THE UNIVERSITY OF ARIZONA

Evelyn F. McKnight Brain Institute
Arizona Research Laboratories

Life Sciences North Building
P.O. Box 245115
Tucson, AZ 85724-5115
Tel: (520) 626-2312
Fax: (520) 626-2618

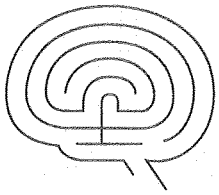
January 21, 2010

MEMORANDUM

TO: Trustees, The McKnight Brain Research Foundation
J.G. Clarkson, M.D.
J. L. Dockery, M.D.
M.L. Dockery, M.D.
N. Ellenbogen Raim, M.D., J.D.
J.A. Salerno, M.D.
T. Borcheck, Corporate Trustee

FROM: C.A. Barnes, Ph.D.
Regents' Professor, Psychology and Neurology
Evelyn F. McKnight Chair for Learning and Memory in Aging
Director, Evelyn F. McKnight Brain Institute
Director, ARL Division of Neural Systems, Memory and Aging
Associate Director, BIO5

Please find enclosed six copies of the Annual Report for the University of Arizona Evelyn F. McKnight Brain Institute, which covers the period of July 1, 2008 through June 30, 2009.



Evelyn F. McKnight
Brain Institute

Annual Report

McKnight Brain Research Foundation Sponsored Institutes and Research Programs

Report Period: July 1, 2008 – June 30, 2009
Institution: University of Arizona

Submitted January 21, 2010

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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. The Director has pioneered and developed two primary scientific tools that are used by her laboratory and in collaboration with others. The first involves the ability to monitor cognitive decline in aged rodents and nonhuman primates, in combination with live imaging methodologies, state-of-the-art ensemble electrophysiological recording in behaving animals and molecular analyses of brain tissue. The second is a molecular imaging technology that allows the examination of individual cells that participate in circuits critical for memory, and in combination with other methods can detect transcriptional and epigenetic factors that are altered in these circuits by behavior and aging.

The Scientific Advisory Board and affiliate members have met and interacted regularly throughout the year. A major paper was published this year describing pharmacological manipulation of the molecular cascade in the pathway of the "memory gene" KIBRA. A portion of the funding for the study came from the EMBI and the work involved the efforts of several EMBI affiliates and collaborators (Huentelman, Reiman, Alexander, and Bimonte-Nelson), including the Director. Additionally, an important paper was published on the role inflammation can play in altering the dynamics of memory circuits that was supported by EMBI. The Tucson Institute continues active collaboration with the Alabama Institute (with two papers in press), and the Tucson (lead by Alexander) and Miami (Wright) Institutes are actively coordinating efforts to share normal human aging populations. In addition to the educational benefits that arise from bringing scientists to the Institute from outside Arizona who can inform our future directions for cutting-edge research, the EMBI speaker series continues to be an effective tool for facilitating interaction among the affiliate members.

One of the decisions that the Scientific Advisory Board made this year was to focus our efforts on developing one or more fundable Program Project (PO1) grants among us. We began meeting twice monthly in the spring, and the first of these projects will focus on the mechanisms underlying individual differences that result in successful rather than unsuccessful cognitive aging in a given organism. The grant will involve both human and animal experiments that will define and examine mechanisms conducive to cognitive competence. Dr. Gene Alexander will be PI, Barnes co-PI, and affiliate members Ryan, Huentelman, and Coleman all have Projects and Cores. We had a meeting with Dr. Molly Wagster in Chicago at the Society for Neuroscience annual meeting, and she is giving us guidance on this process to reach our target submission date of May 2010.

2. Publications in peer reviewed journals

From Barnes

Huentelman MJ, Stephan DA, Talboom J, Corneveaux JJ, Reiman DM, Gerber JD, Barnes CA, Alexander GE, Reiman EM and Bimonte-Nelson HA (2009) Peripheral delivery of a ROCK inhibitor improves learning and working memory. Behavioral Neuroscience, 123: 218-223.

Jenstad M, Quazi AZ, Zilberter M, Haglerød C, Berghuis P, Saddique N, Goiny M, Buntup D, Davanger S, Haug FM, Barnes CA, McNaughton BL, Ottersen OP, Storm-Mathisen J, Harkany T and Chaudhry FA (2009) System A transporter SAT2 mediates replenishment of

dendritic glutamate pools controlling retrograde signaling by glutamate. Cerebral Cortex, 19:1092-1106.

Lister J and Barnes CA (2009) Neurobiological changes in the hippocampus during normative aging. Archives of Neurology, 66: 829 - 833.

Rosi S, Ramirez-Amaya V, Vazdarjanova A, Esparza EE, Larkin PB, Fike JR, Wenk GL, Barnes CA (2009) Accuracy of hippocampal network activity is disrupted by neuroinflammation: rescue by memantine. Brain, 132:2464-2477.

Burke, S.N. and Barnes, C.A. (2010) Senescent synapses and hippocampal circuit dynamics. Trends in Neurosciences, in press.

Schimanski, L.A. and Barnes, C.A. (2010) Neural protein synthesis during aging: Effects on plasticity and memory. Frontiers in Aging Neuroscience, in press.

Penner, M.R., Roth, T.L., Barnes, C.A. and Sweatt, J.D. (2010) An epigenetic hypothesis of aging-related cognitive dysfunction. Frontiers in Aging Neuroscience, in press.

Penner, M.R., Roth, T.L., Chawla, M.K., Hoang, L.T., Roth, E.D., Lubin, F.D., Sweatt, D.J., Worley, P.F. and Barnes C.A. (2010) Age-related changes in *Arc* transcription and DNA methylation within the hippocampus. Neurobiology of Aging, in press.

From Selected Affiliates

Caselli RJ, Dueck AC, Osborne D, Sabbagh MN, Connor D, Ahern GL, Baxter LC, Rapcsak SZ, Shi J, Woodruff BJ, Locke DEC, Snyder CH, Alexander GE, Rademakers R, Reiman EM. (2009) Longitudinal Growth Modeling of Cognitive Aging and the APOE e4 Effect. New England Journal of Medicine, 361:255-263.

Chen K, Reiman EM, Zhongdan H, Caselli RJ, Bandy D, Alexander GE. (2009) Linking functional and structural brain images with multivariate network analyses: A novel application of the partial least square method. Neuroimage, 47:602-610.

Drag LL, Bieliauskas LA, Kaszniak AW, Bohnen NI and Glisky EL (2009) Source memory and frontal functioning in Parkinson's disease. Journal of the International Neuropsychological Society, 15:399-406.

Drag LL, Kaszniak AW, Bieliauskas L and Glisky EL (2009) Source memory and frontal functioning in Parkinson's disease. Journal of the International Neuropsychological Society, 15:399-406.

Glisky EL and Marquine MJ (2009) Semantic and self-referential processing of positive and negative trait adjectives in older adults. Memory, 17:144-157.

Hua X, Lee S, Yanovsky I, Leow AD, Chou YY, Ho AJ, Gutman B, Toga AW, Jack CR, Bernstein MA, Reiman EM, Harvey DJ, Kornak J, Schuff N, Alexander GE, Weiner MW, Thompson PM; the Alzheimer's Disease Neuroimaging Initiative. (2009) Optimizing power to track brain degeneration in Alzheimer's disease and mild cognitive impairment with tensor-based morphometry: An ADNI study of 515 subjects. Neuroimage, 49:668-681.

Huentelman MJ, Stephan DA, Talboom J, Reiman DM, Gerber JD, Barnes CA, Alexander GE, Reiman EM, Bimonte-Nelson HA. (2009) Peripheral Delivery of a ROCK inhibitor improves learning and working memory. Behavioral Neuroscience, 123:218-223.

Lane RD, McRae KL, Reiman EM, Chen K, Ahern GL, Thayer JF (2009) Neural correlates of heart rate variability during emotion. NeuroImage, 44:214-223.

Langbaum JBS, Chen K, Lee W, Reschke C, Bandy D, Fleisher AS, Alexander GE, Foster NL, Weiner MW, Koeppe RA, Jagust WJ, Reiman EM, and the Alzheimer's Disease Neuroimaging Initiative. (2009) Categorical and correlational analyses of baseline fluorodeoxyglucose positron emission tomography images from the Alzheimer's Disease Neuroimaging Initiative (ADNI). Neuroimage, 45:1107-1116.

Leow AD, Yanovsky I, Parikshak N, Hua X, Lee S, Toga AW, Jack CR, Bernstein MA, Britson PJ, Gunter JL, Ward CP, Borowski B, Shaw LM, Trojanowski JQ, Fleisher AS, Harvey D, Kornak J, Schuff N, Alexander GE, Weiner MW, Thompson PM; for the ADNI study. (2009) Alzheimer's Disease Neuroimaging Initiative: A one-year follow up study using tensor-based morphometry correlating degenerative rates, biomarkers and cognition. Neuroimage, 45:645-655.

McFarland CP and Glisky EL (2009) Frontal lobe involvement in a task of time-based prospective memory. Neuropsychologia, 47:1660-1669.

Reiman EM, Chen K, Liu X, Bandy D, Yu M, Lee W, Ayutyanont N, Keppler J, Reeder SA, Langbaum JBS, Alexander GE, Klunk WE, Mathis CA, Price JC, Aizenstein HJ, DeKosky ST, Caselli RJ. (2009) Fibrillare amyloid-β burden in cognitively normal people at three levels of genetic risk for Alzheimer's disease. Proceedings of the National Academy of Sciences USA, 106:6820-6825.

Ryan L, Lin CY, Ketcham K and Nadel L (2009 Epub). The role of medial temporal lobe in retrieving spatial and nonspatial relations from episodic and semantic memory. Hippocampus, epub.

Thayer JF, Sollers JJ, Labiner DM, Weinand ME, Herring AM, Lane RD and Ahern GL (2009) Age related differences in prefrontal control of heart rate in humans: A pharmacological blockade study. International Journal of Psychophysiology, 72:81-88.

Walther K, Bendlin B, Glisky E, Trouard T, Lisse J, Posever J and Ryan L. (2009 Epub). Anti-inflammatory drugs protect against age-related differences in brain volume measured by voxel-based morphometry. Neurobiology of Aging, epub.

Weinand M, Serxner B, Labiner D, Ahern GL. (2009) Interhemispheric propagation time and temporal lobe epileptogenicity. Pathophysiology, 16:39-42.

Zhang W, Gardell S, Zhang D, Xie JY, Agnes RS, Badghisi H, Victor J, Hruby VJ, Rance N, Ossipov MH, Vanderah TW, Porreca F and Lai L (2009) Neuropathic pain is maintained by brainstem neurons co-expressing opioid and cholecystokinin receptors. Brain, 132:778-787.

Reiman EM, Chen K, Langbaum JB, Lee W, Reschke C, Bandy D, Alexander GE, Caselli RJ (2010) Higher serum total cholesterol levels in late middle age are associated with glucose hypometabolism in brain regions affected by Alzheimer's disease and normal aging. Neuroimage, 49:169-176.

Bergfield KL, Hanson KD, Chen K, Teipel SJ, Hampel H, Rapoport SI; Moeller JR, Alexander GE. Age-Related Networks of Regional Covariance in MRI Gray Matter: Reproducible Multivariate Patterns in Healthy Aging. Neuroimage, in press.

Corneveaux JJ, Liang WS, Reiman EM, Webster JA, Myers AJ, Zismann VL, Joshipura KD, Pearson JV, Hu-Lince D, Craig DW, Coon KD, Dunckley T, Bandy D, Lee W, Chen K, Beach TG, Mastroeni D, Grover A, Ravid R, Sando SB, Aasly JO, Heun R, Jessen F, Kolsch H, Rogers J, Hutton ML, Melquist S, Petersen RC, Alexander GE, Caselli RJ, Papassotiropoulos A, Stephan DA, Huentelman MJ. Evidence for an association between KIBRA and late-onset Alzheimer's disease. Neurobiology of Aging, in press.

Dacks PA and Rance NE. Effects of Estradiol on the Thermoneutral Zone and Core Temperature in Ovariectomized Rats. Endocrinology, in press.

Ho A, Hua X, Lee S, Leow AD, Yanovsky I, Gutman B, Dinov ID, Lepore N, Stein J, Toga AW, Jack CR, Bernstein MA, Reiman EM, Harvey DJ, Kornak J, Schuff N, Alexander GE, Weiner MW, Thompson PM. Comparing 3 Tesla and 1.5 Tesla MRI for Tracking Alzheimer's Disease Progression with Tensor-Based Morphometry. Human Brain Mapping, in press.

