsible for the clear “age changes” in transcription that we found in DG, or the “cognitive changes” in transcription observed in CA1. These data will be used as background to inform and generate hypotheses concerning the pattern of genomic and epigenomic changes that may be expected across age and levels of cognitive competence in humans. With this information we plan targeted analyses using these predictions, in groups of cognitively characterized older humans that exist across the McKnight Institutes.

Burke, Barnes, Bauer, Bizon, Roberson, Ryan

We are working on a review entitled: *The Perirhinal Cortex Comes of Age: Perception, Discrimination and Recognition Memory Across the Lifespan*. This is a collaborative effort by researchers at multiple Evelyn F. McKnight Brain Institutes who ask questions regarding the neurobiological basis of cognitive decline in aging, with a focus on the perirhinal cortex. In this review, we propose a framework that accounts for discrepancies in published reports regarding perirhinal cortical function in the elderly by discussing how the perirhinal cortex supports both perception and complex sensory discrimination, as well as high-level associations and memory. Our expertise spans rodent pre-clinical models, monkeys and humans, thus bridges basic science to translational disciplines for the most complete understanding of perirhinal cortical function in old age. The importance of the current emphasis on this structure, stems from recent behavioral, imaging, electrophysiological and biochemical data that indicate that impairments in sensory discrimination abilities supported by the perirhinal cortex, may occur prior to the manifestation of memory deficits. Specifically, understanding the differential susceptibility of the dual functions of the perirhinal cortex in old age may help to elucidate the neurobiological mechanisms of both memory and perception. We hope to have this submitted before the Cognitive Aging Summit this spring.

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

Beach/Barnes

Although it appears that no other animal other than humans develop the hallmark distribution of both of the neuropathological markers of Alzheimer’s disease (amyloid plaques and neurofibrillary tangles), a variety of animals have been found to have some extracellular amyloid accumulation, and others scattered intraneuronal tangles. Because of Barnes’ tissue bank of behaviorally-characterized macaques, a systematic analysis is being performed in these animals of the distribution and extent of the appearance of these markers in the monkey brain in relation to memory. Barnes has identified tissue samples from 28 young and aged monkeys most of which has been sent to Tom Beach to perform several different stains that histologically identify amyloid and tau distribution in these brains, identical to what Beach uses on brains that come to

autopsy to receive an Alzheimer's disease diagnosis. In humans, the "transentorhinal area" (i.e., perirhinal cortex) shows the earliest signs of tau accumulation and amyloid plaques in the brains of people with Alzheimer's disease, and even in normative human aging, this region shows at least some tangles (not considered pathological). Beach was, therefore surprised at the frank absence of tangles in the monkey. For this reason, we have recently identified tissue from four additional levels of the perirhinal cortex in all of these monkeys, to ensure we have not 'undersampled' in this critical region. We will be shipping this extra tissue in January 2016. The present data constitute the only thorough analysis of tau and amyloid deposition staging (by an expert human neuropathologist), of cognitively-characterized primates that exists. Thus we believe that this thorough treatment of this important topic will result in a landmark manuscript.

15. Plans for future research

My laboratory remains in a strong position in the coming year to conduct significant research that is funded through five RO1 grants, and in our collaborations with colleagues in the other McKnight Brain Institutes. In addition, my colleagues and I here at the University of Arizona (Roberta Brinton and Yves Lussier) were allowed to go forward to apply for the \$100,000,000 MacArthur100 & Change grant. The title of this grant is "Precision Aging". If we are chosen as one of the finalists, then MacArthur will provide experts to help us implement our proposed grand solution, by assisting us to develop an organizational infrastructure. At that point all 4 Evelyn F. McKnight Brain Institutes would be funded to 'get to work' on the problem of brain aging and cognition. The gaps that we believe we fill in our Precision Aging solution is, for example, the current lack of integration across scientific and technological domains that target brain health in aging. Another is the involvement of the aging community (end user) into the scientific and innovation process. Our proposal will enable the integration across discovery, translation and big data domains to create personalized brain health for the aged. The tools we develop with our Precision Aging framework aims to transform the ways that individuals and healthcare providers can actively optimize aging – creating a landscape shift that integrates our solutions into the fabric of medicine itself. The long-term goal, of course, is regulatory approval, healthcare system integration and an open source system for all. Regardless of whether we are chosen finalists – the opportunity to 'think without typical monetary constraints' is incredibly stimulating – these ideas cannot now be 'put back into the box' – we must find a way to realize these goals, and a way to work together to achieve them.

