Evelyn F. McKnight Brain Institute

Full Lives Through Healthy Minds

Annual Report 2019
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Summary of scientific achievements since last report

The director and other members of the Evelyn F. McKnight Brain Institute at the University of Arizona have had another productive year. The full list of publications can be found on pages 12 through 19. The following outlines some of these accomplishments that directly relate to mechanisms of age-related memory loss, first from the Director’s and Associate Director’s laboratories, and then from other Evelyn F. McKnight Brain Institute (EMBI) Affiliate Faculty laboratories.

Barnes

The Barnes laboratory collaborated with four other EMBI Affiliate Faculty (Coleman, Trouard, Alexander and Huentelman) to examine the effect of gradual hypertension induction on cognition in a rat model of hypertension. While the impact of hypertension on the function of the renal and cardiovascular systems is well studied, its influence on brain regions important for cognition has garnered less attention. Our collaborator Kenneth Mitchell (Tulane) generated a novel transgenic rat model (Cyp11a1 Ren2) in which hypertension could be induced by a xenobiotic compound at an age of choice. Renin-dependent hypertension was gradually induced over a 6 week period in middle aged rats, to mimic the age at which hypertension begins to be observed in human populations. Significant elevations in blood pressure was induced in the animals given the xenobiotic compound, while the transgenic rats not fed the compound maintained stable blood pressure. The hypertension was associated with cardiac, aortic and renal hypertrophy as well as increased collagen deposition in the left ventricle and kidney of the treated rats. Additionally, rats with hypertension showed reduced savings from prior spatial memory training on a hippocampus-dependent task, but they did not show deficits in sensory or motor tasks. These data indicate a profound effect of hypertension not only on the cardiovascular-renal axis, but also on brain systems critically important for learning and memory (reported in Willeman et al. 2019). This finding clearly warrants replication and further study.

Barnes collaborated with four other individuals (Stern, Grady, Jones and Raz) in writing a summary of the session in the Cognitive Aging Summit III on “Brain Reserve, Cognitive Reserve, Compensation and Maintenance” (reported in Stern et al., 2019). The goal of the session was to begin to operationalize, explore validity and mechanisms of cognitive resilience. Significant individual difference in the trajectories of cognitive aging and age-related changes of brain structure and function have been reported in the past half-century. In some individuals, significant pathological changes in the brain are observed in conjunction with relatively well-preserved cognitive performance. Multiple constructs have been invoked to explain this paradox of resilience, including brain and cognitive reserve, maintenance and compensation. We examine the overlap and distinction in definitions and measurement of these constructs. We proposed a continued dialog
among investigators as a means to help refine the language used across broad fields, so that faster progress can be made in understanding both the resistance and vulnerability to cognitive decline during aging.

Barnes and Gray from the Tucson EMBI authored an invited chapter describing results that Barnes presented for the Sacker Colloquium of the National Academy of Sciences, the topic being: “Using Monkey Models to Understand and Develop Treatments for Human Brain Disorders” (reported in Gray and Barnes, 2019). The use of animal models in brain aging research has led to numerous fundamental insights into the neurobiological processes that underlie changes in brain function associated with normative aging. The present review highlights how nonhuman primates provide a critical bridge between experiments conducted in rodents and development of therapeutics for humans. Several studies from the Barnes laboratory were discussed to illustrate how this work has been important for translating mechanistic implications derived from experiments conducted in rodents to human brain aging research.

The Barnes laboratory collaborated with Rapp (NIA Intramural) to examine the behavioral impact of long-term chronic implantation of neural recording devices in the monkey. While there is widespread use of invasive recording methods with animal models and in humans, little is known of their effect on behavior in healthy populations. We were able to quantify the effect of chronic electrode implantation that targeted the hippocampus on recognition memory performance in macaques ranging in age from 7 to 26 years. Memory on the delayed non-matching-to-sample task was not significantly affected by chronic electrode implants targeting the hippocampus in healthy monkeys (reported in Kyle et al., 2019). These data indicate that the tissue damage and subsequent foreign body response caused by hyperdrive implantation was not sufficient to disrupt hippocampal circuits and impair memory performance, even though small lesions have been shown to influence this behavior.

The Barnes laboratory and EMBI Affiliate Faculty member Ekstrom collaborated on the creation of a cytoarchitectonically-driven MRI atlas of the nonhuman primate hippocampus. Identification of human and nonhuman primate hippocampal subfields in vivo using structural MRI imaging relies on variable anatomical guidelines and signal intensity differences to differentiate between regions. Methods are currently being developed for human experiments to use ex vivo histology or MRI methods that have the potential to inform subfield demarcations of in vivo images. For optimal results, however, ex vivo and in vivo images should ideally be matched within the same brains with the goal to develop a neuroanatomically-driven basis for in vivo structural MRI images. We report here a novel method that uses Nissl stained histological sections in which we can identify the dentate gyrus, CA3, CA2, CA1, subiculum, presubiculum and parasubiculum guided by morphological cell properties. The histologically identified boundaries were merged with in vivo structural MIRS via iterative rigid and diffeomorphic registration resulting in probabilistic atlases of young and old rhesus macaques. Our results indicate stability in hippocampus subfield volumes over an age range of 13 to 32 years (reported in Kyle et al., 2019). Our approach has the potential to provide a ‘ground truth’ for more accurate identification of hippocampal subfield boundaries on human in vivo MIRs.

The Barnes laboratory developed a new method to remove background autofluorescence from aging primate brain tissue. Age-related accumulation of molecules with autofluorescent properties such as lipofuscin, can possess spectral profiles that invade the typical emission range of fluorophores commonly utilized in fluorescent microscopy. The traditional method for dealing with native fluorescence is to apply lipophilic dyes that are able to sequester these unwanted signals. While effective, such dyes can present a range of problems including the obstruction of fluorescent probe emissions relevant to the experiment. This study compared the Sudan Black dye method to spectral imaging and linear unmixing methods. We found that the linear unmixing approach yielded significantly higher cell numbers counted than the dye-based Sudan black approach (results in Pyon

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et al., 2019). These results suggest an alternative method for aging studies in which brain tissue accumulates large quantities of lipofuscin.

The Barnes laboratory along with the Trouard laboratory (EMBI Faculty Affiliate) has begun to examine the contribution that sensory system function plays in age-related cognitive decline. Recent evidence suggests that hearing-impaired individuals have a greater risk of developing cognitive impairment and dementia compared to people with intact auditory function. The neurobiological basis of this association is poorly understood. To begin to better understand this relationship we examined a colony of young and older bonnet macaques. They completed a battery of behavioral tests designed to probe frontal and temporal lobe-dependent cognition, were tested electrophysiologically for auditory brainstem responses and visual evoke potentials, and were imaged using structural and diffusion methods. Animals showing higher cognitive function had significantly better auditory processing capacities, and these associations were selectively observed with tasks that depend on temporal lobe brain structures. Tractography analyses revealed that fractional anisotropy of the fimbria-fornix and hippocampal commissure were associated with temporal lobe-dependent cognitive performance and auditory sensory function (reported in Gray et al., 2019). Frontal cortex white matter integrity, on the other hand, was not associated with frontal lobe-dependent memory or with sensory function. The visual sensory measures were not related to any of the cognitive tests given. This study demonstrates significant and selective relationships between auditory processing, white matter connectivity and higher-order cognitive ability.

Barnes was invited to contribute an opinion piece for Trends in Neurosciences. Along with EMBI Affiliate Faculty Matt Huentelman, and U19 Precision Aging Network grant participant Zhao Chen, they proposed a reinvention of experimental approaches taken to study the brain and aging, with the aim of better matching cognitive healthspan with human lifespan. Past studies of cognitive aging have included sample sizes that tended to be underpowered, were not sufficiently representative of national population characteristics, and often lacked longitudinal assessments. As a step to address these shortcomings, they propose a framework that encourages interaction between electronic-based and face-to-face study designs. We argue that this will achieve the necessary synergy to accelerate progress in the discovery and application of personalized interventions to optimize brain and cognitive health (reported in Huentelman et al., in press).

**Ryan**

Barnes, Ryan, Hay, Mehl and Huentelman from the Tucson EMBI collaborated with Levin and Rundek from the Miami EMBI, and colleagues participating in our U19 Precision Aging Network grant from Johns Hopkins (Solden and Pettigrew) and from Georgia Tech (Duarte) to co-author a review article on the importance of applying concepts from precision medicine to the field of cognitive aging (reported in Ryan et al., 2019). We contend in this article that the current “one size fits all” approach to our cognitive aging population is not adequate to close the gap between cognitive health span and human lifespan. We present a novel model for understanding, preventing and treating age-related cognitive impairment based on concepts borrowed from precision medicine. This Precision Aging model is meant as a starting point to guide future research. To that end, we discuss key risk categories, genetic risks, and brain drivers involved in setting cognitive trajectories across age and suggest steps needed to move the field forward.

The Ryan laboratory along with the Grilli laboratory (EMBI Faculty Affiliate) published a report on the impact of cardiovascular risk factors on cognition in Hispanic and non-Hispanic whites. Among non-Hispanic whites, cardiovascular risk factors are associated with increased mortality and poorer cognition. Prevalence of cardiovascular risk factors among aging Hispanics is also high. While Hispanics generally have poorer access to healthcare, they tend to have advantageous cardiovascular disease rates and outcomes and live longer than do non-Hispanic whites. This epidemiological phenomenon is commonly referred to as the Hispanic or Latino health paradox. Whether the
Hispanic paradox with respect to greater longevity with respect to greater longevity with the disease extends to the impact of cardiovascular disease on cognition was not known. In this study Hispanics and non-Hispanic whites were matched on age, education, sex, cognitive status and apolipoprotein E4 status. History of hypertension and higher body mass index were associated with poorer executive functions among Hispanics. This relationship was not observed in non-Hispanic whites (reported in Stickel et al., 2019). These findings do not fit with the notion of a Hispanic health paradox for cognitive aging and suggest greater vulnerability to impairments in executive functions among Hispanics with hypertension and obesity.

**Alexander**

The Alexander laboratory collaborated with the Raichlen lab to investigate the relationship between physical activity, cardiorespiratory fitness and brain volume in middle-aged to older adults. Two measures of exercise that might account for the benefits of aerobic exercise (time spent in moderate-to-vigorous physical activity and cardiorespiratory fitness) were examined. Using the UK Biobank, 7,148 males and 4,086 females were studied and time spent in moderate-to-vigorous physical activity and cardiorespiratory fitness were measured along with neuroimaging. They found that moderate-to-vigorous physical activity was associated with overall gray matter volume, while cardiorespiratory fitness was associated with left and right hippocampal volumes (but not overall gray matter volume) (reported in Raichlen et al., 2019). This suggests that there are separable effects of specific kinds of exercise on brain health.