Langbaum JBS, Chen K, Caselli RJ, Lee W, Reschke C, Bandy D, Alexander GE, Burns CM, Kaszniak AW, Reeder SA, Corneveaux J, Huentelman MJ, Fleisher AS and Reiman EM. Hypometabolism in Alzheimer's-affected brain regions in cognitively normal Latinos carrying the apoliproprotein E e4 allele. Archives of Neurology, in press.

Smith JF, Alexander GE, Chen K, Husain FT, Kim J, Pajor N, Horwitz B. Imaging systems level consolidation of novel semantic-like memories: A longitudinal neuroimaging study. Neuroimage, in press.

Walther K, Bendlin B, Glisky E, Trouard T, Lisse J, Posever J and Ryan L. Anti-inflammatory drugs protect against age-related differences in brain volume. Neurobiology of Aging, in press.

Walther K, Birdsill A, Glisky E and Ryan L. Structural brain differences and cognitive functioning related to body mass index in older females. Human Brain Mapping, in press.

3. Publications (other)

Bondi M, Salmon D and Kaszniak AW (2009) The neuropsychology of dementia. In: I. Grant and K. Adams (Eds.), Neuropsychological Assessment of Neuropsychiatric & Neuromedical Disorders (pp. 159-198). New York: Oxford University Press.

Glisky EL (2009) Foreword. In: B.A. Wilson (Ed), Memory rehabilitation: Integrating theory and practice. New York: Guilford.

Glisky EL (in press) Forgetting. In: J. S. Kreutzer, J. DeLuca and B. Caplan (Eds.), Encyclopedia of Clinical Neuropsychology. New York: Springer.

Glisky EL (in press) Implicit memory. In: J. S. Kreutzer, J. DeLuca and B. Caplan (Eds.), Encyclopedia of Clinical Neuropsychology. New York: Springer.

Glisky EL (in press) Incidental memory. In: J. S. Kreutzer, J. DeLuca and B. Caplan (Eds.), Encyclopedia of Clinical Neuropsychology. New York: Springer.

Glisky EL (in press) Memory. In: J. S. Kreutzer, J. DeLuca, & B. Caplan (Eds.), Encyclopedia of Clinical Neuropsychology. New York: Springer.

Glisky EL (in press) Method of vanishing cues. In: J. S. Kreutzer, J. DeLuca, & B. Caplan (Eds.), Encyclopedia of Clinical Neuropsychology. New York: Springer.

Kaszniak AW and Edmonds E. Anosognosia and Alzheimer's disease: Behavioral studies. In: G. Prigatano (Ed.), The study of anosognosia (pp. 189-228). New York: Oxford University Press, in press.

4. Presentations at scientific meetings

From Barnes

Barnes, C.A. Age-related Changes in Object Recognition and "Object Fields" in Perirhinal Cortical Cells, Centre for the Biology of Memory, Norwegian University of Science and Technology, January 2009 (Invited)

Barnes, C.A. Memory and the Aged Hippocampal Circuit Dynamics, Hungarian Neuroscience Meeting, January 2009 (Invited)

Barnes, C.A. Memory Changes in Normal Aging: Neural Correlates in Rats and Monkeys, 19th Annual Rotman Research Institute Conference, Toronto, Ontario, Canada, March 2009 (Invited)

Barnes, C.A. New and Exciting Discoveries at the Arizona Evelyn F. McKnight Brain Institute, Evelyn F. McKnight Inter-Institutional Meeting, University of Alabama at Birmingham, April 2009 (Invited)

Barnes, C.A. Brain and behavioral aging: Molecules, maps and memory, M.R. Bauer Colloquium Series Speaker, Brandeis University, May 2009 (Invited)

Barnes, C.A. Looking under the street light: Surely the hippocampus isn't the only contributor to age related memory deficits, Brandeis University, May 2009 (Invited)

Barnes, C.A. Cognitive changes in aging: Neural correlates in rats and monkeys. Keynote Speaker, Ohio Miami Valley Chapter, Society for Neuroscience Meeting Miami University, June 2009. (Invited)

Barnes, C.A. Neural Correlates of Memory Change in Normal Aging, Biomedical Institute, Bergen, Norway, June 2009. (Invited)

Barnes, C.A. Effects of aging on memory and temporal lobe cell ensembles. In: Symposium, "Neural Correlates of Normal Age-Related Memory Decline" Spring Hippocampal Research Conference, Verona, Italy, June 2009. (Invited)

Barnes, C.A. Age-related changes in hippocampal circuits: disrupted sequence patterning. RIKEN Brain Science Institute Forum on Hippocampus, RIKEN, Japan, September 2009. (Invited)

Barnes, C.A. Weakening of replay of temporal patterns may result in memory consolidation failures in older animal. Symposium entitled, "The awake and sleeping brain - Processing of sequential information and memory consolidation." 32nd Annual Meeting of the Japan Neuroscience Society, Nagoya, Japan, September 2009. (Invited)

Barnes, C.A. Aging and Arc expression in the hippocampus: Unique changes in pyramidal versus granule cells. Eighth Annual Meeting of the International Molecular and Cellular Cognition Society, Chicago, Illinois, October 2009. (Invited)

Insel, N.E., Patron, L.A., Vega, J.N., Takehara-Nishiuchi, K., and Barnes, C.A. (2009) Neuron population activity in the rat anterior cingulate cortex tracks the advancement through a trial during a decision-making task. Program No. 481.15. Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, Online.

Maurer, A.P., Burke, S.N., Lipa, P., and Barnes, C.A. (2009) Hippocampal sequence compression increases with increasing velocity. Program No. 481.16. Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, Online.

Glatting, A.F., Schimanski, L.A., Broersma, B.M., and Barnes, C.A. (2009) Pre-activation of hippocampal CA1 activity patterns is reduced in old rats. Program No. 481.17. Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, Online.

Schimanski, L.A., Broersma, B.M., Lipa, P., and Barnes, C.A. (2009) Hippocampal CA1 place representations stabilize as young and old rats gain experience in a novel environment. Program No. 481.18. Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, Online.

Nematollahi, S., Burke, S.N., Maurer, A.P., Wallace, J.L., Uprety, A., and Barnes, C.A. (2009) CA1 pyramidal cell activity characteristics are modulated by 3-dimensional objects. Program No. 481.19. Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, Online.

Burke, S., Maurer, A.P., Nematollahi, S., Wallace, J.L., Uprety, A., and Barnes, C.A. (2009) Age effects on neuronal activity in the perirhinal cortex. Program No. 481.20. Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, Online.

Uprety, A.R., Hoang, L.T., Lipa, P., Egurrola, A.E., Thome, A., and Barnes, C.A. (2009) Electrophysiological responses of rostral versus caudal ventral tegmental neurons. Program

No. 481.21. Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, Online.

Hoang, L.T., Wann, E.G., Fellous, J.M., and Barnes, C.A. (2009) Characterization of behaviorally-induced Arc expression in ventral tegmental neurons during aging. Program No. 481.22. Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, Online.

Lister, J.P., Inglis, A., Anand, K., Cruz, L., Barnes, C.A. and Rosene, D.L. (2009) Statistical analysis of microcolumn structure in the rodent neocortex. Program No. 481.23. Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, Online.

Takehara-Nishiuchi, K., Wagner, Z., Insel, N., Chawla, M.K., Olson, K., Burke, S.N., Barnes, C.A., and McNaughton, B.L. (2009) Spatial context sensitivity partially explains differences in episodic encoding between deep and superficial neocortical layers. Program No. 481.24. Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, Online.

Penner, M.R., Roth, T.L., Lubin, F.D., Roth, E.D., Hoang, L.T., Sweatt, J.D., and Barnes, C.A. (2009) DNA methylation of zif268 is not dynamically regulated within the aged hippocampus following spatial behavior. Program No. 481.25. Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, Online.

Buzzetti, R., Penner, M.R., Hoang, L.T., Lister, J.P., and Barnes, C.A. (2009) Arc transcriptional responses are modulated by degree of context familiarity. Program No. 481.26. Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, Online.

Chawla, M.K., Penner, M.R., Olson, K., Barnes, C.A. (2009) Maximal electro-convulsive shock induced *c-fos* mRNA expression is reduced in the hippocampus of aged rats. Program No. 481.27. Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, Online.

Angulo, A., Chawla, M.K., Rosi, S., Barnes, C.A. and Ramirez-Amaya, V. (2009) Effect of actinomycin D on the sustained transcription of Arc in the rat hippocampal granule cells. Program No. 481.28. Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, Online.

Samson, R.D., Lipa, P., and Barnes, C.A. (2009) Age differences in performance of appetitive instrumental tasks. Program No. 481.29. Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, Online.

Plange, K., Burke, S.N., Nematollahi, S., Huerta, D., Gazzaley, A., Barnes, C.A. (2009) The effects of distraction and interruption forms of interference on delayed-nonmatching to sample task performance. Program No. 481.30. Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, Online.

Barnes, C.A. Research in Memory and Aging: From Rodents to Primates. University Animal Care Department Seminar, October 2009. (Invited)

Barnes, C.A. Effects of Aging on Memory and Temporal Lobe Networks. Colloquium Speaker, Department of Psychology, University of Pennsylvania, Pittsburgh, November 2009 (Invited)

Barnes, C.A. Normative Decline in Memory and Function in the Aging Brain, 23rd Annual Roland Pinkham Basic Science Conference, Swedish Medical Center, Seattle, WA, November 2009 (Invited)

Barnes, C.A. Neural Correlates of Memory Decline in Aging, 9th International SONA Conference, Sharm El Sheikh, Egypt, December 2009 (Invited).

From Selected Affiliates

Kaszniak AW. Emotion, equanimity, compassion, and selflessness in long-term meditators. Presentation given at the Conference/Retreat on Compassion and Selflessness: Zen, Neuroscience, and

Complexity Theory (A.W. Kaszniak & J. Halifax, Organizers), Upaya Zen Center and Institute, Santa Fe, NM, January 2009.

Kaszniak AW. Recognizing the symptoms and understanding the experience of neuropsychological disorders. Invited full-day workshop presented to the Oregon Psychological Association, Lake Oswego, OR, January 2009.

Alexander GE. Network Analyses of MRI Gray Matter: Implications for Translational Studies of Aging and Alzheimer's disease. Presentation at the Neuroscience Community Data Blitz, Tucson, AZ, January 2009.

Alexander GE. Neuroimaging in Aging and Alzheimer's Disease: Implications for Translational Research in Healthy and Pathological Aging. Presentation at the Department of Neurobiology, Tucson, AZ, 2009.

Ahern GL. Practical Aspects of Diagnosis and Treatment of Alzheimer's Disease and Other Dementias. Current Clinical Practice; Psychopharmacology Review. University of Arizona Department of Psychiatry, Ventana Canyon Resort, Tucson, AZ, February 2009.

Cox C, Forbes C, Ryan L, Schmader T. I want my mind off stereotypes, but stereotypes are on my mind: Motivation to not be prejudiced moderates memory for outgroup faces in a negative stereotypic context. Talk presented at the 10th annual conference of the Society for Personality and Social Psychology, Tampa FL, February 2009.

Edmonds EC, Rapcsak SZ, Shastri KK, Glisky EL and Bartlett JC. Cognitive mechanisms of false facial recognition in older adults. International Neuropsychological Society, Atlanta, GA, February 2009.

Grilli MD and Glisky EL. Self-imagining enhances recognition memory in memory-impaired patients. International Neuropsychological Society, Atlanta, GA, February 2009.

Marquine MJ, Glisky EL, Recknor E and Rapcsak S. Self- and other-person knowledge in Alzheimer's disease and mild cognitive impairment. International Neuropsychological Society, Atlanta, GA, February 2009.

McFarland CP, Glisky EL and Gorfein D. Frontal lobe involvement in a verbal switching task. International Neuropsychological Society, Atlanta, GA, February 2009.

Menchola M, Bergfield KL, Hanson KD, Chen K, Reiman EM, Caselli RJ and Alexander GE. Multivariate network of MRI gray matter association with healthy cognitive aging. Abstract presented at the International Neuropsychological Society, Atlanta, GA, February 2009.

Zajonc A and Kaszniak AW. The Science of Meditation, Web-seminar, Association for Contemplative Mind in Higher Education, March 2009.