21. Additional comments

The fund raising efforts continue for the Evelyn F. McKnight Brain Institute in Tucson to meet the challenge of raising private philanthropic funds to match the gift from the McKnight Brain Research Foundation to establish the permanent endowment.

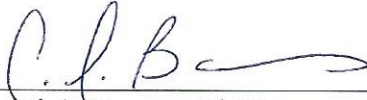
In May, the Office for Research, Discovery & Innovation hired Jeffrey Fischer-Smith as Senior Director of Development. In this role, Jeffrey reports directly to Dr. Kimberly Andrews Espy, Senior Vice President for Research. He will lead a team in raising philanthropic investment for three museums, 11 core facilities and eight centers and institutes, including the Evelyn F. McKnight Brain Institute. Jeffrey has over 25 years of senior-level management, organization, analysis, writing, and design experience—in all aspects of institutional advancement—and is an excellent match for the expertise needed for success in this key position. He is adept in both the individual giving arena as well as the corporate and foundation relations realm. He has served at many institutions and programs that are similar to the units that report to the Senior Vice President for Research, including four public research universities (University of Miami, Florida International University, University of California Davis, and Arizona State University). Jeffrey has acquired strong expertise in closing principal and major gifts, and has a keen ability to work with donors at the seven and eight figure level. He also possesses a strong proficiency in estate and gift planning. We have already been working closely with Jeffrey—as an example, he led the University’s proposals to the MacArthur Foundation’s 100&Change Award Competition and was very involved in our proposal.

We have also hired a Director of Development for Life Sciences who will work with Jeffrey and whose focus will be the Evelyn F. McKnight Brain Institute and BIO5 Institute. Elaine Cunningham’s tenure will begin on February 13, 2017—and we cannot be more excited. Elaine Cunningham is an accomplished fundraising professional with tenures at a healthcare foundation and leading public research universities and a skill set in major and principal gifts, corporate and foundation relations, prospect identification and qualification, donor stewardship, project management, and operational excellence. She also has 18 years of clinical nursing experience with academic medical centers in intensive care, surgery, transplant, and neurology units and a background in home healthcare and hospice administration and marketing. Elaine has cultivated, solicited, and stewarded six- and seven-figure gifts and has a track record of building strong relationships with donors and prospects that lead to significant philanthropic commitments. Throughout her career, she has worked effectively and in partnership with physicians, faculty researchers, administration, central development, colleagues, and volunteers to further institutional objectives and goals. Elaine’s tenacious spirit and desire to impact transformational initiatives motivate her to strive for extraordinary results. She is eager to serve as Director of Development, Life Sciences for the University of Arizona.

The Office of Research, Discovery & Innovation also hired Bentz, Whaley Flessner (BWF) to conduct a predictive modeling project of the nearly one million households in our donor database. This project is underway and we expect to have initial results by late Spring / 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 work to identify ways to grow the effectiveness and scope of prospect research services using increasingly powerful analytics tools. Their first project will be to develop a prospect pool for the Evelyn F. McKnight Brain Institute.

In conclusion, we now feel that we have the Team onboard to successfully raise the private matching funds for the very generous gift from the McKnight Brain Research Foundation. It has taken some time to recruit this Team – but it is an excellent, experienced, and extraordinarily skilled one.



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

1/13/17

Date