The Alexander and Raichlen laboratories collaborated on a study to examine best methods for analysis of accelerometer data that monitor and track physical activity for health-related applications. They examined the potential for fractal complexity of actigraphy data to serve as a clinical biomarker for mortality risk. The results suggest that fractal complexity of physical activity decreased significantly with age and was lower in women compared with men. Higher levels of moderate-to-vigorous physical activity in older adults were associated with greater fractal complexity. Lower fractal complexity of activity was associated with greater mortality (reported in Raichlin et al., 2019). These data suggest that wearable accelerometers can provide a noninvasive biomarker of physiological aging.

**Andrews-Hanna**

The Andrews-Hanna laboratory has explored how age alters off-task, self-generated thought (mind-wandering) under conditions of low cognitive demand. They explored the frequency, temporal focus and self-referential/social content of spontaneous decoupled thought in younger and older adults in the Shape Expectations task. The participants also completed the daydreaming subscale of the Imaginal Process Inventory as a trait measure of mind-wandering propensity. Their findings indicate a distinct attenuation of off-task, self-generated thought processes with increasing age, and evidence for a shift in temporal focus and self-referential quality during periods of low cognitive demand (reported in Irish et al., 2019).

Andrews-Hanna and collaborators explored the neural correlates of mind wandering in normal older adults and adults with a behavioral variant of frontotemporal dementia (bvFTD) and Alzheimer’s disease (AD). Relative to controls the bvFTD patients displayed significantly reduced mind wandering capacity, offset by a significant increase in stimulus-bound thought. In contrast, AD patients exhibited comparable levels of mind wandering as controls, but some increase in propensity towards stimulus-bound thought. The altered profiles of mind-wandering were associated with structural and functional brain changes in the hippocampus, default and frontoparietal networks (reported in O’Callaghan et al., 2019).

Andrews-Hanna and collaborators examined the long-held notion that memory and ‘the self’ are intertwined, and that a loss of memory in dementia results in a diminished sense of self. Their data
led them to propose a new framework for understanding and managing everyday functioning and behavior in dementia. They suggest that the temporally-extended self changes in healthy and pathological aging (but is not lost in neurodegenerative disease), and that this has important ramifications for development of person-centered care (reported in Strikwerda-Brow et al., 2019).

Andrews-Hanna and collaborators have explored mind-wandering in Parkinson’s disease (PD) patients with hallucinations. In PD patients with visual hallucinations, they found abnormal activity within the default mode network, and altered pattern of connectivity patterns of this network to early visual regions. To test the hypothesis that individuals with hallucinations experience an increased frequency of mind-wandering, patients were compared to PD patients without hallucinations and controls. The results showed that patients with hallucinations exhibited significantly higher mind-wandering relative to non-hallucinators, who in turn had reduced levels of mind-wandering compared to controls (reported in Walpola et al., 2019). Taken together the data suggest that elevated mind-wandering and increased default-visual network coupling is a distinguishing feature of the hallucinatory phenotype. The data suggest that top-down influences over perception is involved in visual hallucinations.

**Brinton**

The Brinton laboratory reported the results of a study that examined mechanisms responsible for neuroendocrine aging and perimenopause. Because age of perimenopause onset is only 47% heritable, they hypothesized that additional factors regulate this endocrine aging transition. They characterized transcriptional and epigenomic changes across endocrine aging using a rat model that recapitulates characteristics of the human perimenopause. RNA-seq analysis revealed that hypothalamic aging precedes onset of perimenopause. Epigenetic analysis revealed changes in DNA methylation in genes required for hormone signaling, glutamate signaling and melatonin and circadian pathways (reported in Bacon et al., 2019). When treatment with a DNA-methyltransferase inhibitor was given, this delayed the onset of perimenopause and endocrine aging, suggesting that there is a critical period of female neuroendocrine aging in brain that precedes ovarian failure, regulated by DNA methylation.

The Brinton laboratory reviewed what is known about autoimmune disease in women across the lifespan. Women have a higher incidence and prevalence of autoimmune disease than do men. Women also undergo dramatic endocrinological changes during lifetime, including puberty and menopause, and frequently also pregnancy. They provide evidence from human epidemiological data and animal studies that endocrine transitions exert profound impact on the development of autoimmune diseases through complex mechanisms, and suggest that a greater understanding of endocrine transitions could aid in prediction and prevention of autoimmune diseases in women (reported in Desai and Brinton, 2019).

The Brinton laboratory and collaborators reported an association of the apolipoprotein E4 genotype, metabolic profile and cognition in women. In a sample of 407 women, verbal memory was lower in the poor metabolic profile women, and performance in all cognitive domains was lowest in the APOE4 carriers in the poor metabolic cluster. Differences in executive functions were detected only in women carrying the APOE4 genotype (reported in Karim et al., 2019). Reduction in cognitive performance is more apparent in women who carry an APOE4 allele, especially in conjunction with a poor metabolic profile, suggesting a window of opportunity for interventions in postmenopausal women.

The Brinton laboratory has reported on the safety and feasibility of an estrogen receptor-β targeted phytoSERM formulation for menopausal symptoms. The Phase 1b/2a randomized clinical trial suggested that the phytoSERM formulation was well tolerated at 50 and 100mg daily doses. Based on safety outcomes, vaginal bleeding at the 100mg dose and vasomotor symptoms and cognitive
outcomes at 12 weeks, a daily dose of 50mg was considered preferable for a Phase 2 efficacy trial (reported in Schneider et al., 2019).

The Brinton laboratory conducted a pilot study on the pharmacogenomic effects of mitochondrial haplogroup and APOE genotype on therapeutic efficacy of a phytoSERM. They conducted a retrospective analysis to identify potential responders to phytoSERM treatment, and to determine the optimal populations to pursue in a Phase 2 clinical trial of efficacy. The population was stratified by 2 genetic risk modulators for Alzheimer’s disease – mitochondrial haplogroup and APOE genotype. When examined in this way, 50mg of daily phytoSERM for 12 weeks reduced hot flash frequency and preserved cognitive function in certain aspects of verbal learning and executive function (reported in Wang et al., 2019). They conclude that these data provide a reasonable rationale to extend analyses to a larger study set that is sufficiently powered statistically.

Chou

The Chou laboratory and collaborators reviewed the impact of yoga as a form of advanced cognitive training. Specifically, they examined the neural effects and benefits of a yogic practice on the default mode network in post-traumatic stress disorder. Symptom severity in this disorder is related to decreased neural connectivity in the default mode network. The particular practice of Kirtan Kriya yoga involving a series of repetitive, sequential movements that are synchronized with a self-produced mantra in Kundalini yoga appears to be a powerful intervention for symptoms of this brain injury, and hold promise for neural repair (as reported in Sales and Chou, 2019).

The Chou laboratory conducted a systematic review and meta-analysis of repetitive transcranial magnetic stimulation (rTMS) effects on cognitive enhancement in mild cognitive impairment (MCI) and Alzheimer’s disease (AD). The meta-analysis of thirteen studies focused on characterizing the effectiveness of various combinations of rTMS parameters on different cognitive domains in MCI and AD. There was an overall medium-to-large effect size favoring active rTMS over sham rTMS in the improvement of cognitive functions. Specific rTMS frequencies used over left dorsolateral prefrontal cortex and right dorsolateral prefrontal cortex significantly improved memory, while rTMS that targeted the right inferior frontal gyrus significantly improved executive functions. The effects of these treatments could last for 4-12 weeks, and they conclude could be effective for treatment of cognitive dysfunction (reported in Chou et al., 2019).

Cowen

The Cowen laboratory collaborated with the Barnes laboratory to examine hippocampal sharp-wave ripples during waking states in young and aged rats. Several novel observation emerged from these studies, including the fact that aged rats express more ripples, but that young rats express higher ripple rates, and that while during periods of rest ripple frequencies were lower, aged rats could increase ripple rates during behavior to levels equivalent to young rats (reported in Cowen et al., 2018). The suggested role played by waking ripples in memory may indicate that slower movement speeds of aged rats may provide more opportunity to replay task-relevant information, and thus may result in some reduction of age-related declines in memory.

Ekstrom

The Ekstrom laboratory conducted a study to examine the question of how we use environmental boundaries to anchor spatial representations during navigation. They conducted an experiment in which participants freely ambulated on an omnidirectional treadmill while viewing novel, town-sized environments in virtual reality on a head-mounted display. Participants performed interspersed judgments of relative direction to assay their spatial knowledge and to determine when during learning they employed environmental boundaries to anchor their spatial representations. Their results suggest that the use of spatial boundaries as an organizing schema during navigation of large-
scale space occurs in an experience-dependent fashion (reported in Starrett et al., 2019). These finding help bridge the gap between neurophysiological models of location-specific firing in rodents and human behavioral models of spatial navigation.

The Ekstrom laboratory published a study focusing on the networks that underlie the retrieval of large-scale spatial environments in the human brain. Recent breakthroughs in immersive virtual reality technology allowed examination of how body-based cues influence spatial representations of large-scale environments in humans. Availability of body-based cues were directly manipulated during navigation using an omnidirectional treadmill and a head-mounted display. The behavioral and neuroimaging results support the idea that there is a core, modality-independent network that supports spatial memory retrieval in the human brain (reported in Huffman and Ekstrom, 2019). This suggests that, at least in humans, primarily visual input may be sufficient for expression of complex representations of spatial environments.

The Ekstrom laboratory in collaboration with several other groups conducted a study on the role that the fornix plays in human navigation learning. Experiments in rodents have demonstrated that transecting the white matter fiber pathway linking the hippocampus with an array of cortical and subcortical structures (including the hippocampus) impairs flexible navigational learning in the Morris watermaze. Human diffusion MRI methods have linked individual differences in fornix microstructure to episodic memory abilities, but the fornix had not been examined in relation to spatial memory. They found a statistically significant correlation between spatial learning rate and mean diffusivity of the fornix but not in another tract that links occipital and anterior temporal cortices (the inferior longitudinal fasciculus) (reported in Hodgetts et al., 2019). These findings extend previous animal studies by demonstrating the functional relevance of the fornix for human spatial learning in a virtual reality environment.

Fernandez

The Fernandez laboratory completed a longitudinal study of sleep and diurnal rhythms in Drosophila anassae. In this study they used high-resolution monitors to track how circadian patterns of locomotor activity change in female flies as they enter mid-to-late life. Daily actograms were generated for each animal, along with a time series of activity across the observational period. Consistent with findings from older rodents and humans, older flies exhibited degraded patterns of wake and sleep that were fragmented – but still rhythmic – across the 24 hour cycle (reported in Kaladchibachi et al., 2019). Overall levels of daily activity declined with age, with particular loss of circadian arousal in the wake-maintenance zone a few hours before bedtime.