Cox C, Nadel L, Ryan L. Perspective differentially modulates neural activation during remembering and imagining autobiographical events. Poster presented at the Cognitive Neuroscience Society Annual Meeting, San Francisco CA, March 2009.

Lin C-Y and Ryan L. The relationship between perceptual/conceptual priming effects and repetition suppression in posterior/frontal cortical regions. Poster presented at the Cognitive Neuroscience Society Annual Meeting, San Francisco CA, March 2009.

Ahern GL. Alzheimer's Disease: What Women Need to Know. 8th Annual Women's Health Symposium. University of Arizona Department of Psychiatry, UA Student Union, Tucson, AZ, April 2009.

Kaszniak AW. Cultivating compassion: Views from contemplative practice and social neuroscience. Presentation given at The Contemplative Heart of Higher Education Conference. 1st Annual Conference of the Association for Contemplative Mind in Higher Education, Amherst, MA, April 2009.

Rance N. Neurokinin B and the hypothalamic regulation of reproduction. Presentation at the Neuroscience Community Data Blitz, Tucson, AZ, April 2009.

Ryan L. Rethinking the role of hippocampus in semantic retrieval. Presentation at the Neuroscience Community Data Blitz, Tucson, AZ, April 2009.

Alexander GE. Voxel based morphometry of MRI gray matter with univaritate and multivariate network analyses from the Alzheimer's Disease Neuroimaging Initiative. Presentation at the Arizona Alzheimer's Consortium Annual Meeting, Glendale, AZ, May 2009.

Edmonds EC, Rapcsak SZ, Shastri KK, Glisky EL and Bartlett JC. Cognitive mechanisms of false facial recognition in older adults. Arizona Alzheimer's Consortium Annual Conference, Glendale, AZ, May 2009.

Walther K, Bendlin BB, Glisky EL, Walker DG., Lue L-F, Ryan L. The relation between APOE gene dosage, diffusion-weighted MRI, and cognition in healthy older adults. Arizona Alzheimer's Consortium Annual Conference, Glendale, AZ, May 2009.

Alexander GE, Chen K, Hanson KD, Bergfield KL, Reiman EM, Valfre M, Ashish D, Bernstein MA, Kornak J, Harvey D, Schuff NW, Thompson PM, Weiner MW, Jack CR, and the Alzheimer's Disease Neuroimaging Initiative. Voxel based morphometry of MRI gray matter with univariate and multivariate network analyses from the Alzheimer's Disease Neuroimaging Initiative. Abstract presented at the meeting of the Alzheimer's Disease Neuroimaging Initiative, Seattle WA, May2009.

Smith JF, Chen K, Horwitz B, Alexander GE. Temporal Evolution of Performance Related Regional Networks for Visual-to-Auditory Memory. Abstract presented at the Organization for Human Brain Mapping meeting, San Francisco, CA, June 2009.

Walther K, Birdsill AC, Glisky EL, Ryan L. Relationship between Body Mass Index, Regional Brain Volume, and Gender in Healthy Older Adults - a Voxel Based Morphometry Study. Poster presented at the annual meeting of the Organization of Human Brain Mapping, San Francisco CA, June 2009.

Kaszniak AW. The relationship of spirituality and compassion in health care. Invited panelist, Fetzer Summit on the Linkage between Spirituality and Compassion. Kalamazoo, MI, July 2009.

Ewers M, Walsh C, Trojanowski JQ, Shaw LM, Petersen RC, Jack CR, Bokde AWL, Feldman H, Alexander GE, Scheltens P, Vellas B, Dubois B, Hampel H, in collaboration with the North American Alzheimer's Disease Neuroimaging Initiative (ADNI). Multi-Modal Biological Marker Based Signature and Diagnosis of Early Alzheimer's Disease. Abstract presented at the International Conference on Alzheimer's Disease, Vienna, Austria, July 2009.

Kaszniak AW. Toward a neuropsychology of metamemory. Invited colloquium presentation given to the Department of Neuroscience, University of Arizona, Tucson, AZ, September 2009.

Kaszniak AW. The neuroscience of attention, emotion, and meditation: Implications for education. Invited presentation, Mindfulness: Foundations for Teaching and Learning Conference, Oakland, CA, October 2009.

Bergfield KL, Bergfield, KL, Hanson KD, Chen K, Reiman EM, Bernstein MA, Kornak J, Harvey DJ, Schuff NW, Thompson PM, Weiner MW, Jack CR, Moeller JR, Alexander GE. Multivariate regional network pattern of MRI gray matter preceding conversion to dementia in amnestic mild cognitive impairment. Abstract presented at the Society for Neuroscience meeting, Chicago, IL, October 2009.

Dacks PA, Brown J and Rance NE. NK_3 receptor activation in the median preoptic nucleus reduces core temperature in the. Poster presented at the annual meeting of the Society for Neuroscience. Chicago IL, October 2009.

Hanson KD, Chen K, Ryan L, Glisky EL, Reiman EM, Bernstein MA, Kornak J, Harvey DJ, Schuff NW, Jack CR, Thompson PM, Weiner MW, Alexander GE. Network analysis of MRI gray matter in amnestic mild cognitive impairment: relation to rates of cognitive decline and

conversion to dementia. Abstract presented at the Society for Neuroscience meeting, Chicago, IL, October 2009.

Ho AJ, Hua X, Lee S, Leow AD, Yanovsky I, Gutman B, Dinov ID, Lepore N, Stein JL, Toga AW, Jack DR, Bernstein MA, Reiman EM, Harvey DJ, Kornack J, Schuff N, Alexander GE, Weiner MW, Thompson PM. Tracking Alzheimer's disease progression: Does 3 Tesla or 1.5 Tesla MRI provide greater statistical power? Abstract presented at the Society for Neuroscience meeting, Chicago IL, October 2009.

Hua X, Lee S, Leow AD, Yanovsky I, Parikshak N, Chou YY, Ho AF, Gutman B, Toga AW, Jack CRW, Bernstein MA, Reiman EM, Harvey DF, Kornak J, Schuff N, Alexander GE, Weiner MW, Thompson PM. Neuroimaging biomarkers track brain degeneration in 676 subjects with Alzheimer's disease, mild cognitive impairment, and healthy controls. Abstract presented at the Society for Neuroscience meeting, Chicago IL, October 2009.

Krajewski SJ, Anderson MJ, McMullen NT and Rance NE. An interconnected network of neurokinin B neurons in the arcuate nucleus of the rat. Poster presented at the annual meeting of the Society for Neuroscience. Chicago IL, October 2009.

Lin L, Ashish D, Chen K, Caselli RJ, Reiman EM, Alexander GE. Regional reductions of MRI cortical thickness in cognitively normal late-middle aged adults with the Apoe e4 Allele. Abstract presented at the Society for Neuroscience meeting, Chicago IL, October 2009.

Menchola M, Bergfield KL, Hanson KD, Chen K, Lin L, Teipel SJ, Hampel H, Moeller JR, Rapoport SI, Alexander GE. Distributed regional pattern of gray matter volume in Alzheimer's disease: A comparison with the effects of healthy aging. Abstract presented at the Society for Neuroscience meeting, Chicago, IL, October 2009.

Orseth ML, Schneider LE, Niedzielko TL, Caselli R, Baxter L, Sabbagh M, Ahern GL, Alexander GE, Reiman EM, Valla J. Platelet mitochondrial functional change with age varies by gender. Abstract presented at the Society for Neuroscience meeting, Chicago IL, October 2009.

Ryan L, Pu L, Hoscheidt S and Nadel L. PPI Analysis: Patterns of frontal and posterior brain activation associated with hippocampus during episodic and semantic spatial memory retrieval. Poster presented at the annual meeting of the Society for Neuroscience. Chicago IL, October 2009.

Walther K, Birdsill AC and Ryan L Diffusion measures of white matter integrity in older females related to Body Mass Index. Poster presented at the annual Society for Neuroscience Conference, Chicago IL, October 2009.

Ryan L. The Aging Brain: Neuroimaging studies of memory, aging and risk for Alzheimer's Disease. Invited colloquium on aging and memory at Dalhousie University. Halifax Nova Scotia. October, 2009.

Ahern GL. Dementia: Diagnostic and Treatment Options. Grand Rounds Presentation, Section of Neurosurgery, Department of Surgery, University of Arizona, December 2009, Tucson, AZ.

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

Barnes, C.A. Altered Hippocampal Networks that Result in Age-Related Changes in Memory, Frontiers in Medical Research Series, University of Arizona, May 2009.

Ahern GL. Differential Diagnosis of Dementia. Encore Senior Living Center. Tucson, AZ, October 2009.

Ryan L and Alexander G. The Aging Brain: Neuroimaging studies of aging, memory, and Alzheimer's disease. Frontiers in Medical Research Seminar Sponsored by the College of Medicine Research Office. Tucson AZ, October 2009.

Kaszniak AW. Multitasking, neuroscience, and contemplative practice. Invited presentation at The One Who Is Not Busy: Living and Working Calmly and Effectively in an Accelerating, Information-Saturated World. Conference held at The Information School, University of Washington, Seattle, WA, November 2009.

Reiman E and Kaszniak AW. Progress in Alzheimer's disease research and the Arizona Alzheimer's Consortium. Invited community presentation given to the University of Arizona Retirees Association, Tucson, AZ, November 2009.

Kaszniak AW. Alzheimer's disease: Research progress. Invited community presentation given at the Memory Matters Conference, Tucson, AZ, November 2009.

Rance, N.E. Role of NKB in the hypothalamic regulation of reproduction. Magee-Women's Research Institute and University of Pittsburgh, Pittsburgh, Pennsylvania (Invited), 2009.

6. Awards

APA Division 6 D.B. Marquis Behavioral Neuroscience Award for Behavioral Neuroscience.

7. Faculty

There are two levels of faculty participation in the Evelyn F. McKnight Brain Institute at the University of Arizona. The Scientific Advisory Board (all of whom are Affiliate Faculty members), and Affiliate Faculty members. The Scientific Advisory Board consists of Dr. Geoff Ahern, Dr. Gene Alexander, Dr. Carol Barnes (Director), Dr. Betty Glisky, Dr. Al Kaszniak, Dr. Naomi Rance and Dr. Lee Ryan. The Advisory Board's one-year abbreviated curricula vitae are included in the following pages.

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Carol A. Barnes, Ph.D.	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, Dept. Psychology, Halifax, Canada
1979 - 1980	**NRSA Postdoctoral Fellow**, Institute of Neurophysiology, Oslo, Norway
1981	**NATO Postdoctoral Fellow**, Cerebral Functions Group, University College, London, England
1982 - 1985	**Assistant Professor**, Department of Psychology, University of Colorado, Boulder
1985 - 1989	**Associate Professor**, Department of Psychology, University of Colorado, Boulder
1989 - 1990	**Professor**, Department of Psychology, University of Colorado, Boulder
1990 - 1996	**Professor**, Psychology, Neurology, ARL Div Neural Systems, Memory & Aging, Univ. Arizona, Tucson
2006 -	**Regents' Professor**, Psychology, Neurology, Bio5, ARL Division of Neural Systems, Memory & Aging, University of Arizona, Tucson
2006 -	**Director**, Evelyn F. McKnight Brain Institute, University of Arizona, Tucson, AZ
2006 -	**Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging**, University of Arizona
2008 -	**Director**, ARL Division of Neural Systems, Memory and Aging, University of Arizona, Tucson
2009 -	**Associate Director**, Bio5, 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	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	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

2009 Publications

Huentelman, M.J., Stephan, D.A., Talboom, J., Corneveaux, J.J., Reiman, D.M., Gerber, J.D., Barnes, C.A., Alexander, G.E., Reiman, E.M., and Bimonte-Nelson, H.A. (2009) Peripheral delivery of a ROCK inhibitor improves learning and working memory. Behavioral Neuroscience, 123: 218-223.

Jenstad, M., Quazi, A.Z., Zilberter, M., Haglerød, C., Berghuis, P., Saddique, N., Goiny, M., Buntup, D., Davanger, S., Haug, F.M., Barnes, C.A., McNaughton, B.L., Ottersen, O.P., Storm-Mathisen, J., Harkany, T., and Chaudhry, F.A. (2009) System A transporter SAT2 mediates replenishment of dendritic glutamate pools controlling retrograde signaling by glutamate. Cerebral Cortex, 19:1092-1106.