The Fernandez laboratory conducted a systematic study to examine the optimal parameters to use for adjusting the circadian pacemaker. Recent work suggests that the circadian pacemaker responds optimally to millisecond flashes of light, not continuous light exposure as has been historically believed. This study stimulated Drosophila with 8, 16 or 120 millisecond flashes, with the energy content for each duration being systematically varied. The results suggested that when considering per microjoule investment, the 8 msec flashes were more effective than flashes at 16 or 120 msec (reported in Kaladchibachi et al., 2019). This suggests that the circadian pacemaker’s photosensitivity declines within milliseconds of light contact, and that very little light can optimize circadian responses.

Fernandez wrote a review on circadian responses to fragmented light, summarizing findings from a family of experiments conducted over two decades in the research wing of the Brigham and Women’s Hospital that examined the human circadian pacemaker’s responses to standardized changes in light patterns generated from overhead fluorescent lighting. Across several hundred days of laboratory recording, the research group observed phase-shifts in body temperature and melatonin rhythms that scaled with illuminance. Phase resetting was optimized, however when exposure occurred as a series of minute-long episodes separated by periods of intervening darkness.
These results suggest that ultra-short duration light pulses can elicit pacemaker responses rivaling those created by continuous hour-long stimulation, if those few seconds of light are evenly distributed across the hour as discreet 2 millisecond pulses (as described in Fernandez, 2019). He suggests that these findings have important potential application in future phototherapy techniques. The Fernandez laboratory and collaborators at the University of Arizona reviewed the data concerning the common denominators of sleep, obesity and psychopathology. The high comorbidity between sleep problems, obesity and mental illness suggest that common mechanisms are at work between them. While several variables — obstructive sleep apnea, food intake and inflammation — appear to covary as mechanisms underlying these relationships, there is actually little current experimental evidence to draw strong conclusions at the present time (as reported in Tubbs et al., 2019). They emphasize the importance of experiments aimed at a better understanding of the moderating/mediating influences between sleep, obesity and mental health.

Glisky
The Glisky laboratory reported data that suggests that working memory predicts subsequent episodic memory decline during healthy cognitive aging. To assess the relationship between working memory and episodic memory during healthy cognitive aging, they performed neuropsychological assessments at multiple time points to understand how these cognitive processes interact over time. They demonstrated that working memory performance was able to predict later episodic free recall, suggesting that working memory may be a useful metric of future episodic memory decline (reported in Memel et al., 2019).

The Glisky and Grilli (EMBI Faculty Affiliate) laboratories investigated whether the strategy of self-reference can benefit memory for multi-element events. Young and older adults imagined different person-object-location events with reference to themselves or in reference to two famous others. They found that self-reference enhanced memory for object-location and person-object pairs in both age groups (reported in Hou et al., 2019). This suggests that self-reference can benefit multiple types of associations and is effective at improving memory in both younger and older adults.

Grilli
The Grilli laboratory and Associate Director Ryan’s laboratory explored the relationship between episodic detail generation and anterotemporal, postero medial and hippocampal white matter tracts. In this study they combine an autobiographical interview and diffusion MRI to investigate the relationships of two types of episodic detail – details about entities of an event (people and objects) and details about spatiotemporal context. Specifically, the integrity of the uncinate fasciculus, cingulum bundle and fornix pathways were examined. They found that only episodic detail generation was significantly related to cortical and hippocampal pathways. The uncinate fasciculus was more strongly related to event element details than it was to spatiotemporal context detail. The cingulum bundle was also related to these details. The fornix was related to both types of episodic detail (reported in Memel et al., 2019). These findings suggest that anterotemporal cortical regions are related to the retrieval of episodic details about autobiographical events.

The Grilli laboratory conducted experiments that suggest that an “episodic mode of thinking” facilitates encoding of perceptually rich memories for naturalistic events. In a between-subjects design, participants were given an episodic mode of thinking task while encoding events. The control was a “gist mode of thinking” task. Participants who received the episodic-generated narrative that contained more perceptual details, encoded memories more effectively that did the gist-generated tasks (reported in Grilli et al., 2019). This suggests that an episodic mode of thinking facilitates encoding of perceptually rich memories for naturalistic events.
**Huentelman**

The Huentelman laboratory collaborated with four other EMBI Affiliate Faculty (Barnes, Ryan, Glisky, Hay) and published the first report from the MindCrowd web-based cognitive testing study cohort. While it is known that a first-degree family history of dementia is a risk factor for Alzheimer’s disease, the influence of family history on cognition across the lifespan is poorly understood. This study addresses this issue. An internet-based paired-associate learning task was developed and was used to test 59,571 participant between the ages of 18 and 85 years of age. We showed that family history was associated with lower memory performance in both males and females under 65 years of age. The modifiers of this effect of family history of Alzheimer’s disease included age, sex, education and diabetes. The apolipoprotein E4 allele was also associated with lower paired-associate learning scores in family history-positive individuals. Perhaps the most surprising finding in this study is the fact that family history is associated with reduced memory performance four decades before the typical onset of Alzheimer’s disease (reported in Talboom et al., 2019).

**Mehl**

The Mehl laboratory, along with several others who are participating in the Precision Aging Network U19 grant (Sternberg, Najafi) reported findings on the health benefits of controlling relative humidity in the workplace. They examined the association between relative humidity and objective measures of stress responses, physical activity and sleep quality in a group of office workers from four federal buildings, who wore chest-mounted heart rate variability monitors for three consecutive days, while relative humidity and temperature were measured in their work places. Those who spend the majority of time at the office in conditions ranging from 30-60% relative humidity experienced 25% less stress and better sleep quality than those outside that range (reported in Razjouyan et al., 2019). The study also suggested that optimal values may reside in an even narrower range around 45%.

The Mehl laboratory in collaboration with Sbarra (EMBI Affiliate Faculty) examined the use of language in a depressed population. Depressive symptomatology is associated with greater first-person singular pronoun use (i.e., I-talk), but the extent to which this is specific to depression remains unclear. Using pooled data from 6 laboratories across 2 countries, they studied “I-talk” in 4,754 participants. There was a small but reliable positive correlation between depression and I-talk for both females and males, with no evidence of gender differences (reported in Tackman et al., 2019). There was also a significant contribution from negative emotionality, suggesting that the use of first-person singular pronouns may be better described as a linguistic marker of general distress proneness or negative emotionality rather than a marker of depression.

The Mehl laboratory studied the prevalence of gender-biased language in everyday language. They investigated two forms of gender bias – paternalism through use of the infantilizing label ‘girl’ to refer to women and androcentrism through a tendency to use more masculine (i.e., man, guy) than feminine (e.g., girl, woman) labels in everyday speech. They found that the label girl surpassed all other labels for women and also found evidence of masculine-label bias (reported in MacArthur et al, 2019). It will be interesting to conduct studies that take a lifespan perspective to determine whether the age of the person being labeled shows the same pattern of gender bias.

**O’Connor**

The O’Connor laboratory examined the role of personal and communal religiosity in the context of bereavement. Interviews and questionnaires from 33 bereaved adults were collected and associations with self-reported religious coping and grief symptoms were assessed. Personal and communal religiosity predicted positive religious coping as well as negative religious coping and grief severity. The data suggest that after loss, personal religiosity by itself is not necessarily protective.
(reported in Stelzer et al., 2019). The presence of personal and communal religiosity contributes to positive religious coping, and the absence of communal religiosity indicates vulnerability.

O’Connor and colleagues conducted a systematic review of the association between bereavement and biomarkers of immune function. A meta-analysis was conducted to synthesize 41 years of research, and 33 publications met inclusion criteria. The overall conclusions were that individual differences in psychological response to bereavement (e.g., depression, grief) influence the association between bereavement and immune function (reported in Knowles et al., 2019). Going forward, this research area would benefit from longitudinal design, larger sample sizes and inclusion of advanced immunological methods.

O’Connor reviewed the history of research on how body, mind and brain adapt to grief. Morbidity and mortality following the death of a loved one has long been a topic of research, and it has long been known that there are immune cell changes in the bereaved. Newer neuroimaging methods have suggested that the greatest impact of the death of a loved one is in those who have the most severe psychological grief reactions. Differences in rumination, inflammation and cortisol dysregulation are clear between those who adapt well and those who do not (reported in O’Connor et al., 2019).

Rance

The Rance laboratory examined how the glutamateric neurokinin 3 receptor neurons in the median preoptic nucleus modulate heat-defense pathways in female mice. To characterize the thermoregulatory role of median preoptic nucleus neurons and their role in producing hot flushes, these neurons were selectively ablated. This resulted in increasing the core temperature of these female mice during the light phase and was independent of ambient temperature or estrogen status (reported in Krajewski-Hall et al., 2019). They conclude that glutamatergic median preoptic nucleus neurons that express the neurokinin 3 receptor modulate thermosensory pathways for heat defense.

Rance and colleagues examined whether noise-induced sleep disruption increases weight gain and decreases energy metabolism in female rats. Inadequate sleep increases obesity and environmental noise contributes to poor sleep. Women may be more vulnerable to noise than men, and this study investigated this in female rats who were monitored for sleep quality, feeding behavior, weight gain and estrous cycle length. The results showed that noise exposure disrupted sleep and increased weight gain in females but did not alter the length of the estrous cycle (reported in Coborn et al., 2019).

Sbarra

The Sbarra laboratory in collaboration with Mehl (EMBI Affiliate Faculty) examined the effect of a stressful life transition (divorce) on mental and physical health outcomes. To identify individual differences that may predict risk for adverse outcomes following divorce, they examined the association between DNA methylation across the serotonin transporter gene and self-reported emotional distress following marital separation. The results suggest that relatively greater methylation of this gene was associated with less subjective separation-related psychological distress, even when accounting for age, length of the relationship and time since separation (reported in Sbarra et al., 2019). These findings raises interesting research questions regarding the mechanisms of psychosocial adaptation to stressful life events.

Sbarra and Mehl examined psychological overinvolvement, emotional distress and daily affect following marital dissolution. In a sample of recently separated adults they examined rumination, language use and judge-rated recounting and reconstruing in relation to daily affect and psychological distress (reported in Bourassa et al., 2019). The results suggest that people’s tendency
to become overinvolved in their psychological experience after divorce predicts increased risk for distress in the months following marital separation.

**Wilson**

The Wilson laboratory have examined the reasons that humans and other animals exhibit biases in foraging and intertemporal choice tasks. Via extensive behavioral testing and quantitative modeling, they showed that rats exhibit similar time preferences in both cases: they prefer immediate versus delayed rewards and they are sensitive to opportunity costs of delays to future decisions (reported in Kane et al., 2019). The model appears to explain individual rats’ time preferences across both contexts and provides evidence for a common mechanism for myopic behavior in foraging and intertemporal choice.

The Wilson laboratory has examined the reasons that humans and other animals integrate evidence over time to make decisions, but do so suboptimally. This could arise because of neuronal noise, weighting evidence unequally over time, previous trial effects or overall bias. Using an auditory evidence accumulation task in humans, they report that people exhibit all four suboptimalities (reported in Keung et al., 2019). Pupilometry shows that only noise and unequal evidence weighting are related to different aspects of the pupil responses, and these could be related to tonic and phasic norepinephrine activity.

The Wilson laboratory has suggested an approach to successful modeling of behavioral data, using ten simple rules. Such modeling of behavior has revolutionized psychology and neuroscience by allowing us to probe the algorithms underlying behavior. This makes it more likely that neural correlates of these behaviors will be discovered with more precision, to yield a better understanding of optimal and suboptimal behaviors and the effect of interventions on these. To do this they applied their rules to both the simplest and more advanced modeling techniques to share the power of these methods and to point out potential pitfalls (reported in Wilson and Collins, 2019).
Publications in peer-reviewed journals


Gray DT, Umapathy L, De La Peña NM, **Burke SN**, Engle JR, **Trouard TP**, and **Barnes CA** (2019) Auditory processing deficits are selectively associated with medial temporal lobe mnemonic function and white matter integrity in aging macaques. Cerebral Cortex, in press.


Pottier C, ..., Ahern GL, Reiman EM, ... (2019) Genome-wide analyses as part of the international FTLD-TDP whole genome sequencing consortium reveals novel disease risk factors and increases support for immune dysfunction in FTLD. Acta Neuropathologica, 137:879-899.


Raichlen DA and Alexander GE (in press) Why your brain needs exercise: Key transitions in the evolutionary history of humans may have linked body and mind in ways that we can exploit to slow brain aging. Scientific American.


Satizabal CL, ... Huentelman M, ... (2019) Variants affecting diverse domains of MEPE are associated with two distinct bone disorders, a craniofacial bone defect and otosclerosis. Genetics in Medicine, 21:1199-1208.


Publications (other)


Presentations at scientific meetings


Barnes CA. Impact of age on neural circuits critical to memory. HKIAS Symposium on Advances in Neuroscience, City University of Hong Kong, March 2019.


Fernandez, F. Impact of sleep on cognition and AD in DS. Alzheimer’s and Down Syndrome Workshop, Bethesda, MD, March 2019.


Alexander GE. Patterns of daily activity in the oldest old: Findings from the McKnight Brain Aging Registry. Eleventh McKnight Inter-Institutional Meeting, University of Florida, Gainesville FL, April 2019.

Barnes CA. Memory and the Aging Brain, New Member Research Briefings, Class II, National Academy of Sciences, April 2019.


Barnes CA. Memory and the Aging Brain, Annual Scientific Meeting of the European Society for Clinical Investigation (ESCI 2019), Coimbra, Portugal, May 2019.


Cowen SL. Panel Speaker: Preparation for graduate admission for underrepresented students. Undergraduate Research Opportunities Consortium (UROC), University of Arizona, Tucson, AZ, June 2019.


Brinton, RD. Innovations in brain science of the future for those who need a cure today. Faculty Showcase, University of Arizona, Tucson, AZ, October 2019.


Han E, Schimanski LA, Ali K, Barnes CA, and Tatsuno M. Detection of hippocampal cell assemblies while rats learn a place-dependent eyeblink conditioning task. Undergraduate Neuroscience Symposium, University of Alberta, August 2019.


Gray DT, Umapathy L, DeLaPena NM, Burke SN, Engle JR, Trouard TP, and Barnes CA. Auditory processing deficits are selectively associated with medial temporal lobe mnemonic function and white matter integrity in aging macaques. Arizona Postdoctoral Research Conference, University of Arizona Phoenix Campus, Phoenix, AZ., September 2019.

Barnes CA. Life trajectories for successful aging: evidence from animal models of aging. Life Trajectories and Interventions that Support Successful Neurocognitive Aging Meeting, Montreal Neurological Institute, McGill University, Montreal, Canada, September 2019.


Ekstrom AD. Testing the influence of enriched body-based cues on how we encode and retrieve space. Memory Disorders Research Society, New York City, NY, October 2019.


Ekstrom AD. Decoding how we represent space when we navigate. Colloquium Series, Department of Psychology, University of Arizona, Tucson, AZ, October 2019.

Rance N. Brain circuits mediating the generation of menopausal hot flushes. Brain Research Initiative, Brigham and Women's Hospital, Boston, MA, October 2019.

Chen S, Wang T, and Brinton RD. Allopregnanolone prevent the loss of neuronal differentiative capacity in 3xTgAD mice. Program No. 651.10. 2019 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, October 2019.


Program No. 535.03, 2019 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, October 2019.


Shang Y, Mishara A, Desai MK, Wang T, and Brinton RD. APOE and chromosomal sex shows significant effect on the lipid pathways from multiple scale analysis of aged mice. Program No. 651.05. 2019 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, October 2019.

Srivathsa SV, Khattab SO, Lester AW, and Barnes CA. Role of prefrontal-hippocampal interactions in age-related deficits in spatial working memory, Program No. 600.08. 2019 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, October 2019.


Andrews-Hanna JR. Constructing and Deconstructing the Dynamics of Autobiographical Thought. 60th Annual Meeting Psychonomic Society, Montreal, Quebec, Canada, November 2019.


Grilli MD. The cognitive and neural bases of personal semantics: Insights from individuals with medial temporal lobe amnesia. 60th Annual Meeting Psychonomic Society, Montreal, Quebec, Canada, November 2019.

Oyao AV, Forloines MR, Robertson A, Grilli MD, and Ekstrom AD. Older adults show impairments in learning new spatial environments compared to younger adult. 60th Annual Meeting Psychonomic Society, Montreal, Quebec, Canada, November 2019.

Presentations at public (non-scientific) meetings or events

Cowen SL. Your Brain on Dopamine. Tucson Community Science Café, Tucson, AZ, January 2019.


Cowen SL. Dopamine, Neuroscience, and Science Fiction, Tucson Science Fiction Writers Association., Tucson, AZ, February 2019.


Cowen SL. The Aging Mind and Brain. UA Retired Faculty Dinner, Tucson, AZ. July 2019.


Awards

Gene Alexander, Ph.D., Elected Fellow, American Psychological Association Division 20, Adult Development and Aging .

Jessica Andrews-Hanna, Ph.D., Curie Award for Outstanding Research, University of Arizona (2019)

Jessica Andrews-Hanna, Ph.D., Galileo Circle Curie Award for “Rising Star” in Academic Scholarship, University of Arizona (2019)

Lynn Nadel, Ph.D., William James Fellow Award, Association of Psychological Societies (APS), 2019

Lynn Nadel, Ph.D., Distinguished Scientific Contribution Award, American Psychological Association (APA), 2020.

Matthias Mehl, Ph.D., Miegunyah Distinguished Visiting Fellow, University of Melbourne (2019)

Mary Peterson, Ph.D., Clifford T. Morgan Leadership Award, Psychonomic Society (2019)

Mary Peterson, Ph.D., Excellence in Mentoring Award, Office of Inclusion and Multicultural Engagement, UA Successful Scholars Faculty Mentoring Program (2019)

Mary Peterson, Ph.D., Early Career Psychologist Champion Award, American Psychological Association (2019)

Eric Reiman, M.D., Appointment to National Advisory Council on Aging

Dave Sbarra, Ph.D., Graduate Teaching and Mentoring Award from the Graduate College
Faculty

Complete Faculty List

Director

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

Associate Director

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

Strategic Advisory Committee

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

Scientific Advisory Committee

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

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

(Select biographical sketches included in following pages)

- Jessica Andrews-Hanna, Ph.D., Assistant Professor, Psychology, University of Arizona
- E. Fiona Bailey, Ph.D., Associate Professor, Physiology, University of Arizona
- Heather Bimonte-Nelson, Ph.D., Associate Professor, Honors Disciplinary Faculty; Behavioral Neuroscience Program Director, Arizona State University
- Ying-hui Chou, Ph.D., Assistant Professor, Psychology, University of Arizona
- Paul Coleman, Ph.D., UA Associate, Evelyn F. McKnight Brain Institute, University of Arizona; Research Professor, The Biodesign Institute, Neurodegenerative Disease Research Center, Arizona State University
- Fabian Fernandez, Ph.D., Assistant Professor, Psychology, University of Arizona
- Ralph F. Fregosi, Ph.D., Professor, Physiology, University of Arizona
- Andrew J. Fuglevand, Ph.D., Associate Professor, Physiology, University of Arizona
- Katalin M. Gothard, M.D., Ph.D., Professor, Physiology, University of Arizona
- Matt Grilli, Ph.D., Assistant Professor, Psychology, University of Arizona
- Meredith Hay, Ph.D., Professor, Physiology, University of Arizona
- Matthew J. Huentelman, Ph.D., UA Associate, Evelyn F. McKnight Brain Institute, University of Arizona; Associate Professor, Neurogenomics Division, Translational Genomics Research Institute
- Anita Koshy, M.D., Assistant Professor, Neurology, University of Arizona
- Lalitha Madhavan, MBBS, Ph.D., Assistant Professor, Neurology, University of Arizona
- Diano Marrone, Ph.D., UA Associate, Evelyn F. McKnight Brain Institute; Assistant Professor, Psychology, Wilfrid Laurier University
- Matthias R. Mehl, Ph.D., Professor, Psychology, University of Arizona
- Lynn Nadel, Ph.D., Regents’ Professor, Psychology, University of Arizona
- Janko Nikolic-Zugich, M.D., Ph.D., Professor and Chairman, Immunobiology; Co-Director, Arizona Center on Aging, University of Arizona
- Mary-Frances O’Conner, Ph.D., Assistant Professor, Psychology, University of Arizona
- Mary Peterson, Ph.D., Professor, Psychology, University of Arizona
- Steve Rapcsak, M.D., Professor, Neurology, Psychology and Speech, Hearing and Language Pathology, University of Arizona; Chief, Neurology Section, VA Medical Center
- Steve Rapcsak, M.D., Professor, Neurology, Psychology and Speech, Hearing and Language Pathology, University of Arizona; Chief, Neurology Section, VA Medical Center
- Linda L. Restifo, M.D., Ph.D., Professor, Neurology, Neuroscience, Cell Biology and Anatomy, andBiO5 Institute, University of Arizona
- David A. Sbarra, Ph.D., Professor and Director of Clinical Training, Psychology, University of Arizona
- Anne C. Smith, Ph.D., Associate Research Scientist, Evelyn F. Brain Institute, University of Arizona
- Ted P. Trouard, Ph.D., Professor, Biomedical Engineering, University of Arizona
- Robert C. Wilson, Ph.D., Assistant Professor, Psychology, University of Arizona
**Biographical Sketch**