Lister, J. and Barnes, C.A. (2009) Neurobiological changes in the hippocampus during normative aging. Archives of Neurology, 66: 829 - 833.

Rosi, S., Ramirez-Amaya, V., Vazdarjanova, A., Esparza, E.E., Larkin, P.B., Fike, J.R., Wenk, G.L., Barnes, C.A. (2009) Accuracy of hippocampal network activity is disrupted by neuroinflammation: rescue by memantine. Brain, 132:2464-2477.

Burke, S.N. and Barnes, C.A. (2009) Senescent synapses and hippocampal circuit dynamics. Trends in Neurosciences, in press.

Schimanski, L.A. and Barnes, C.A. (2009) Neural protein synthesis during aging: Effects on plasticity and memory. Frontiers in Aging Neuroscience, in press.

Penner, M.R., Roth, T.L., Barnes, C.A. and Sweatt, J.D. (2009) An epigenetic hypothesis of aging-related cognitive dysfunction. Frontiers in Aging Neuroscience, in press.

Penner, M.R., Roth, T.L., Chawla, M.K., Hoang, L.T., Roth, E.D., Lubin, F.D., Sweatt, D.J., Worley, P.F. and Barnes C.A. (2009) Age-related changes in *Arc* transcription and DNA methylation within the hippocampus. Neurobiology of Aging, in press.

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Geoffrey Lawrence Ahern, M.D., Ph.D.	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

1994-1995 Cited in S Naifeh & GW Smith(eds.), The Best Doctors in America, 2nd Ed, Woodward/White
1996-1997 Cited in S Naifeh & GW Smith(eds.), The Best Doctors in America, Pac Reg, Woodward/White
1997 Elected, American Neurological Association
1998-1999 Cited in S Naifeh & GW Smith(eds.), The Best Doctors in America, 4th Ed. Woodward/White
2003 Cited in S Naifeh and GW Smith (eds.), The Best Doctors in America, 2003-2004

2009 Publications:

Thayer JF, Sollers JJ, Labiner DM, Weinand ME, Herring AM, Lane RD, and Ahern GL. (2009) Age related differences in prefrontal control of heart rate in humans: A pharmacological blockade study. International Journal of Psychophysiology, 72: 81-88.

Lane RD, McRae KL, Reiman EM, Chen K, Ahern GL, Thayer JF. (2009) Neural correlates of heart rate variability during emotion. NeuroImage, 2009, 44:214-223.

Weinand M, Serxner B, Labiner D, Ahern GL. Interhemispheric propagation time and temporal lobe epileptogenicity. Pathophysiology, 16, 39-42.

Caselli RJ, Dueck AC, Osborne D, Sabbagh MN, Connor DJ, Ahern GL, Baxter LC, Rapcsak SZ, Shi J, Woodruff BK, Locke DEC, Snyder CH, Alexander GE, Rademakers R, Reiman EM. (2009) Longitudinal modeling of age-related memory decline and the APOE ε4 effect. New England Journal of Medicine, 361:255-263.

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Gene E. Alexander, Ph.D.	Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	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 & Behav. 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, AZ
1999- date Director, MRI Morphology Core, Arizona Alzheimer's Disease Research Ctr, Phoenix, AZ
2001-2009 Director, Data Management Program/Core, NIA AZ Alzheimer's Disease Core Center, AZ
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, AZ
2007-date Professor, Psychology & Evelyn F. McKnight Brain Institute, Univ of Arizona, Tucson, AZ
2007-date Director, Brain Imaging, Behavior, & Aging Lab, Univ of Arizona, Tucson, AZ

Honors and Awards

1995- date Ad Hoc Reviewer, 15 journals in Neuropsychology, Psychiatry, Neurology, and Neuroscience
1996-1999 Staff Recognition Awards (annual), Laboratory of Neurosciences, National Institute 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- date External Adv, Aging Brain:Vasculature, Ischemia & Behav. Prog Proj, USC, UCSF/Davis
2005-2007 Member, Specialist Peer Review Comm, Psychology: Exp/Clinical, 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 and Aging, ZAG1 ZIJ-5 JF, NIA

2009 Publications

Caselli RJ, MD, Dueck AC, Osborne D, Sabbagh MN, Connor DJ, Ahern GL, Baxter LC, Rapcsak SZ, Shi J, Woodruff BJ, Locke DEC, Snyder CH, Alexander GE, Rademakers R, Reiman EM. (2009)

Longitudinal Growth Modeling of Cognitive Aging and the APOE e4 Effect. New Eng J Med, 361, 255-63.

Chen K, Reiman EM, Zhongdan H, Caselli RJ, Bandy D, Alexander GE. (2009) Linking functional and structural brain images with multivariate network analyses: A novel application of the partial least square method. Neuroimage, 47, 602-10.

Hua X, Lee S, Yanovsky I, Leow AD, Chou YY, Ho AJ, Gutman B, Toga AW, Jack CR Jr, Bernstein MA, Reiman EM, Harvey DJ, Kornak J, Schuff N, Alexander GE, Weiner MW, Thompson PM; the Alzheimer's Disease Neuroimaging Initiative. (2009) Optimizing power to track brain degeneration in Alzheimer's disease and mild cognitive impairment with tensor-based morphometry: An ADNI study of 515 subjects. Neuroimage, 49, 668-81

Huentelman MJ, Stephan DA, Talboom J, Reiman DM, Gerber JD, Barnes CA, Alexander GE, Reiman EM, Bimonte-Nelson HA. (2009) Peripheral Delivery of a ROCK inhibitor improves learning and working memory. Behav Neurosci, 123, 218-23.

Langbaum JBS, Chen K, Lee W, Reschke C, Bandy D, Fleisher AS, Alexander GE, Foster NL, Weiner MW, Koeppe RA, Jagust WJ, Reiman EM, and the Alzheimer's Disease Neuroimaging Initiative. (2009) Categorical and correlational analyses of baseline fluorodeoxyglucose positron emission tomography images from the Alzheimer's Disease Neuroimaging Initiative (ADNI). Neuroimage, 45, 1107-16.

Leow AD, Yanovsky I, Parikshak N, Hua X, Lee S, Toga AW, Jack CR, Bernstein MA, Britson PJ, Gunter JL, Ward CP, Borowski B, Shaw LM, Trojanowski JQ, Fleisher AS, Harvey D, Kornak J, Schuff N, Alexander GE, Weiner MW, Thompson PM; for the ADNI study. (2009) Alzheimer's Disease Neuroimaging Initiative: A one-year follow up study using tensor-based morphometry correlating degenerativerates, biomarkers and cognition. Neuroimage, 45, 645-55.

Reiman EM, Chen K, Liu X, Bandy D, Yu M, Lee W, Ayutyanont N, Keppler J, Reeder SA, Langbaum JBS, Alexander GE, Klunk WE, Mathis CA, Price JC, Aizenstein HJ, DeKosky ST, Caselli RJ. (2009)Fibrillare amyloid-β burden in cognitively normal people at three levels of genetic risk for Alzheimer's disease. Proc Natl Acad Sci USA, 106, 6820-5.

Reiman EM, Chen K, Langbaum JB, Lee W, Reschke C, Bandy D, Alexander GE, Caselli RJ. (2010) Higher serum total cholesterol levels in late middle age are associated with glucose hypometabolism in brain regions affected by Alzheimer's disease and normal aging. Neuroimage, 49, 169-76.

Bergfield KL, Hanson KD, Chen K, Teipel SJ, Hampel H, Rapoport SI; Moeller JR, Alexander GE. Age-Related Networks of Regional Covariance in MRI Gray Matter: Reproducible Multivariate Patterns in Healthy Aging. Neuroimage, in press.

Corneveaux JJ, Liang WS, Reiman EM, Webster JA, Myers AJ, Zismann VL, Joshipura KD, Pearson JV, Hu-Lince D, Craig DW, Coon KD, Dunckley T, Bandy D, Lee W, Chen K, Beach TG, Mastroeni D, Grover A, Ravid R, Sando SB, Aasly JO, Heun R, Jessen F, Kolsch H, Rogers J, Hutton ML, Melquist S, Petersen RC, Alexander GE, Caselli RJ, Papassotiropoulos A, Stephan DA, Huentelman MJ. Evidence for an association between KIBRA and late-onset Alzheimer's disease. Neurobiol Aging, in press.

Ho A, Hua X, Lee S, Leow AD, Yanovsky I, Gutman B, Dinov ID, Lepore N, Stein J, Toga AW, Jack CR, Bernstein MA, Reiman EM, Harvey DJ, Kornak J, Schuff N, Alexander GE, Weiner MW, Thompson PM. Comparing 3 Tesla and 1.5 Tesla MRI for Tracking Alzheimer's Disease Progression with Tensor-Based Morphometry. Human Brain Mapping, in press.

Langbaum JBS, Chen K, Caselli RJ, Lee W, Reschke C, Bandy D, Alexander GE, Burns CM, Kaszniak AW, Reeder SA, Fleisher AS, Reiman EM. Hypometabolism in Alzheimer's-affected brain regions in cognitively normal Latinos carrying the Apolipoprotein E ε4 allele. Arch of Neurology, in press.

Smith JF, Alexander GE, Chen K, Husain FT, Kim J, Pajor N, Horwitz B. Imaging systems level consolidation of novel semantic-like memories: A longitudinal neuroimaging study. Neuroimage, in press.

BIOGRAPHICAL SKETCH

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

EDUCATION/TRAINING

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**, Department of Psychology, Univ 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**, Dept of Psych, Univ of Arizona, Tucson
2007 -	**Professor**, Evelyn F. McKnight Brain Institute, University of Arizona, Tucson
2008 – 2009	**Acting Head,** Department of Psychology

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

2009 Publications

Glisky, E. L., & Marquine, M. J. (2009). Semantic and self-referential processing of positive and negative trait adjectives in older adults. Memory, 17, 144-157.

Drag, L. L., Kaszniak, A. W., Bieliauskas, L., & Glisky, E. L. (2009). Source memory and frontal functioning in Parkinson's disease. Journal of the International Neuropsychological Society, 15, 399-406.

Glisky, E. L. (2009). Foreword. In B. A. Wilson, Memory rehabilitation: Integrating theory and practice. New York: Guilford.

McFarland, C. P., & Glisky, E. L. (2009). Frontal lobe involvement in a task of time-based prospective memory. Neuropsychologia, 47, 1660-1669.

Walther, K., Bendlin, B., Glisky, E., Trouard, T., Lisse, J., Posever, J., & Ryan, L. (in press). Anti-inflammatory drugs protect against age-related differences in brain volume. Neurobiology of Aging.

Walther, K., Birdsill, A., Glisky, E., & Ryan, L. (in press). Structural brain differences and cognitive functioning related to body mass index in older females. Human Brain Mapping,

Glisky, E. L. (in press). Forgetting. In J. S. Kreutzer, J. DeLuca, & B. Caplan (Eds.), Encyclopedia of Clinical Neuropsychology. New York: Springer.

Glisky, E. L. (in press). Implicit memory. In J. S. Kreutzer, J. DeLuca, & B. Caplan (Eds.), Encyclopedia of Clinical Neuropsychology. New York: Springer.

Glisky, E. L. (in press). Incidental memory. In J. S. Kreutzer, J. DeLuca, & B. Caplan (Eds.), Encyclopedia of Clinical Neuropsychology. New York: Springer.

Glisky, E. L. (in press). Memory. In J. S. Kreutzer, J. DeLuca, & B. Caplan (Eds.), Encyclopedia of Clinical Neuropsychology. New York: Springer.

Glisky, E. L. (in press). Method of vanishing cues. In J. S. Kreutzer, J. DeLuca, & B. Caplan (Eds.), Encyclopedia of Clinical Neuropsychology. New York: Springer.