Geoffrey Lawrence Ahern, M.D., Ph.D.
Professor, Neurology, Psychology, and Psychiatry

**Education/Training**

<table>
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<th>Institution &amp; Location</th>
<th>Degree</th>
<th>Year(S)</th>
<th>Field Of Study</th>
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<td>SUNY, Purchase College</td>
<td>B.A.</td>
<td>1976</td>
<td>Psychology</td>
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<td>Yale University, New Haven</td>
<td>M.S.</td>
<td>1978</td>
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<td>1981</td>
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<tr>
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<td>M.D.</td>
<td>1984</td>
<td>Medicine</td>
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<td>Waterbury Hospital, Waterbury</td>
<td>Intern</td>
<td>1984 – 1985</td>
<td>Medicine</td>
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<td>Boston University, Boston</td>
<td>Resident</td>
<td>1985 – 1988</td>
<td>Neurology</td>
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<tr>
<td>Beth Israel Hospital, Boston</td>
<td>Fellow</td>
<td>1988 – 1990</td>
<td>Behavioral Neurology</td>
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**Personal Statement**

I am a professor of neurology, psychology, and psychiatry at the University of Arizona College of Medicine. I also have an appointment as professor in the Evelyn F. McKnight Brain Institute at the University of Arizona and hold the Bruce and Lorraine Cumming Endowed Chair in Alzheimer’s Research. I am a board-certified neurologist with subspecialty board certification in behavioral neurology and neuropsychiatry. Over the past 25 years, I have served as principal investigator or sub-investigator in more than 45 clinical trials in Alzheimer’s disease, including those from the pharmaceutical industry as well as the Alzheimer’s Disease Cooperative Study (ADCS). I am the director of the University of Arizona clinical arm of the Arizona Alzheimer’s Disease Core Center. For the Brain Imaging and Fluid Biomarkers Core, I will provide oversight in the acquisition of CSF and blood samples at the University of Arizona and will work with the nurse practitioners and with Drs. Alexander, Beach, and Blennow in helping to augment efforts in the coordination of the CSF and blood sample acquisition, processing, and analyses as part of the Fluid Biomarkers Workgroup for the BI-FB Core. I will work with Drs. Alexander and Caselli (Clinical Core leader) and BI-FB Core staff to help identify interested ADCC Clinical Core participants for inclusion in the neuroimaging and fluid biomarker standardization cohort. My extensive experience in performing LPs for CSF acquisition and storage for both clinical and research protocols make me well suited to be an investigator on this new core.


**Positions**

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

**Honors and Awards**

2009        Cited in S Naifeh and GW Smith (eds.) The Best Doctors in America 2009 – 2010
2010        Cited in S Naifeh and GW Smith (eds.) The Best Doctors in America 2011 – 2012
2013        Cited in S Naifeh and GW Smith (eds.) The Best Doctors in America 2013
2014        Cited in S Naifeh and GW Smith (eds.) The Best Doctors in America 2014

**Contribution to Science**

Paraneoplastic syndromes are entities in which the body produces an antibody against a malignancy, which occasionally reacts against tissues and the brain, leading to a number of characteristic syndromes. During my fellowship, I came upon a patient with intractable epilepsy and severe memory difficulties. Ultimately, he was found to have testicular cancer. In collaboration with the group at Memorial Sloan-Kettering in New York, we were able to identify and characterize a new paraneoplastic antibody, anti-Ta (named after the first two initials of the patient). This antibody was ultimately found to be one of the causes of limbic encephalitis. The field has clearly grown over the past 25 years, and now the anti-Ta antibody has been characterized as coming from the family of the anti-Ma1/ Ma2 paraneoplastic antibody class.

In graduate school, I developed an interest in cerebral lateralization, particularly for emotional processes. Without going into a great deal of detail about the evidence for same, the general principal that appears to have emerged over the past three decades is that while the right hemisphere seems to be more involved in handling emotional issues in general, the left hemisphere tends to be a bit more ‘positive’ in terms of the emotional valence it handles and the right hemisphere tends to be more ‘negative.’ Over the years, I have investigated this phenomenon with such wide-ranging techniques as lateral eye movements, facial EMG, EEG spectral analysis, FDG PET scanning, and unilateral hemispheric inactivation produced in the Wada test (the latter studies are considered below under the Wada test).


The intracarotid amobarbital test, otherwise known as the Wada test (after its inventor, Juhn Wada), is a technique in which each cerebral hemisphere is transient and activated via the use of sodium amytal injected into the ipsilateral carotid artery. This test is done to determine language dominance, as well as the potential for memory dysfunction, in patients in whom unilateral temporal lobectomy is being considered for intractable epilepsy. Utilizing this technique, I was able to make a number of observations regarding how each cerebral hemisphere handles positive and negative emotion. This includes not only self-report, but the ability to perceive emotion in the faces of others.


I was also able to show that the two hemispheres are different in their ability to control heart rate and heart rate variability.


Finally, using EEG spectral analysis, I was able to quantify the time course and spatial extent of hemispheric inactivation during the Wada test.

Hemispatial neglect is a well-known neurological phenomenon that is usually associated with lesions in the right hemisphere. Having trained under Dr. Marsel Mesulam, I was exposed to this phenomenon early in my career. In association with my colleagues, we published a number of reports that elucidated this phenomenon. For instance, we were able to show (in the same patient) that posterior lesions in the right hemisphere led to a greater involvement of the sensory aspects of neglect, while anterior lesions in the right hemisphere led to greater involvement in the motoric intentional aspects of neglect.


We were also able to demonstrate that right hemispatial neglect, which is usually a transient phenomenon, might be more long lasting if there were to be bilateral involvement of attentional systems in the brain.


In a later study, I was able to show that neglect was not an all-or-none phenomenon, but that it could vary in severity depending on the degree of hemispheric dysfunction. This study was performed in patients undergoing the Wada test. During maximal inactivation of the right hemisphere, left hemispatial neglect was quite severe. But as the Amytal wore off, the neglect became profound and this phenomenon correlated perfectly with other measures of right hemispheric function, including the degree of EEG slowing.


Complete list of published work in MyBibliography


Research Support


2018-2019 A Randomized, Double-Blind, Placebo-Controlled, Two-Cohort Parallel Group Study to Evaluate the Efficacy of CAD106 and CNP520 in Participants at Risk for the Onset of Clinical Symptoms of Alzheimer’s Disease. (Generation 1) Protocol # CAPI015A2201J. Novartis. Total grant: $100,702 / patient. 2% salary support, 2% effort.

2018-2019 A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study to Evaluate the Efficacy and Safety of CNP520 in Participants at Risk for the Onset of Clinical Symptoms of Alzheimer’s Disease. (Generation 2) Protocol # CCNP520A2202J. Novartis. Total grant: $95,456 / patient. 2% salary support, 2% effort.
**Biographical Sketch**

Gene Alexander, Ph.D.
Professor, Psychology and Psychiatry

**Education/Training**

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<tr>
<td>Pomona College, Claremont, CA</td>
<td>B.A.</td>
<td>1983</td>
<td>Psychology</td>
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<tr>
<td>Loyola University of Chicago, Chicago, IL</td>
<td>M.A.</td>
<td>1987</td>
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<td>Ph.D.</td>
<td>1992</td>
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**Personal Statement**

I am a professor in the Departments of Psychology and Psychiatry, the Evelyn F. McKnight Brain Institute, the BIO5 Institute, and the Neuroscience and Physiological Sciences Graduate Programs at the University of Arizona. I also am director of the Brain Imaging, Behavior and Aging Lab; a member of the Internal Scientific Advisory Committee for the state-supported Arizona Alzheimer’s Consortium; a member of the ADCC Executive Committee, and director of the Brain Imaging and Fluid Biomarkers Core for the NIA Arizona Alzheimer’s Center. Prior to coming to Arizona, I was chief of the Neuropsychology Unit in the Laboratory of Neurosciences in the Intramural Research Program at the NIA. I serve as a member of the NIA Neuroscience of Aging Study Section and am a fellow of the Association for Psychological Sciences and the American Psychological Associations Society for Clinical Neuropsychology. My research is supported by the NIA, the State of Arizona and Arizona Department of Health Services, and the McKnight Brain Research Foundation. I have 20 years of experience as a neuroimaging researcher on the effects of aging and risk factors for age-related neurodegenerative disease. I use structural and functional magnetic resonance imaging (MRI) and positron emission tomography (PET) to investigate the effects of multiple health and lifestyle factors on the cognitive and brain changes associated with healthy and pathological aging, with the goal of developing new interventions for the effects of cognitive aging.


**Research and Professional Experience**

1988 – 1989 Clinical Psychology Intern, Department of Psychiatry & Behavioral Science, University of Washington, Seattle
1989 – 1992 Research Fellow, Dept. of Brain Imaging, NYSPI and Columbia University, NY
1991 – 1993 Research Scientist I, Dept. of Brain Imaging, NYSPI and Columbia University, NY
1993 – 1999 Staff Fellow to Sr. Staff Fellow, Laboratory of Neurosciences, NIA, NIH, Bethesda
1993 – 1999 Chief, Neuropsychology Unit, Laboratory of Neurosciences, NIA, NIH, Bethesda
1999 – 2003 Research Assoc Professor, Dept. of Psychology, Arizona State University, Tempe
2001 – 2009 Director, Data Management and Statistics Program/Core, Arizona ADC
2003 – 2007 Professor, Psychology Dept., Arizona State University, Tempe
2007 – Present Professor, Psychology Dept & Evelyn F McKnight Brain Institute, University of Arizona, Tucson
2007 – Present Director, Brain Imaging, Behavior & Aging Lab, Psychology Dept., University of Arizona, Tucson
2007 – Present Professor, Neuroscience Graduate Interdisciplinary Program, University of Arizona, Tucson
2011 – Present Professor, Physiological Sciences Graduate Interdisciplinary Program, University of Arizona
2017 – Present Member, BIO5 Institute, University of Arizona, Tucson
2017 – Present Member, Department of Psychiatry, College of Medicine Tucson, University of Arizona

Honors and Awards

1995 – Present Ad Hoc Reviewer, more than 20 journals in Neuropsychology, Psychiatry, Neurology, and Neuroscience.
1996 – 1999 Staff Recognition Awards (annual), Laboratory of Neurosciences, IRP, NIA, NIH
2000 – Present Reviewer, Alzheimer’s Association Research Grant Program
2003 – 2007 Member, Study Section, Clinical Neuroscience and Disease, IRG, CSR, NIH
2003 Member, SEP, Women’s Health Initiative Memory Study, Review Branch, NHLBI, NIH
2004 Member, Special Emphasis Panel, Alzheimer’s Disease Center Grant Review, NIA, NIH
2005 – 2007 Member, Specialist Review Committee, Psychology: Exp/Clinical, Fulbright Scholar Program
2006 Chair, SEP, Clinical Neuroscience & Disease, ZRG1 BDCN-E, IRG, CSR, NIH
2008 Member, SEP, Prog Project Review Group, Recovery from Illness, ZAG1 ZIJ-8 O1, NIA, NIH
2008 Member, Study Section, Brain Injury & Neurovascular Pathology, ZRB 1 BDCN-L (07), CSR, NIH
2008 – Present Member, Neuroimaging Workgroup, International Conf. on Alzheimer’s Disease/ISTAART
2009 Reviewer, SEP, Challenge Grant Panel #10, ZRG1 BDA-A 58 R, CSR, NIH
2009 Member, SEP, P30 Faculty Recruitment in Biomedical Research Core Centers, NIA, NIH
2009 Member, SEP, RC2 Grand Opportunity Grants in Genetics, Epigenetics & Genomics, NIA, NIH
2009 Member, SEP, Program Project Review Group, Brain Dopamine, ZAG1 ZIJ-8 J3, NIA, NIH
2009 Member, SEP, Prog. Project Review. Group, Neuroimaging and Aging, ZAG1 ZIJ-5 JF, NIA, NIH
2010 Member, Neurological Sciences & Disorders K Review Committee, NSD-K, NINDS, NIH
2010 – 2012 Member, Neuroscience of Aging Review Committee, NIA-N, NIA, NIH
2010 Member, SEP, Prog. Project Rev., Exercise, Motor Deficits, & Aging, ZAG1-ZIJ-9, NIA, NIH
2010 Member, SEP, Prog. Project Review, Dopaminergic Dysfunct. Aging, ZAG1 ZIJ-6 J3, NIA, NIH
2011 Chairperson, Member Special Emphasis Panel, ZAG1 ZIJ-7 (J1), NIA, NIH
2011 – 2014 Advisory Editor, Neurobiology of Aging, Elsevier
2011 Member, VA MHBB Merit Review Subcommittee, Veterans Administration
2011 Member, SEP, Biobehavioral Research Award Innovative New Scientists (BRAINS), ZMH1ERBL04, NIMH, NIH
2011 – Present Reviewer, Alzheimer’s Disease Pilot Grant Program, Arizona Alzheimer’s Disease Center
2011 – Present Fellow, Association for Psychological Science
2012 Member, Neurological Sciences & Disorders K Review Committee, NSD-K, NINDS, NIH
2012 – Present Member, Cognitive Workgroup, Evelyn F. McKnight Brain Institute
2012 – Present Member, MRI Standardization Workgroup, Evelyn F. McKnight Brain Institute
2012 – Present Co-Director, Annual Conference on Successful Aging, University of Arizona
2013 Member, SEP, Neurodegenerative & Neurodevelopmental Disease, ZRG1BDCN-Y(02), NIA, NIH
2013 Member, SEP, Psychol. Health, Development & Aging, 10 ZRG1 BBBP-D (02), NIA, NIH
2013 Member, Alzheimer’s Disease Research Centers Review, ZAG1ZIJ4J1, NIA, NIH
2013 – Present Member, Neuroscience of Aging Review Committee, NIA-N, NIA, NIH
2014 Member and Chairperson, Biobehavioral & Behavior. Processes Review Group, ZRG1BBBPY04, CSR, NIH
2015 – Present Guest Assoc. Editor, Neuroimaging Approaches to Cognitive Aging, Frontiers Aging Neuroscience
2015 – Present Chair, Research Committee, Department of Psychology, University of Arizona
2016 Member, SEP, Alzheimer’s Disease Center Review, ZAG1 ZIJ-1 M1, NIA, NIH
2016 Member, SEP, Prevention Trial Review, ZAG1 ZIJ-1 M2, NIA, NIH
2017 – Present Fellow, American Psychological Association Division 40, Society for Clinical Neuropsychology
2019 Member, SEP, Alzheimer Network U19 Review Panel, ZAG1 ZIJ-U M1, NIA, NIH
2019 Member, AD Center Review Panel, ZAG1 ZIJ GJ1, NIA, NIH
2019 Fellow, American Psychological Association Division 20, Adult Development and Aging

**Contribution to Science**

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

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


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


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


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


**Complete list of published work in MyBibliography**

**Research Support**

**NIA R01 AG064587**
Alexander, Bowers, Woods (MPIs) 8/01/19 – 4/30/24

*Revitalizing Cognition in Older Adults at Risk for Alzheimer’s Disease with Near-Infrared Photobiomodulation*

The goal of this project is to determine whether NIR stimulation has potential for enhancing cognition in cognitively normal but “at risk” individuals for Alzheimer’s disease.

Role on project: Dr. Alexander is MPI.

**NIA R01 AG049464**
Alexander, Barnes, Coleman (MPIs) 8/1/14 – 3/31/20

*Epigenetic, Neuroimaging and Behavioral Effects of Hypertension in the Aging Brain*

To determine epigenetic changes induced by hypertension in brain regions important for cognition.

Role on Project: Contact PI

**NIA 3P30AG019610-1951**
Alexander (Core Leader), Reiman (PI) 9/15/18 – 6/30/21

*Brain Imaging and Fluid Biomarkers Core*

The goal of this supplement grant is to establish a new core to support brain imaging and biomarker research as part of the Arizona Alzheimer’s Disease Center.

Role on Project: Core Leader

**McKnight Brain Research Foundation**
Bowers, Alexander, Woods (MPIs) 5/1/18 – 4/30/20

*A Pilot Intervention with Near Infrared Stimulation: Revitalizing Cognition in Older Adults*

To evaluate the potential of near infrared light as an intervention for healthy cognitive aging.

Role on Project: PI

**McKnight Brain Research Foundation**
Alexander, Cohen, Levin, Wadley (MPIs) 9/1/15 – 12/31/18

*McKnight Inter-Institutional Cognitive Aging Assessment Core*

To provide standardized clinical and cognitive measures for multi-institutional brain aging research.

Role on Project: PI

**McKnight Brain Research Foundation**
Williamson (PI) 10/1/19-9/30/21

*Transcutaneous Vagal Nerve Stimulation and Cognitive Training to Enhance Cognitive Performance in Healthy Older Adults*

The goal of this project is to determine whether tVNS augments cognitive training associated improvements in cognition.

Role on Project: Dr. Alexander is PI of the UA subcontract.
AZ Alzheimer’s Consortium (ADHS)  Alexander (PI)  7/1/18 – 6/30/19

**Modifiable Health & Lifestyle Factors in Brain Aging and Alzheimer’s Disease**

The goal of this project is to investigate cerebrovascular risk factors for brain aging and cognitive health in humans and animal models.

Role on Project: PI

AZ Alzheimer’s Consortium (ADHS)  Alexander (PI)  7/1/18 – 6/30/19

**Influence of Health & Lifestyle Factors on Brain Aging and the Risk for Alzheimer’s Disease**

The goal is to study health and lifestyle factors that alter effects of brain aging and cognitive health.

Role on Project: PI

NIA R03 AG055020  Su (PI)  7/1/17 – 4/30/20

**Ultra-sensitive and Label-free Detection of Alzheimer’s Disease Biomarkers**

This goal is to evaluate a highly sensitive method to identify Alzheimer’s biomarkers in fluid samples.

Role on Project: Co-Investigator

NIA P30 AG019610  Reiman (PI)  7/1/16 – 6/30/21

**Arizona Alzheimer’s Disease Core Center**

This center provides core resources to support Alzheimer’s disease research in the Arizona region.

Role on Project: Co-Investigator and member of the Data Management and Statistics Core

NIH 3 R01 AG031581  Reiman, Caselli (MPIs)  4/1/14 – 3/31/20

**Brain Imaging, APOE & the Preclinical Course of Alzheimer’s disease**

The goal is to characterize the brain changes in those at risk for Alzheimer’s disease with the APOE ε4 allele.

Role on Project: Co-Investigator and PI of the UA subcontract.

NIA R01 AG049465  Barnes (PI)  8/1/14 – 3/31/20

**Neural System Dynamics and Gene Expression Supporting Successful Cognitive Aging**

The goal is to use cognitive, neurobiological and molecular methods to test reserve in a rodent model of aging.

Role on Project: Co-Investigator

NIA R01 AG061888  Wilson (PI)  9/1/19 – 8/31/24

**Evaluating the Neurocomputational Mechanisms of Explore-Exploit Decision Making in Older Adults**

The goal is to use cognitive, neurobiological and molecular methods to test reserve in a rodent model of aging.

Role on Project: Co-Investigator
Biographical Sketch

Jessica Andrews-Hanna, Ph.D.
Assistant Professor, Psychology

Education/Training

<table>
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<th>Institution &amp; Location</th>
<th>Degree</th>
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<th>Field Of Study</th>
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<tr>
<td>Duke University, Durham, NC</td>
<td>B.A.</td>
<td>2003</td>
<td>Biology, Psychology</td>
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<td>Washington University, St. Louis, MO</td>
<td>M.A.</td>
<td>2006</td>
<td>Neuroscience</td>
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<td>Harvard University, Cambridge, MA</td>
<td>Ph.D.</td>
<td>2009</td>
<td>Psychology</td>
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<tr>
<td>University of Colorado, Boulder, CO</td>
<td>Postdoc</td>
<td>2014</td>
<td>Cognitive Neuroscience</td>
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Personal Statement

Despite constant sensory input from our busy environment, the human mind has the capacity to overcome external constraints in favor of a different time, place, or perspective. By imagining what was or what might be, and by reflecting on our emotions and simulating the mental states of other people, we become better adapted to predict our future mental states and navigate our social world. My research seeks insight into the psychological and neural mechanisms underlying these internally guided processes and their top-down regulation. Related to this central theme, I am also passionate about exploring these questions across the lifespan and in a variety of mental health disorders and neurodegenerative diseases, with an ultimate goal of developing interventions to help individuals harness the beneficial aspects of internally guided cognition and live happier, healthier lives.