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Alfred W. Kaszniak, Ph.D.	Head of Psychology Professor of Psychology, Neurology & Psychiatry

EDUCATION/

INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
University of Illinois, Chicago	B.S.	1970	Psychology
University of Illinois, Chicago	M.A.	1973	Clinical Psychology
University of Illinois, Chicago	Ph.D.	1976	Clinical Psychology
Rush Medical College, Chicago	Postdoc	1973-1974	Clinical

Positions

1976 - 1979 **Assistant Professor**, Dept of Psychology, Rush College of Medicine, Chicago
1979 - 1985 **Assistant to Associate Professor**, Dept of Psychiatry, Univ of Arizona, Tucson
1985 - 1987 **Associate Professor**, Depts of Psychology & Psychiatry, Univ of Arizona, Tucson
1987 - present **Professor,** Depts of Psychology, Psychiatry, Neurology, Univ of Arizona, Tucson
2002 - present **Head**, Department of Psychology, University of Arizona, Tucson
2007 - present **Professor**, Evelyn F. McKnight Brain Institute, University of Arizona, Tucson

Fellowships, Honors and Awards:

1978 Distinguished Contribution Award (for dissertation research), Division 20 (Adult Development and Aging), American Psychological Association
1989 Commendation for special contributions as a member of the Veterans Administration Geriatrics and Gerontology Advisory Board, Washington, DC
1989 Fellow, American Psychological Assoc; 1988 Fellow, Amer Psychological Society
1995 President, Section on Clinical Geropsychology, Div 12, Amer Psychological Assoc
2004 Koffler Prize for Outstanding Accomplishments in Public Service/Outreach
2006 University of Arizona Alumni Association Extraordinary Faculty Award
2007 Distinguished Contribution to the Science of Psychology Award, Arizona Psychological Association
2008 Contemplative Practice Fellow, Center for Contemplative Mind in Society

2009Publications

Bondi, M., Salmon, D., & Kaszniak, A.W. (2009) The neuropsychology of dementia. In I. Grant, & K. Adams (Eds.), Neuropsychological Assessment of Neuropsychiatric & Neuromedical Disorders (pp. 159-198). New York: Oxford University Press.

Drag, L.L., Bieliauskas, L.A., Kaszniak, A.W., Bohnen, N.I., & Glisky, E.L. (2009). Source memory and frontal functioning in Parkinson's disease. Journal of the International Neuropsychological Society, 15, 399-406.

Kaszniak, A.W., & Edmonds, E. (2010). Anosognosia and Alzheimer's disease: Behavioral studies. In G. Prigatano (Ed.), The study of anosognosia (pp., 189-228). New York: Oxford University Press.

Langbaum, J.B.S., Chen, K., Caselli, R.J., Lee, W., Reschke, C., Bandy, D., Alexander, G.E., Burns, C.M., Kaszniak, A.W., Reeder, S.A., Corneveaux, J., Huentelman, M.J., Fleisher, A.S., & Reiman, E.M. (in press). Hypometabolism in Alzheimer's-affected brain regions in cognitively normal Latinos carrying the apoliproprotein E e4 allele. Archives of Neurology.

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Lee Ryan, Ph.D.	Associate 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- present **Associate Professor**, Departments of Psychology and Neurology, University of Arizona, Tucson, AZ

2007- present **Associate Professor**, Evelyn F. McKnight Brain Institute, University of Arizona, Tucson, AZ

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

2009 Publications

Walther, K., Bendlin, B., Glisky, E., Trouard, T., Lisse, J., Posever, J., & Ryan, L. (2009 Epub). Anti-inflammatory drugs protect against age-related differences in brain volume measured by voxel-based morphometry. Neurobiology of Aging.

Ryan, L., Lin, C.Y., Ketcham, K., & Nadel, L. (2009 Epub). The role of medial temporal lobe in retrieving spatial and nonspatial relations from episodic and semantic memory. Hippocampus.

Walther K, Birdsill AC, Glisky EL, Ryan L. Structural Brain Differences and Cognitive Functioning Related to Body Mass Index. Human Brain Mapping, in press.

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

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 Basic Science Educator of the Year, University of Arizona College of Medicine
2000 Basic Science Educator of the Year, University of Arizona College of Medicine
2001 Basic Science Educator of the Year, University of Arizona College of Medicine
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
2004 Invited Speaker, Annual Meeting of the Endocrine Soc of Australia, Sidney
2004 Invited Speaker, Reproductive Endocrine Unit, Massachusetts General Hospital, Boston
2007 Invited Speaker, Symposium Session entitled "Lifecycle of the GnRH neuron", Annual Meeting of the Endocrine Society in June, Toronto
2007 Vernon and Virginia Furrow Award for Excellence in Innovation in Teaching, Univ Arizona
2008 Invited Speaker, First World Conf on Kisspeptin Signaling in the Brain, Cordoba Spain
2009 Invited Speaker, "Role of NKB in the hypothalamic regulation of reproduction" Magee-Women's Research Institute and University of Pittsburgh, Pittsburgh, Pennsylvania

2009 Publications

Zhang, W., Gardell, S., Zhang, D, Xie, J.Y., Agnes, R.S., Badghisi, H. Victor J. Hruby, V.J., Rance, N., Ossipov, M.H., Vanderah, T.W., Porreca, F. and Lai, L. Neuropathic pain is maintained by brainstem neurons co-expressing opioid and cholecystokinin receptors. Brain 132: 778-87, 2009.

Dacks, P., and Rance, N.E. Effects of Estradiol on the Thermoneutral Zone and Core Temperature in Ovariectomized Rats. Endocrinology, in press.

7. **Faculty** (continued)

The full Affiliate faculty list is given below:

- 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
- E. Fiona Bailey, Ph.D., Assistant Professor of Physiology, University of Arizona
- Carol A. Barnes, Ph.D., Regents' Professor, Psychology and Neurology; Director, Evelyn F. McKnight Brain Institute; Evelyn F. McKnight Chair for Learning and Memory in Aging; Director, ARL Division of Neural Systems, Memory and Aging, Associate Director, Bio5, University of Arizona
- Paul Coleman, Ph.D., Co-Director and Senior Scientist, J. Roberts Center for Alzheimer's Research; Professor of Neurobiology and Anatomy, University of Rochester Medical Center
- Jean-Marc Fellous, Ph.D., Associate Professor 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
- Elizabeth Glisky, Ph.D., Professor, Department of Psychology, University of Arizona
- Katalin M. Gothard, M.D., Ph.D., Associate Professor of Physiology, University of Arizona
- Marco Herrera-Valdez, Ph.D., UA Associate: Assistant Research Scientist, Evelyn F. McKnight Brain Institute, University of Arizona; Assistant Research Professor, Mathematical, Computational and Modeling Sciences Center, Arizona State University
- Matthew J. Huentelman, Ph.D., Investigator, Neurobehavioral Research Unit, Translational Genomics Research Institute
- Alfred W. Kaszniak, Ph.D., Head, Department of Psychology; Director, Coordinated Clinical Neuropsychology Program, University of Arizona
- Diano Marrone, Ph.D., UA Associate: Assistant Research Scientist, Evelyn F. McKnight Brain Institute; Assistant Professor, Psychology, Wilfrid Laurier University
- 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 Peterson, Ph.D., Professor 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
- Steve Rapcsak, M.D., Professor of Neurology, Psychology, and Speech, Hearing and Language Pathology, University of Arizona; Chief, Neurology Section, VA Medical Center
- 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)
- Linda L. Restifo, M.D., Ph.D., Professor, Neuroscience, Cell Biology & Anatomy, and BIO5 Institute, University of Arizona
- Lee Ryan, Ph.D., Associate Professor, Psychology; Director, Cognition and Neuroimaging Labs, University of Arizona

- Robert S. Sloviter, Ph.D., Professor of Pharmacology and Neurology, University of Arizona
- Ted P. Trouard, Ph.D., Associate Professor, Biomedical Engineering
- Andrea J. Yool, Ph.D., UA Research Associate, Department of Physiology; Professor, Molecular and Biomedical Science, University of Adelaide

The six new additions to the faculty affiliates include Drs. Paul Coleman, Marco Herrera-Valdez, Matt Huentelman, Diano Marrone, Steve Rapcsak and Ted Trouard. Drs. Marrone and Herrera-Valdez are collaborating on a computational model of the effects of loss of hippocampal granule cell function in normal aging that is observed in rats, monkeys and humans. Drs. Coleman, Huentelman and Trouard are participating in the creation of a program project grant being developed by the EMBI. Dr. Rapcsak is a Neurologist and active clinician/scientist who is interested in language and face recognition in aging.

8. Trainees (advisor in brackets)

Postdoctoral

Sara Burke (Barnes)
Area of Interest: Ensemble recording approaches to determine age-related changes in perirhinal cortical function.

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

Lan Lin, Ph.D. (Alexander)
Area of Interest: Development and implementation of MRI methods for small animal models and human studies of aging.

James Lister, Ph.D. (Barnes)
Area of Interest: Large-scale genetic imaging.

Andrew Maurer, Ph.D. (Barnes)
Area of Interest: Temporal lobe circuits involved in memory.

Marisa Menchola, Ph.D. (Alexander and Kaszniak)
Areas of Interest: Cognitive and neuroimaging affects in healthy aging and Alzheimer's disease. (Alexander)
Aging and the Psychophysiology of Emotion Response; Aging and Frontal Lobe Changes. (Kaszniak)

Marsha Penner (Barnes)
Area of Interest: Selectivity of gene expression changes across hippocampal regions in aging.

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

Lesley Schimanski, Ph.D. (Barnes)
Area of Interest: Ensemble recording of aged rat hippocampus: evaluation of map dynamics.

Katrin Walther, Ph.D. (Ryan)
Area of Interest: Brain imaging and cognitive changes in normal older adults.

Predoctoral

Elsa Baena (Ryan)

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

Kaitlin Bergfield (Alexander)

Area of Interest: Imaging and cognitive functioning associated with pathological and healthy aging in humans.

Christine Burns (Kaszniak)

Area of Interest: Ethnicity, Metabolic Syndrome, and AD Genetic Risk as Predictors of PET Regional Glucose Metabolism in Middle-Aged and Older Adults.

Marina Cholanian (Rance)

Area of Interest: First year graduate student with interest in the morphology and electrophysiology of Neurokinin B neurons.

Emily Connally (Glisky)

Area of Interest: Source memory, neuroimaging, training in virtual reality environments. (all in normal aging)

Penny Dacks (Rance)

Area of Interest: Age-related changes in temperature regulation in menopause.

Emily Edmonds (Glisky and Kaszniak)

Areas of Interest: Metamemory, decision-making, face recognition in normal aging and dementia. (Glisky)

Frontal brain system functioning and facial memory in healthy older adults .(Kaszniak)

Alaina Glatting (Barnes)

Area of Interest: Mechanisms of sleep disturbance that can affect memory.

Matt Grilli (Glisky)

Area of Interest: Self-referential processing, self-imagination, prospective memory, and memory rehabilitation (in normal aging).

Krista Hanson (Alexander)

Area of Interest: Imaging and cognitive functioning associated with healthy aging and age-related neurodegenerative disease.

Lan Hoang (Barnes)

Area of Interest: Age-related changes in dopaminergic systems.

Nathan Insel (Insel)

Area of Interest: Prefrontal cortical function in aging rats.

Kevin Kawa (Ryan)

Area of Interest: fMRI studies of memory and aging.

Thabelo Khoboko (Barnes)

Area of Interest: Age-related changes in population dynamics of hippocampal granule cells.

Gittan Mansson (Glisky)

Area of Interest: Prototype learning (of faces) in older adults.

Craig McFarland (Glisky)

Area of Interest: Executive function in older adults; prospective memory.

Rose Marie O'Donnell (Kaszniak)

Area of Interest: Developing Stress Resiliency in Middle-Aged and Older Adult Caregivers of Persons with Neurodegenerative Disorders

Lilian Patron (Barnes)

Area of Interest: Frontal lobe contributions to memory decline in the rat.

Angelina Polsinelli (Glisky)
Area of Interest: First year student with interests in emotion and memory in normal aging.
Melinda Smith (Rance)
Area of Interest: Role of neurokinin B in menopausal flushes and the hypothalamic regulation of gonadotropin.
Alex Thome (Barnes)
Area of Interest: Age-related changes in alpha and gamma oscillations in primate neocortex.
Michelle Valfre (Alexander)
Area of Interest: Biomarkers and gray matter atrophy in older adults experiencing cognitive decline.
Janelle Wohltmann (Glisky)
Area of Interest: Integration, inhibition, and strategic processing in source memory and associative learning in normal aging; executive function

Undergraduate Students (from Barnes' lab with graduate student or postdoctoral mentor in brackets)
Keshav Anand (Lister)
Neha Bandekar (Chawla)
Amy Chamberlain (Chawla)
Sarah Clasen (Lister)
Ana Egurrola (Hoang)
Andrew Flores (Burke)
Andrea Hartzell (Burke)
Danah Huerta (Burke)
Anthony Murata (Lister)
Kim Lind (Burke)
Anthony Murata (Lister)
Dhara Patel (Samson)
Nima Sekhadia (Chawla)
Khoa Truong (Chawla)
Jennifer Vega (Insel)
Zachary Wagner (Insel)

Staff
Caroline Garcia, Assistant to the Vice President for Research
Kojo Plange, Research Specialist, Non-human Primates
Luann Snyder, Department Administrator

9. Clinical/translational programs

2008-present Ahern, PI: A Phase 3, Multicenter, Randomized, Double-Blind,Placebo-Controlled, Parallel-Group, Efficacy and Safety Trial of Bapineuzumab (AAB-001, ELN115727) in Patients with Mild to Moderate Alzheimer's Disease Who Are Apolipoprotein Eε4 Non-Carriers. Protocol # ELN115727-301. Elan Pharmaceuticals, Inc.

2008-present Ahern, PI: A Phase 3, Multicenter, Randomized, Double-Blind,Placebo-Controlled, Parallel-Group, Efficacy and Safety Trial of Bapineuzumab (AAB-001, ELN115727) in Patients with Mild to Moderate Alzheimer's Disease Who Are Apolipoprotein Eε4 Carriers. Protocol # ELN115727-302. Elan Pharmaceuticals, Inc.

2008-present Ahern, PI: A Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging, Safety and Efficacy Study of Oral ELND005 (AZD-103) in Alzheimer's Disease. Protocol # ELND005-AD201. Elan Pharmaceuticals, Inc.

2008-present Ahern, PI: An Open Label, Parallel Group, Multicenter Study, Comparing the Safety and Imaging Characteristics of ^{18}F-AV-45 for Brain Imaging of Amyloid in Healthy Volunteers, Patients with Mild Cognitive Impairment (MCI) and Patients with Alzheimer's Disease (AD). Protocol # ^{18}F-AV-45-A05. Avid Radiopharmaceuticals, Inc.

2009-present Ahern, PI: Immunoglobulin Intravenous (IgIV) for Treatment of Alzheimer's Disease. Protocol # ADC-031. National Institute on Aging - Alzheimer's Disease Cooperative Study.

2009-present Ahern, PI: Observational Study of Long-Term (18 Month) Cognitive Outcomes in Healthy Volunteers, Patients with Mild Cognitive Impairment (MCI) and Patients with Alzheimer's disease (AD) Who Have Previously had PET Imaging with Florpiramine F 18 (^{18}F-AV-45) Injection. Protocol # ^{18}F-AV-45-A11. Avid Radiopharmaceuticals, Inc.

2009-present Ahern, co-PI (Hishaw PI): CONCERT: A Phase 3 Multicenter, Randomized, Placebo-Controlled, Double-Blind Twelve-Month Safety and Efficacy Study Evaluating Dimebon in Patients with Mild-to-Moderate Alzheimer's Disease on Donepezil. Protocol # DIM18. Medivation, Inc.

<u>New Hiring Initiative in Translational Biomedical Research at the University of Arizona</u>
This year Provost Hay committed significant funding to develop a Translational Biomedicine Program at the University of Arizona. Part of this initiative will be the submission of a Clinical and Translational Science Award (CTSA) application to the NIH. Dr. Fernando Martinez, Director of the BIO5 Institute, will take the lead as P.I. on this grant, and the Director of the Evelyn F. McKnight Institute and Associate Director of BIO5 (Barnes) will play an active role in the recruitment of clinician/scientists for this initiative. It is my hope that we will find applicants that will help the Evelyn F. McKnight Institute move forward with our translational goals in the upcoming years.

10. Technology transfer

None

11. Budget update

(a) **Last year's budget and actual results - July 1, 2008 to June 30, 2009**

	Budget	**Expenditures**
Personnel	$ 600,000	$1,011,933
Operations	$ 400,000	$ 341,157
Recruitment	$ 300,000	$ 18,964
Total	$1,300,000	$1,372,114

(b) **Status of matching funds – FY 07, 08, 09**

Year	**MBRF Gift**	**Match**
FY 06-07	$1,000,000	$1,779,500
FY 07-08	$1,000,000	$ 851,918
FY 08-09	$1,300,000	$1,251,309
Total	$3,300,000	$3,882,727

(c) **Projected budget for coming year (FY 09/10)**

Personnel	$ 700,000
Operations	$ 300,000
Recruitment	$ 281,036
Total	$1,281,036

d) **Extramural funding (covering period July 1, 2008 to June 30, 2009)**

Grants Received – from Barnes

5 RO1 AG012609-15 (P.I.: Barnes)
Title: Cell Assemblies, Pattern Completion and the Aging Brain*
Dates: 07/01/08 – 06/30/09
Amount: $298,162/year ($197,458 direct)
*This project received a competitive renewal award for an additional five years (7/09 – 6/14)

5 RO1 AG003376-25S1 (P.I.: Barnes)
Title: Neurobehavioral Relations in Senescent Hippocampus**
Dates: 9/30/08 – 01/31/10
Amount: $197,592/year ($130,856 direct) in bridging funds
**This project received a Director's bridge award (8/09 – 6/10) as well as a 4% priority score for the competitive renewal application to begin in the summer 2010.

1 P30 AG019610-08 (PI: Reiman – Barnes, Director, Ad Hoc Review Program)
Title: Arizona Alzheimer's Disease Core Center Ad Hoc Review
Dates: 07/01/2008 – 06/30/2009 (7/06 – 7/11 project period)
Amount: $19,331/year ($12,802 direct)

State of Arizona, DHS Grant
Title: Arizona Alzheimer's Consortium - UA Evelyn F. McKnight Brain Inst
Date: 07/01/08 – 06/30/09
Amount: $158,793/year (direct costs)

State of Arizona, DHS Grant
Title: Arizona Alzheimer's Consortium – ISAC Support
Date: 07/01/08 – 06/30/09
Amount: $19,508/year (direct costs)

Canadian Institutes of Health Research
Postdoctoral Fellowship to Dr. Rachel Samson
Title: Age-related changes in network activity of the amygdale during emotional learning
Date: 07/01/08 – 3/31/09 (7/08 – 6/11 project period)
Amount: $50,000 Canadian dollars

1 RC1 AG036053-01 (P.I.: Barnes)
Title: Functional Activity Mapping of Brain Networks
Date: 09/30/09 – 08/31/10 (9/09 – 8/11 project period)
Amount: $323,615 (direct costs)

NIA 1 F32 AG033460-01A1 (Sponsor: Barnes; NRSA to J. Lister)
Title: Age effects on grid cell and scene recognition systems of entorhinal cortex"
Date: 09/01/09 – 08/31/10 (9/09 – 8/11 project period
Amount: $50,054 (direct costs)

Grants Received - From Selected Affiliates

1 P30 AG019610-08 (PI: Reiman – Ahern co-PI, UAHSC Clinical Core)
Title: Arizona Alzheimer's Disease Core Center
Dates: 07/01/2008 – 06/30/2009 (7/06 – 7/11 project period)
Amount: $68,688/year ($45,489direct costs)

State of Arizona, DHS Grant (PI: Reiman – Ahern: co-PI)
Title: Clinical Core
Date: 07/01/08 – 06/30/09
Amount: $34,200/year (direct costs)

1 R01 AG025526 (PI: Alexander)
Title: Neuroanatomical Substrates of Aging & Cognitive Decline
Dates: 4/01/07-6/30/12
Amount: $533,970/year ($358,104 direct costs)

2 R01 MH57899 (PI: Reiman – Alexander co-PI)
Title: PET, APOE, & the Preclinical Course of Alzheimer disease
Dates: 07/1/98 – 6/30/13
Amount: 172,324/year ($115,764 direct costs)

1 UO1 AG024904 (PI: Weiner – Alexander co-PI)
Title: Alzheimer's Disease Neuroimaging Initiative
Dates: 10/1/04-9/30/10
Amount: $50,200/year ($33,245 direct costs)

5 RO1 EB000343 (PI: Trouard – Alexander co-PI)
Title: Non-Invasive Monitoring of NPC Disease Progression and Therapy
Dates: 04/02/01-1/31/2011
Amount $335,808/yr ($222,389 total costs)

State of Arizona, DHS Grant (PI: Reiman – Alexander co-PI)
Title: Magnetic Resonance Imaging of Amyloid Plaques in a Mouse Model of Alzheimer's Disease
Dates: 7/1/08-6/30/09
Amount: $11,342/year (direct costs)

State of Arizona, DHS Grant (PI: Reiman – Alexander co-PI)
Title: Image Acquisition and Analysis
Dates: 7/1/08-6/30/09
Amount: $50,678 /year (direct costs)

State of Arizona, DHS Grant (PI: Reiman – Alexander co-PI)
Title: Biomarkers Project
Dates: 7/1/08-6/30/09
Amount: $4,534 /year (direct costs)

State of Arizona, DHS Grant (PI: Reiman – Alexander co-PI)
Title: Arizona Alzheimer's Center Database
Dates: 7/1/08-6/30/09
Amount: $16,288 /year (direct costs)

State of Arizona, DHS Grant (PI: Reiman – Glisky: co-PI)
Title: Longitudinal study of neuropathologic markers in Alzheimer's disease
Date: 07/01/08 – 06/30/09
Amount: $19,509/year (direct costs)

AG 014792 (PI: Van Petten – Glisky: co-PI)
Title: Cognitive and Neural Bases of Aging and Memory
Date 09/01/05 –07/30/10
Amount: $420,038 /year ($281,237 direct costs)

9 RO1AG 031581 (PI: Reiman; Kaszniak: co-PI)
Title: PET, APOE and the Preclinical Course of Alzheimer's Disease
Date: 07/01/07 – 06/30/12 (7/1/07 – 6/30/12 project period)
Amount: $45,181/year (subcontract total costs)

1 P30 AG019610-08 (PI: Reiman – Kaszniak co-PI, Education and Information Core)
Title: Arizona Alzheimer's Disease Core Center
Dates: 07/01/2008 – 06/30/2009 (7/06 – 7/11 project period)
Amount: $71,922/year ($48,862 direct costs)

State of Arizona, DHS Grant
Title: Arizona Alzheimer's Consortium (PI: Reiman – Kaszniak: co-PI)
Diversity Education and Outreach Program
Date: 07/01/08 – 06/30/09
Amount: $8,121/year (direct costs)

State of Arizona, DHS Grant
Title: Arizona Alzheimer's Consortium (PI: Reiman – Kaszniak: co-PI)
Outreach and Information Dissemination Program
Date: 07/01/08 – 06/30/09
Amount: $45,370 /year (direct costs)

1 F31 AG030881-01
NRSA to Penny Letts, graduate student (Advisor: Dr. Naomi Rance)
Title: The Neuronal Circuitry Underlying Estrogen Effects in Thermoregulation
Dates: July 1, 2008 – June 30, 2009 (7/07 – 6/10 project period)
Amount: $26,556/year

2 R56 AG009215-15A1 (PI: Rance)
Title: Reproductive Aging and the Human
Dates: 07/15/07 – 06/30/09
Amount: $540,277 ($366,243 direct costs)

Arizona Biomedical Research Committee (PI: Rance)
Title: Effects of Estrogen Withdrawal on Hypothalamic Thermoregulation
Dates 07/01/06 – 06/30/09
Amount: $49,504/year ($45,000 direct costs)

RO1 AG032315 (PI: Rance)
Title: The Role of Neurokinin B in the Generation of Menopausal Flushes
Dates: 08/01/08 – 06/30/13
Amount: $277,576 ($183,325 direct costs)

R01 NS044107 (PI: Ryan)
Title fMRI Studies of Episodic and Semantic Memory Retrieval
Date: 3/1/2003 – 2/28/2009
Amount: $223,845/year ($161,379 direct costs)

R01 NS044107-S1 (PI: Ryan; minority supplement to Michelle Valfre)
Title: fMRI Studies of Episodic and Semantic Memory Retrieval
Date: 8/1/2005 – 2/28/2009
Amount: $36,794/year ($24,367 direct costs)

State of Arizona, DHS Grant
Title: Arizona Alzheimer's Consortium (PI: Reiman – Ryan: co-PI)
Cognition & Neuroimaging Laboratories
Date: 07/01/1998 – 06/30/2009 (renewable)
Amount: $172,811/year direct costs (w/$172,811 institutional match)

Grants Submitted – from Barnes

2 R01 AG003376-26A2 (PI: Barnes)
Title: Neurobehavioral Relations in Senescent Hippocampus
Dates: 07/01/10 - 6/30/15 (requested dates of project)
Amount: $790,208 (requested annual direct costs)
Status: Award pending (received a priority score of 22; 4th percentile)

1 RC1 AG036053-01 (PI: Barnes)
Title: Functional Activity Mapping of Brain Networks
Dates: 10/1/09 – 8/31/11 (dates of project)
Amount: $407,257 (annual total costs)
Status: This challenge grant was funded in October 2009

1 R44 AG035446-01(P.I.: LaComb; co-PI Barnes)
Title: Whole-brain fluorescence and brightfield imaging at single-cell level
Dates: 12/1/09 – 11/30/14 (requested dates of project)
Amount: $19,791 (requested annual direct costs for Barnes project)
Status: Under consideration (priority score: 39). A revised application will be prepared if not funded this round.