I currently direct the Neuroscience of Emotion & Thought (NET) Laboratory at the University of Arizona, where I am also an assistant professor in the Department of Psychology and the Interdisciplinary Cognitive Science Program. I have a strong record of collaboration and research funding and have received grant support as PI or Co-I on several neuroimaging grants examining the neural underpinnings of functional and dysfunctional memory, prospection, and other forms of internally guided cognition. I employ a multimodal approach in my research, combining methods spanning task-related functional MRI, resting state functional connectivity MRI (RSFC-MRI), fMRI meta-analyses, and laboratory and naturalistic behavioral assessments. I have particular expertise in RSFC-MRI and brain network analyses, including graph theory. Using these techniques, my research has revealed important insight into the functional-anatomic organization of the brain’s default mode network (DMN) and the frontoparietal control network, delineated how these large-scale brain systems develop throughout adolescence and change in normal and pathological aging, pointed to hyperconnectivity of the DMN in the first meta-analysis of RSFC-MRI in depression, and applied dynamic RSFC-MRI to clinical populations.

Positions

2017 – Present  Assistant Professor, Department of Psychology; Interdisciplinary Program in Cognitive Science, University of Arizona
2014 – 2016  Research Scientist/Associate, Institute of Cognitive Science, University of Colorado, Boulder
2009 – 2014  Postdoctoral Fellow, Institute of Cognitive Science, University of Colorado, Boulder

Honors

2003  Graduated with Distinction at Duke University
2006  Washington U. in St. Louis Alzheimer’s Disease Research Center Travel Fellowship
2007 – 2008  Harvard University Sosland Family Graduate Fellowship Award
2008  Thompson Reuter’s Science Watch Award for Fast-Breaking Paper
2009  Harvard Psychology Department Excellence in Teaching Award
2011  NIMH Summer Institute in Cognitive Neuroscience Fellow
2011 – 2014  Ruth L. Kirschstein National Research Service Award (NRSA) Postdoctoral Fellowship
2012  Intermountain Neuroimaging Consortium Pilot Funding Award
2013  Mind & Life Summer Research Institute Fellow
2013  Neuron 25 Year Anniversary: Featured influential paper from 2010
2015  Science of Prospection Award, Templeton Foundation
2016  Neuroimage Editor’s Choice Award best paper (2016)
2017  Kavli Foundation / U.S. National Academy of Science Frontiers of Science Fellow
2018  Fellow of the Psychonomics Society
2018  Early Investigator Award, Society of Experimental Psychologists
2018  Galileo Circle Curie Award for “Rising Star” in Academic Scholarship, University of Arizona

Contribution to Science

Across a series of studies employing task-related fMRI and fMRI meta-analyses, resting-state functional connectivity, graph theory, and experience sampling methods, my research was the first to demonstrate that the brain’s default network is organized into interacting subsystems that support different aspects of internally-guided cognition. These components allow us to retrieve past information and flexibly recombine this information into imagined episodes, reflect upon ours and others’ mental states, and guide decision making by computing the affective significance and personal meaning of incoming information. Collectively, this line of work led to a novel neurocognitive model of autobiographical thought as a multi-faceted phenomenon comprising several interacting component processes.

Since it’s delineation in the early 2000s, the brain’s default network has largely been viewed as a passive, task-negative brain system with minimal contributions to goal-directed cognition. My work is widely recognized for challenging these predominant views, revealing that the default network plays a key role in several active and goal-directed forms of internally-guided cognition spanning autobiographical and imaginative thought, and theory of mind. Some of my more recent work uses dynamic behavioral approaches and dynamic functional connectivity to explore how network interactions between the default network and other large-scale brain networks unfold and change over time.


A large portion of my research involves developing new methods to examine autobiographical thought, including its spontaneous emergence. My work in this domain has revealed that spontaneous thought is a frequent, heterogeneous, and often adaptive phenomenon that can be quantified through rigorous, ecologically-valid experimental investigation. My 2010 paper in the Journal of Neurophysiology was the first to link individual differences in resting state connectivity within the default network to spontaneous autobiographical thoughts. In later work, I developed a novel Autobiographical Thought Sampling Task, and used clustering approaches to distill autobiographical thoughts into major content dimensions that explain nearly 50% of the variance in traits relevant to mental health. My team also developed a smartphone application called MindMirror to assess the content, correlates and consequences of spontaneous and deliberate autobiographical thoughts as they emerge in real-world settings.


Several of my completed and ongoing research projects characterize the nature of internally-guided cognition, and the brain systems that support it, in aging and neurodegenerative disease. For example, my 2007 Neuron article was the first to reveal that normal aging is associated with functional connectivity alterations in default and external attention systems (even in individuals confirmed by PIB-PET to have no known amyloid deposition), and that these alterations relate to
individual differences in white matter integrity and cognition. My more recent work has shown that changes in default network connectivity in older adults are accompanied by alterations in the content and frequency of task-unrelated thought, and also extends these questions to Alzheimer’s disease, behavioral variant Frontotemporal dementia, Semantic dementia and Parkinson’s disease. In a theoretical review, MPI Grilli and I integrated research in this field into a neurocognitive theory of normal and pathological aging that we aim to test in the proposed work.


While much of my research provides support for the adaptive functions of autobiographical thought, the experience can also be associated with significant costs, disrupting task performance and hindering psychological well-being. My work reveals that the ability to regulate the content of one’s thoughts as well as the occurrence of self-generated thought based on contextual demands are two important factors that constrain the costs and benefits of self-generated cognition. Of particular interest are several recent and ongoing projects that examine dysfunctional styles of thinking in depression, anxiety, and maladaptive repetitive thought as a transdiagnostic construct. Integrating neuroimaging with behavioral assessments reveals that dysfunctional self-generated thought in depression and anxiety is accompanied by alterations in the function of - and interaction between - default and executive control networks.


Complete list of published work in MyBibliography  

Research Support  
NIA 1R03AG060271-01A1  
Grilli: PI  
4/15/19-3/31/21

The episodic autobiographical memory hypothesis of preclinical Alzheimer’s disease: Developing a new approach for early cognitive detection and measurement of Alzheimer’s disease.
Role on Project: Co-Investigator

NIA R56 AG061888  Wilson: PI  9/30/18 – 8/31/20
Evaluating the Neurocomputational Mechanisms of Explore-Exploit Decision Making in Older Adults

Role on Project: Co-Investigator

Maladaptive repetitive thought and psychopathology: The mediating role of neural dyadic empathy.

Role on Project: PI

AZ Alzheimer’s Consortium (ADHS) Andrews-Hanna: PI  7/01/19 - 6/30/20
Uncovering neurocognitive links between Alzheimer’s disease and depression in mid-life to early aging

Role on Project: PI

AZ Alzheimer’s Consortium (ADHS) Grilli: PI  7/01/19 - 6/30/20
Improving clinical neuropsychological assessment of subtle cognitive decline and mild cognitive impairment

Role on Project: Co-Investigator

NIA P30 AG019610 Reiman: PI  7/1/18 – 6/30/19
Uncovering Neurocognitive Links between Alzheimer’s Disease and Depression in Mid-Life to Early Aging

Role on Project: Pilot Grant PI

NIA 1R01 AG043452 Bryan: PI  8/1/14 – 7/31/19
Enhancing Function in Later Life: Exercise and Functional Network Connectivity

Role on Project: Co-Investigator

NIMH 1R21 AG108848 Banich: PI  6/20/16 – 3/31/19
Clearing the Contents of Working Memory: Mechanisms and Representations

Role on Project: Co-Investigator
**Biographical Sketch**

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

**Education/Training**

<table>
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<th>Institution &amp; Location</th>
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<th>Field Of Study</th>
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<td>University of California, Riverside, CA</td>
<td>B.A. (Honors)</td>
<td>1971</td>
<td>Psychology</td>
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<tr>
<td>Carleton University, Ottawa, Ontario, Canada</td>
<td>M.A.</td>
<td>1972</td>
<td>Psychology</td>
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<tr>
<td>Carleton University, Ottawa, Ontario, Canada</td>
<td>Ph.D. (Cum laude)</td>
<td>1977</td>
<td>Psychology</td>
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**Personal Statement**

I have been interested in the brain circuits responsible for memory and how these circuits change during aging for more than four decades. I have applied behavioral and electrophysiological methods to the study of plasticity and circuit properties of the medial temporal lobe over that time, including in vivo evoked field potential recordings in chronically implanted freely behaving rats, and intracellular and extracellular recordings in vitro. I was instrumental (with McNaughton) in the development of ensemble tetrode recording methods for single units in awake young and old rats. More recently I have extended these methods to young and aged nonhuman primates, with chronic implants of hyperdrive recording devices that are capable of individually lowering multiple tetrodes into the hippocampus while monkeys behave. Another approach use to understand behavior-driven circuits is the single cell gene expression imaging method “catFISH,” which was developed in her laboratory. The immediate early gene Arc is induced in a cell-specific fashion in the brain by neural activity associated with attentive, active behavior. With this method, the activity history of individual cells in a population can be determined for two different time points within the same animal (ex vivo). This method contributed to moving the field closer to the goal of behavior-driven whole brain imaging with single cell resolution. I direct the Evelyn F. McKnight Brain Institute at the University of Arizona and the Division of Neural Systems, Memory and Aging. I am actively involved in collaborative projects with scientists within the state of Arizona, across the United States and around the world. I have a track record of conducting difficult, systematic, and thorough studies with interdisciplinary teams, as well as with my own students and postdoctoral fellows – projects that have been followed through to publication (274 total, H index 101), a number of which are now classic references on brain aging and behavior.