1 F32 AG033460-01A1
Postdoctoral fellowship application for Dr. Jim Lister (Barnes sponsor)
Title: Age effects on grid cell and scene recognition systems of entorhinal cortex
Dates: 09/01/09 – 08/31/11 (dates of project)
Amount: $50,054/year (direct costs)
Status: This fellowship was funded in September 2009

1 F32 NS070464-01
Postdoctoral fellowship application for Dr. Drew Maurer (Barnes sponsor)
Title: Hippocampal ensembles dynamics during active ambulation, passive movement & rest
Dates: 04/01/10 – 03/31/13 (requested dates of project)
Amount: $47,210/year (requested direct costs)
Status: Priority Score: 57; 66% percentile (to be resubmitted)

2 T32 AG007434-11A1 (P.I.: Zinsmaier; co-PI: Barnes)
Title Predoctoral Training Program in Neuroscience
Dates: 05/01/10 – 04/30/15 (requested dates of project)
Status: Not funded – will be revised and resubmitted in May 2010

Grants Submitted - From Selected Affiliates

RFA-OD-09-003 (P.I.: Moeller; co-PI: Alexander)
Title Multivariate Network Analyses of MRI & PET to Enhance Prediction & Tracking of AD
Dates: 9/30/09-9/29/10 (requested dates of project)
Status: Not Funded

National Institute on Aging (PI: Glisky)
Title Longitudinal Changes in Frontal and Medial Temporal Lobe Function in Older Adults
Date: Revised Application Submitted 2008
Status: Unfunded

National Institute on Aging (PI: Glisky; co-PI: Ryan)
Title Reducing Age-Related Cognitive Decline: Cognitive Training and Aerobic Exercise
Date: 10/1/09 – 9/30/11
Status: Unfunded

National Science Foundation (PI: Ryan; co-PI: Nadel)
Title Interactions between episodic and semantic memory in the medial temporal lobe
Date: Submitted August 2009
Status: Under review

12. Educational programs focusing on age related memory loss

Event: *Evelyn F. McKnight Brain Institute Seminar Series*
Summary: This Seminar Series is designed to bring together people across campus as well as the EMBI affiliates to hear state of the art presentations from leading investigators in the field of normal aging, and provide opportunities for one-on-one interactions that may foster future collaborations.

Date: September 22, 2008
Title: Compensatory Brain Activity in Older Adults
Presenter: Roberto Cabeza, Ph.D., Center for Cognitive Neuroscience, Duke University

Date: March 6, 2009
Title: Lifelong Bilingualism: Linguistic Costs, Cognitive Benefits, and Long-term Consequences
Presenter: Ellen Bialystok, Ph.D., Distinguished Research Professor, Bilingualism and Cognition Laboratory, York University

Date: May 8, 2009
Title: Race, language, education and cognitive aging
Presenter: Jennifer Manly, Ph.D., Sergievsky Center, New York

Event: *6th Forum of European Neuroscientists*
Date: July 12-17, 2008
Venue: Geneva, Switzerland
Symposium: Molecular Cellular and Circuit Contributions to Cognitive Decline in Normal Aging
Chairperson: Carol A. Barnes (Tucson, Arizona)

Presentations: Threshold changes in plasticity: relation to memory decline
T.C. Foster (Gainesville, Florida)

Modulating the age-related increase in microglian activation attenuates the neuroinflammatory changes which are associated with deficits in LTP
M.A Lynch (Dublin, Ireland)

Differential outcomes in neurocognitive aging
M. Gallagher (Baltimore, Maryland)

New models of cognitive aging emerging from gene array and calcium-related physiological studies
P.W. Landfield (Lexington, Kentucky)

Summary: Normal aging leads to subtle, but reliable alterations in brain function and behavior. Speakers in this symposium have contributed substantively to identifying age-related gene expression changes, altered cellular homeostatic mechanisms, selective changes in synaptic plasticity, and altered network dynamics in the circuits responsible for cognition. As the mechanisms of age-related memory change become unraveled, predictions for therapeutic targets aimed at postponing or alleviating age-related memory impairment can be made. Barnes will discuss age-related changes in behaviorally-induced plasticity and consolidation mechanisms in hippocampal networks, and treatments that affect the function of aging circuits through modification of the NMDA receptor. Foster discussed how alterations in Ca2+ sources, including NMDA receptors, can alter the thresholds for synaptic plasticity, and how behavioral and pharmacological treatments can avert or ameliorate threshold changes. Gallagher reviewed the neurobiology of differential outcomes in aging with a focus on cellular alterations in the CA3 region of hippocampus that distinguish dysfunction underlying cognitive decline from adaptive adjustments that support preserved cognitive capacities. Landfield discussed new integrative models of hippocampal cell type-specific processes in aging-related cognitive decline emerging from studies that combine gene/protein expression profiling, electrophysiology and behavioral analyses.

Event: *Presidential Special Lecture*
Date: November 16, 2008
Venue: 38thAnnual Meeting of the Society for Neuroscience
Washington, DC (November 15-19, 2008)
Speaker: Carol A. Barnes, Ph.D.
Talk Title: Memory and Hippocampal Networks: The Impact of Aging
Summary: An understanding of the neural basis of cognition requires examination of the dynamics of large populations of neurons in behaviorally-driven networks. Developments in ensemble electrophysiological recording and functional imaging methods provide a framework for understanding how the hippocampus stores and retrieves information. This lecture reviews

how changes in plasticity mechanisms and network dynamics during aging impact the computations that presumably underlie initial episodic memory formation and contribute to cognitive deficits observed in older mammals. Attended by approximately 7,500 members of the Society for Neuroscience.

Event: *McKnight Inter-Institutional Meeting*
Date: April 21-23, 2009
Venue: Evelyn F. McKnight Brain Institute, University of Alabama
Participating Institutions:
UA Evelyn F. McKnight Brain Institute, University of Arizona,
UAB Evelyn F. McKnight Brain Institute, University of Alabama
Evelyn F. McKnight Brain Institute, University of Florida,
Evelyn F. McKnight Center for Age-Related Memory Loss, Univ of Miami
Summary: 22 members of the University of Arizona Evelyn F. McKnight Brain Institute attended the McKnight Brain Research Foundation 2nd Inter-Institutional Meeting in Birmingham, Alabama.

Event: *Spring Hippocampal Research Center*
Date: June 14-19, 2009
Venue: The Palazzo Verita-Poeta, Verona, Italy
Symposium: Neural Correlates of Normal Age-related Decline
Chairperson: Carol A. Barnes, Ph.D.
Invited Speakers:

Calcium homeostatis and modulation of neural function in aged brain
Thomas Foster, University of Florida, Gainesville

Effects of aging on memory and temporal lobe cell ensembles
Carol Barnes, University of Arizona, Tucson

Imaging-guided microarray applied to cognitive aging: from dentate gyrus dysfunction to histone dysregulations
Scott Small, Columbia University, New York

Age-related changes in diffusion weighted MRI and BOLD fMRI and their relationships to memory performance in older adults with and without risk for Alzheimer's disease
Lee Ryan, University of Arizona, Tucson

Exploring the crossroads of memory and attention in the aging brain
Adam Gazzaley, University of California, San Francisco

13. Collaborative Programs with McKnight institutions and research programs

Gene Alexander/ Matt Huentelman/Paul Coleman/Ted Trouard/Lee Ryan/Carol Barnes
Alexander and Barnes are going to serve as PI and co-PI, respectively on a program project grant (PO1) that will be submitted in May 2010. Additional collaborators are Huentelman, Coleman, Trouard and Ryan, and we all have been meeting frequently this past year to refine our conceptualization of how to approach the question of what factors result in individual differences in successful aging. To this end we have conducted a series of pilot projects to include in the

grant proposal, and have been working with Dr. Molly Wagster from NIA, who is providing feedback both on our ideas and on the grant submission process. We are excited about the development of this collaborative grant proposal which will include both human and animal experiments. This should lay the foundation for stronger interactions among faculty across the state of Arizona that participate in the Evelyn F. McKnight Brain Institute.

Marsha Penner/Lan Hoang/Tanya Roth/Eric Roth/ David Sweatt/ Carol Barnes
We were able to successfully guide our collaborative project through the manuscript submission and acceptance process (Penner, Roth, Chawla, Hoang, Roth, Lubin, Sweatt, Worley, Barnes, 2010). This manuscript reflects the combination of expertise at the University of Arizona using the catFISH imaging methodology, along with the expertise in epigenetics at the University of Alabama. Additionally, our groups at Arizona and Alabama have written a review for Frontiers in Aging Neuroscience (Penner, Roth, Barnes, and Sweatt, in press) that highlights the potential relevance of the data contained in the Neurobiology of Aging manuscript, and emphasizes the potential use of these findings for the development of therapeutic strategies to treat age-related memory impairment.

Huentelman /Coleman/Barnes
We have begun to explore the possibility of using laser microdissection technologies for capturing specific cells in the hippocampus. Barnes has provided the tissue from young and aged rats to Huentelman and Coleman to determine whether the microdissection procedures will work with our brain extraction techniques. One test will be to examine transcriptional fidelity and methylation processes in known cell types in old animals. Additionally, we are working out the details for a method that will allow us to select out single *Arc*-positive and *Arc*-negative cells in the hippocampus of young and old rats. If we can achieve this, it will be the first time that experience-driven gene expression is examined in the precise cells that are activated by specific behaviors.

14. Collaborative programs with non-McKnight institutions:

Collaborators at Non-McKnight Institutions
Heather Bimonte-Nelson, Ph.D., Assistant Professor, Department of Psychology, Arizona State University
Veronique Bohbot, Ph.D., Assistant Professor, Department of Psychiatry, McGill University
Adam M. Brickman, Ph.D., Assistant Professor of Neurology, Taub Institute, Columbia University
Leyla de Toledo-Morrell, Ph.D., Jean Schweppe Armour Professor of Neurological Sciences, Rush University
Adam Gazzaley, M.D., Ph.D., Director, Neuroscience Imaging Center, Departments of Neurology and Physiology, University of California, San Francisco.
A. David Redish, Ph.D., Department of Neuroscience, University of Minnesota
Scott A. Small, Ph.D. Associate Professor of Neurology, Sergievsky Center and Taub Institute, Columbia University

Heather Bimonte-Nelson/Matt Huentelman/Dietrich Stephan/Eric Reiman/Carol Barnes
We have collaborated on a project for preclinical screening of a genetically implicated compound for the enhancement of memory in memory-impaired aged rats. It has been suggested

that the biological pathways involving the KIBRA gene play an important role in aging-associated episodic memory decline (in recent studies published by Drs. Reiman, Stephan and colleagues). The experiments conducted here tested compounds that influence KIBRA pathways, and the results suggest selective enhancement of hippocampal-dependent spatial working and reference memory performance in aged rats. This manuscript was published in the journal *Behavioral Neuroscience* (Huentelman et al., 2008).

Veronique Bohbot

The EMBI in Tucson provided seed money that enabled the behavioral testing, as well as functional and structural MRI scanning, of 3 experimental human participants and 3 controls, before and after a spatial memory training program in the Bohbot Memory & Motion Laboratory at the Douglas Hospital, in Montreal Quebec. The spatial memory training program is aimed at promoting growth in hippocampal circuits, and was modeled after a program originally designed for mice that resulted in positive growth. The data suggest that participants in the experimental group felt that their ability to notice details in the real word had improved, a necessary factor for building accurate spatial relationships. This method has the potential to improve spatial orientation, engender more confidence and autonomy, which could lead to a better quality of life for the elderly. With these pilot data, Dr. Bohbot has applied for support to conduct clinical trials for this spatial memory training technique.

Adam Brickman/Scott Small/Gene Alexander/Carol Barnes

Small and Barnes previously assessed basal levels of metabolism in the temporal lobe of Barnes' population of young and old rhesus macaques at the California National Primate Research Center in Davis. Adam Brickman was interested in expanding the analysis of these data to the frontal cortex. He performed univariate voxelwise statistical parametric mapping to derive CBV maps of frontal cortex and to examine the metabolic correlates across age and performance on a spatiotemporal memory test, a delayed response task, and a delayed non-matching to sample task. Correlations between age and CBV were observed bilaterally in prefrontal cortex, and CBV in prefrontal regions was also significantly correlated with performance on the delayed non-matching to sample task. We are currently writing up for publication the data that was presented at the Society for Neuroscience meeting last year (Brickman, Muraskin, Shamy, Steffener, Buonocore, Rapp, Alexander, Barnes, and Small, 2008).

Leyla de Toledo-Morrell/Travis Stoub/Emily Rogalski/Carol Barnes

A prediction from rat aging models is that normal aging leads to axonal pruning of the entorhinal cortical projection cells to the hippocampus. This has been verified electrophysiologically by Barnes and others, as well as anatomically (Geinisman and colleagues). Dr. de Toledo-Morrell and her colleagues have demonstrated that the fiber tract from the entorhinal cortex to the hippocampus declines in Alzheimer's disease patients compared to age-matched controls. The question remained as to whether normal aged individuals would show declines in this important temporal lobe projection pathway to the hippocampus when compared with young subjects. We were able to report that, in fact, there is a white matter volume loss that occurs in humans as a result of the normal aging process, using two different imaging methods. We presented these results at the Society for Neuroscience meeting last year (Stoub, Shah, Barnes, de Toledo-Morrell, 2008; Rogalski, Murphy, de Toledo-Morrell, Barnes, Shah, Stebbins, 2008). The manuscript is in final stages of revisions before submission.

Adam Gazzaley/Sara Burke/Kojo Plange/Carol Barnes

Gazzaley has investigated the ability of young and healthy older adults to ignore information that is not relevant to the performance of simple working memory tasks. He noted that in the elderly that he interacts with as a Neurologist often complain that they are much more distractible than they were when younger, and there have been many psychological experiments that have shown that older individuals are disproportionately affected by distractors in a variety of tasks. While Gazzaley has obtained behavioral, fMRI and event related potential data that show that healthy older adults have a deficit in suppression of cortical activity that is associated with task-irrelevant representations, it remains an open question what underlying mechanisms are responsible for these changes in memory and attention. To understand this better, nonhuman primate aging models will be extremely helpful. In the past year, a behavioral study was completed in our young and old bonnet macaques that examined the affects of distraction and interruption forms of interference on delay non-matching to sample task performance. The results were reported this year at the Society for Neuroscience meeting (Plange, Burke, Nematollahi, Huerta, Gazzaley, and Barnes, 2009). The data suggest that, like humans, monkeys do show disrupted memory performance in conditions in which interfering variables required attention. Over the next months, we will examine several other interference procedures in order to see whether we can find those that are most disruptive to the memory performance of these animals.

A. David Redish/Andrew Maurer/Joe Bohanick/Carol Barnes

Dr. Redish and his students have reported that neural representations of space exist at fast time scales when animals are at decision points on mazes. These location representations reflect future possible choices rather than recently traveled paths. This suggests that the hippocampus is involved in active, forward-shifted spatial representations, as well as instantaneous local neural representations. We continue to collaborate with Dr. Redish to examine whether aged rats show these transient nonlocal representations at critical choice points, and whether the decisions made by the animals at such choices are reflected in an individual animal's ability to accurately represent these nonlocal activity patterns in hippocampal cells. The older rats that we have trained had some difficulty at learning the multiple-choice T maze task in which many decision points can be examined within recording sessions. We have therefore scaled back the number of decision points and have found that the older animals are now able to learn this task. Our prediction for the outcome of this experiment is that old rats may never be as accurate as younger rats, and that the sweeping forward of spiking activity that reflects future spatial locations at decision points will be defective in the old animals and correlated with deficits in spatial behavioral tasks.

Scott Small/Paul Coleman/Carol Barnes

A gene involved in transcriptional silencing was identified that increases over age in Dr. Small's normal aged human population. Barnes looked across the lifespan in the rat, and found that RbAp48 also changes over age in rats, and that lower expression of RbAp48 was correlated with defective spatial memory. We are waiting to publish these data until results from monkey brain tissue can also be analyzed. Barnes has provided brain tissue from hippocampus and entorhinal cortex from young and old behaviorally-characterized monkeys to Dr. Coleman to perform this analysis. Coleman has been able to use his newly developed laser capture technology to facilitate measurement of mRNA content in the fixed tissue that Barnes provided. For additional sensitivity, fluorescent quantum dots have been attached to the RbAp48 probe which was hoped to increase sensitivity for detection of age-related changes. The quantum dot labeling procedures have proven problematic over the past year, but we have enlisted the assistance of Dr. Eberwine

at SUNY (one of the pioneers of this technology) to assist with this preparation. Once these procedures are optimized, then other genes can also be tested using similar methods. We will combine the rat, monkey and human RbAp48 data together for publication when the full dataset is available.

15. Plans for future research

Cognitive Testing of Young and Old Bonnet Macaques

During the past year, we were able to acquire 4 additional monkeys to add to our colony in Tucson from the source at SUNY where our other animals were obtained (for a total of 7 young and 7 old animals). This allows us some flexibility in assuring that, in the end, we will have the 6 young and 6 old animals that will be needed (at minimum) to obtain statistically reliable behavioral, imaging, electrophysiological and other biochemical and molecular data that we plan to collect from these animals . We have begun to train these additional animals to be comfortable with transport to the test apparatus,, and have begun to put them through the identical set of behavioral tests that the others have received in the Wisconsin General Testing Apparatus, beginning with the reinforcer devaluation task. They are responding well to the procedures and adaptation to the testing box.

The primary plans for the upcoming year are to continue the behavioral testing, not only of frontal lobe-dependent tasks, but also medial temporal lobe-dependent tasks. This will allow correlations to be made with the imaging studies that we have planned in the upcoming year. We have tested the new anesthesia system needed for these MRI experiments on one of Dr. Gothard's monkeys here in Tucson, and feel confident that we will be able to set up the MRI procedures for the bonnet macaques when there is a logical break in their behavioral testing schedule.

Technological Innovations

Electrophysiological Methods:

Our plans for the telemetered recordings in freely behaving monkeys is moving forward with our collaborators at Neuralynx, who have designed the recording system, and our collaborators at Yerkes Primate Center in Atlanta who have been training the animal that will be our first subject for these studies. We tested the Neuralynx system on rats here in Tucson, and discovered a noise signal at a frequency that will interfere with our spike recordings. This problem has now been diagnosed, and has led to a redesign of the telemetry unit. The new boards are being made, and we hope to do the test on the new product in March. The behavioral adaptation of carrying the 'back pack' in the freely behaving monkey is progressing, although it is a slow process to get the monkey to accept the pack without attempting to remove it. Dr. Buffalo finally does have a procedure that she believes will work, and Barnes will make a trip out to Atlanta in May or June to assess how the behavioral training is going, and to plan for the implantation of the hyperdrive in this animal. The telemetry system will first be tested in Tucson, and we will only take it out to Atlanta after we are certain that the recording noise levels are within our tolerance levels. Our overall goal will be to be able to record from a primate that is entirely free to move and behave within a large space – the first such recordings ever made in the completely unrestrained state in the monkey. Once we are certain of the success of these procedures, we will determine whether we will be able to apply these methods to our bonnet macaques.

Whole Brain Imaging with Single Cell Resolution
My collaborator at Rensselaer Polytechnic Institute in New York, Dr. Badri Roysam and I received funding in the past year to optimize the data analysis for large areas of brain for the catFISH method. This funding should allow us to move more quickly towards solutions to the next steps that need to be made in brain tissue montaging that will allow us to accurately put tissue sections back together in 3 dimensions. This step is essential before the algorithms for identifying the fluorescent gene product can be implemented over significant portions of the brain. The new associative image analysis procedures that are being developed should allow us to make joint registration possible with little error accumulation that would otherwise limit image registration methods. Our laboratory groups met in December to finalize our plans for the next year, and it was a very productive interaction, with clear milestones identified for moving ahead on this project.

Program Project Grant Development
My colleagues and I (all Affiliate Members of the Evelyn F. McKnight Institute in Tucson) have worked very diligently over the past year to develop our ideas for submission of a major program project grant from the University of Arizona. The overall goal of the project is to advance understanding of the mechanisms underlying why some individuals experience "successful" cognitive aging and others do not. The research approach is to use human and non-human animal models of "normal" aging to elucidate the factors that influence individual differences leading to optimal cognitive aging. We will propose a model of "Normal" Cognitive Aging, and for the purposes of focus, we will emphasize medial temporal and frontal cortical regions as key brain structures preferentially affecting in aging. The methods used will involve a well-selected cognitive test battery for humans and animal studies that can be examined in relation to health status, various types of brain imaging methodologies, electrophysiology as well as examination of normal genetic variation, gene expression and epigenetic profiles of individuals. We will use large cohorts over a wide adult age continuum in both animal and human experiments so that high and low performers can be identified. Furthermore, in terms of gene candidates associated with aging, we will target genes in an hypothesis-driven manner, emphasizing those involved in synaptic function and white matter integrity. We (Gene Alexander, Lee Ryan, Ted Trouard, Matt Huentelman, Paul Coleman and Carol Barnes) are very excited to see this project through to completion in the coming year, and hope to report good progress on these efforts in the next report.

16. Endowment investment results (July 1, 2008 to June 30, 2009)

Evelyn F. McKnight Chair for Learning and Memory in Aging

Endowment Account		
Beginning Balance/Market Value as of July 1, 2008	$	950,359
Fiscal Year Change in Market Value (7/08 - 6/09)	$	(203,433)
Year-end Balance (6/30/09)	$	749,926
Income to Chair (Expendable Account)		
Beginning Balance as of July 1, 2008	$	13,395
Payout from the Endowment	$	39,246
Personnel Expenditures (7/1/08 - 6/30/09)	$	(19,283)
Year End Balance (6/30/09)	$	33,358

Evelyn F. McKnight Brain Institute

Beginning Balance/Market Value as of July 1, 2008	$	886,304
2008/2009 MBRF allocation to the Institute	$	1,000,000
6% Development Fund	$	(60,000)
Entry to the Endowment	$	73,849
Fiscal Year Change in Market Value	$	(391,372)
Year-end Balance (6/30/09)	$	1,508,781

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?

Yes. Due to the reduced projected long-term growth of the McKnight Brain Research Foundation gift, in order to maintain the level of funds available to support the Institute at ~ $750,000 per year, the account will be expended by approximately 2018 rather than 2020.

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

Yes

20. Loss of personnel

Dr. Bruce McNaughton's position was not filled in the past year. With the support of the Trustees of the McKnight Brain Research Foundation, however, three different candidates were at the top of our recruitment list. Two are electrophysiologists with outstanding credentials in ensemble recording methodologies, and one with expertise in the molecular imaging methods used by the EMBI. We made offers to the first two candidates, Knierim and Mehta. Knierim went to the Johns Hopkins University and Mehta accepted an offer at the University of California at Los Angeles. The final candidate we are pursuing had the added complication that his wife is also a scientist, and, in fact, would be an outstanding collaborator for the EMBI if we had two positions. Fortunately, one of EMBI's affiliate faculty, Dr. Nikolich-Zugich, is the Head of the Department of Immunobiology and agreed to use one of his positions to recruit Dr. Lewandowski. Dr. Nikolich-Zugich's latest update is that he is finalizing the offer at the College level, and will send it to the Vice President for Research for the approval of the amounts. Fortunately the VPR is very enthusiastic about this hire, and we are very optimistic that the offer will be outstanding. On the Guzowski hire, the hiring commitments are currently being routed through the College of Science and the VPR for approval. We should know the outcome, at the latest, by March.

21. Additional comments

N/A

22. _____ 1/21/10

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