**Positions**

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

**Honors**

1969  NSF Summer Research Fellowship
1971  Phi Beta Kappa
1972 – 1974  Ontario Graduate Fellowship
1979 – 1981  NRSA Individual Postdoctoral Fellowship, NIH
1981 – 1982  NATO Fellowship in Science, NSF
1984 – 1989  Research Career Development Award, NIH
1987 – 1991  Neuroscience, Behavior and Sociology of Aging Committee A, NIA
1991 – 1997  Medical and Scientific Advisory Board, Alzheimer’s Association
1994 – 1999  Research Scientist Award, NIMH
1996 – 2000  Councilor, Society for Neuroscience
1997 – 2000  Medical and Scientific Advisory Council, Alzheimer’s Association
1999 – 2004  Board of Scientific Counselors, NIMH
2000 – 2002  Secretary, Society for Neuroscience
2004  MERIT Award, National Institute on Aging, NIH
2004  Elected Norwegian Royal Society of Sciences and Letters
2006  Regents’ Professor, University of Arizona
2006  Evelyn F. McKnight Endowed Chair for Learning and Memory in Aging, University of Arizona
2007  Fellow, American Association for the Advancement of Science
2010  Elected: Mika Salpeter Lifetime Achievement Award, Society for Neuroscience
2011  Elected: Galileo Fellow, College of Science, University of Arizona
2013  Ralph W. Gerard Prize in Neuroscience, Society for Neuroscience
2014  American Psychological Association Award for Distinguished Scientific Contributions
2017  Quad-L Award, University of New Mexico
2018  Elected Member, National Academy of Sciences
2018  Museum of Contemporary Art Local Genius Award

**Contribution to Science**

Some of my early work was inspired by two fundamental discoveries in the early 1970s. The first was the discovery of the likely biological basis of memory formation in the brain in 1973 by Terje Lomo, Tim Bliss, and Tony Gardner-Medwin. They used patterned electrical stimulation to experimentally induce changes in synaptic strength in the hippocampus, enabling the study of the process the brain may use to lay down memory traces (long-term potentiation, or LTP). In that same time period, O’Keefe and Nadel were circulating a monograph, which eventually turned into a classic and
influential book (The Hippocampus as a Cognitive Map, 1978) that suggested that hippocampal function could be evaluated in animals by assessing spatial memory. These ideas made it possible to design experiments to interrogate how the brain acquires, stores, and retrieves information across the lifespan. Using awake, freely behaving rats with chronically implanted electrodes that could monitor the induction and decay of LTP over weeks, we obtained the first concrete evidence that LTP persistence and the durability of memory were related, and that a decline in its persistence was associated with poorer spatial memory in old animals. This relationship held in young rats as well – the better the animal’s memory, the more durable was LTP. For these experiments, I developed a novel spatial memory task (“the Barnes maze”), which was conceived of and the methods published long before the more widely used, and conceptually similar, Morris water maze. The 1979 paper referenced below introduced the Barnes maze and provided the first demonstration that LTP and memory are associated – providing the groundwork for an explosion of research on the biophysical and molecular mechanisms of memory across the lifespan.


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


Having established that plasticity mechanisms like LTP are altered at older ages, and that, with some important exceptions, most biophysical properties of aged hippocampal neurons are intact, I extended my work from an assessment of the impact of age on the function of artificially activated networks to those activated by behavior. These were the earliest studies to examine behavior-driven single cell firing characteristics in the aged hippocampus. We developed better recording methods over the years (the tetrode, the hyperdrive device) that enabled recording from many hippocampal
cells simultaneously. This made it possible to characterize how the hippocampus constructs a “cognitive map” (as proposed by O’Keefe and Nadel in 1978) of the surrounding environment. We showed that there are distinct changes in spatial representations within the hippocampus – with the older animals appearing to occasionally retrieve the wrong map (in CA1) upon repeated exposures to an environment. In addition, we have shown plasticity-related defects in the construction of these maps, changes in the replay of these maps during sleep in aged rats, as well as altered network functions of other temporal and frontal lobe structures.


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


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


Complete list of published work in MyBibliography

Research Support
NIA R01 AG003376 Barnes (PI) 1/16 - 11/30/20

Neurobehavioral Relations in Senescent Hippocampus
The research is directed towards an understanding of the decline in spatial cognition and memory with age. Nonhuman primates are assessed behaviorally and electrophysiologically (hippocampus, perirhinal cortex), and the ensemble activity of the entorhinal and perirhinal cortical units in young and old rats are examined.

NIA R01 AG05058 Barnes (PI) 9/1/15 - 5/31/20

Cell Assemblies, Brain Adaptation and Cognitive Aging
The aims of this grant are to better understand the underlying causes of two hallmarks of cognitive aging – behavioral slowing and multi-tasking deficits. We will examine how the aging brain adapts to the changed dynamics intrinsic to both hippocampus and PFC in rats, and how these structures interact or compete during aging, as well as the cellular correlates of multi-tasking in an aging primate model, to assess how aging weakens the resilience of working memory circuits in the face of interference.

NIA R01 AG048907 Huentelman, Barnes (MPI) 9/30/14 - 5/31/19

CATT: Development and Application of a Neuronal Cell Activity-Tagging Toolbox
Our overall goal of this EUREKA award is to develop methods to label cells that were active during a defined temporal period and utilize a new approach to investigate the impact of aging on the circuit elements engaged by those behaviors as well as the transcriptional function of those behavior-driven labeled cells. The “Cell Activity-Tagging Toolbox” will provide a means to “permanently mark” the specific cells that were engaged in a defined behavioral experience. This is an extension of the catFISH methodology that can only labels cells for minutes to hours after a behavior.
Role: Principal Investigator (Multi-PI)

NIA R01 AG049465 Barnes (PI) 8/01/14 3/31/20

Neural System Dynamics & Gene Expression Supporting Successful Cognitive Aging
The major goal of this project is to understand the basis of differing cognitive trajectories that occur even over the lifespan in inbred rat strains. Methods used include cognitive assessment batteries for frontal and temporal lobe regions, 7T MRI scanning methods, transcriptional evaluation, and circuit activity pattern assessment using the Arc catFISH single cell imaging method devised in Barnes’
laboratory. All methods are applied to animals of different ages and aptitudes so that the underlying basis of differential cognitive functioning across the lifespan may be identified.

**NIA R01 AG049464**  Coleman, Barnes, Alexander (MPI)  8/1/14 - 3/31/20

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

Major project goals are to determine what hypertension-induced epigenetic changes occur in a transgenic rat model of hypertension. Blood pressure can be slowly elevated in this rat model from middle to older ages, mimicking the course of hypertension development observed in human aging. Epigenetic changes induced by hypertension that occur in temporal and frontal lobe structures will be measured and related to behavioral assays of these regions as well as with high resolution MRI scans to assess grey and white matter integrity.

Role: Principal Investigator (Multi-PI)

**NIA P30 AG019610**  Reiman (PI)  8/15/16 - 6/30/21

**Arizona Alzheimer’s Disease Core Center**

Dr. Barnes serves as Director of the Ad Hoc review program for research proposals for the Center.

Role: Co-Investigator

**NIA T32 AG044402**  Barnes (PI)  5/1/16 - 4/30/21

**Postdoctoral Training, Neurobiology of Aging and Alzheimer's Disease**

Dr. Barnes serves as Program Director, Dr. Paul Coleman and Eric Reiman as Co-Directors, and Dr. Matthew Huentelman and Health Bimonte-Nelson as Associate Directors of this statewide postdoctoral training grant focused on training postdoctoral fellows in the Arizona Alzheimer’s Consortium (six participating institutions).

Role: Principal Investigator

**NIA R21 AG061421**  Stern (PI)  10/1/18 - 9/30/21

**Collaboratory on Research for Cognitive Reserve and Resilience**

Dr. Barnes role is to serve with a group of 6 Co-I’s to build the infrastructure to organize workshops, databases, and facilitate award of pilot grants that will guide efforts to reach consensus on the most effective operational definitions for brain and cognitive reserve so that experiments can be directed at understanding underlying mechanism of these concepts.

Role: Co-Investigator
Biographical Sketch

Roberta Diaz-Brinton, Ph.D.
Director, Center for Innovation in Brain Science
Professor, Pharmacology and Neurology

Education/Training

<table>
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<tr>
<th>Institution &amp; Location</th>
<th>Degree</th>
<th>Year(S)</th>
<th>Field Of Study</th>
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<td>B.A.</td>
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<td>Psychobiology</td>
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<td>M.A.</td>
<td>1981</td>
<td>Neuropsychology</td>
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<td>University of Arizona, Tucson, AZ</td>
<td>Ph.D.</td>
<td>1984</td>
<td>Psychobiology &amp; Neuropharmacology</td>
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<td>Postdoc</td>
<td>1987</td>
<td>Neuropharmacology &amp; Neuroendocrinology</td>
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Personal Statement

I am the inaugural director of the UA Center for Innovation in Brain Science at the University of Arizona Health Sciences and professor of pharmacology and neurology, College of Medicine, University of Arizona. The Center for Innovation in Brain Science is focused on mechanistically driven therapeutic development and translational research for age-associated neurodegenerative diseases (https://cibs.uahs.arizona.edu/). My research has focused broadly on the mechanisms underlying late onset Alzheimer’s disease (AD) and developing therapeutics to prevent, delay, and cure the disease. Towards that goal, I lead three programs of discovery research and two programs of translational and clinical research. Our discovery research programs focus on systems biology of 1) mechanisms underlying risk of Alzheimer’s during female brain aging, 2) sex differences in mechanisms underlying Alzheimer’s, and 3) regeneration and repair mechanisms to regenerate the Alzheimer’s brain. Fundamental insights that have emerged from our research indicate that the aging brain is dynamic and adaptive. The dynamic adaptive nature of the aging brain has led to an increasing focus on transition states of the aging brain, their plasticity, limits, and vulnerability. We have advanced our basic science discoveries into FDA IND-enabling translational programs and two early phase clinical trials. These programs of research are supported by the National Institute on Aging (R01, P01, U01, U54) and by philanthropic foundations. The breadth and depth of our research requires effective and collaborative team science that is mission focused. Teams that I lead include basic, translational, and clinical scientists and technology transfer professionals.

Positions

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

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

Contribution to Science

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

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

Sex differences in mechanisms leading to late onset Alzheimer’s disease program investigates the underlying mechanisms for the difference between female and male risk of developing late-onset Alzheimer’s disease. Outcomes of which research indicate that the female and male brain bioenergetically age quite differently in remarkable and unanticipated ways that may be beneficial to the Apoe4- male but may be deleterious to the Apoe4+ male.


The Allopregnanolone regenerative systems neurobiology and regenerative therapeutic for Alzheimer’s disease programs of research are devoted to elucidating the regenerative mechanisms of the brain and harnessing those mechanisms to both promote endogenous mechanisms of regeneration while simultaneously targeting mechanisms underlying Alzheimer’s disease. Outcomes of this pioneering research indicate that the neurosteroid allopregnanolone significantly increases endogenous neural stem cell generation, which restores learning and memory functions to age-associated normal in both males and females. Further allopregnanolone reduces the burden of disease by promoting mitochondrial function and beta amyloid clearance. Based on our discovery science of allopregnanolone regenerative mechanisms, we advanced allopregnanolone through IND-enabling research (PK,PD and toxicology), and acquired an FDA IND to conduct a NIA sponsored Phase 1b clinical trial of allopregnanolone in persons with mild cognitive impairment or early Alzheimer’s disease. The NIA-sponsored clinical trial Allopregnanolone for Mild Cognitive Impairment Due to Alzheimer’s Disease or Mild AD is currently ongoing.


Complete list of published work in MyBibliography
Research Support
NIA R01 AG057931 Brinton (PI) 9/1/18 - 8/31/23

**Sex Differences in the Molecular Determinants of Alzheimer’s Disease Risk: Prodromal Endophenotype**

The mission for the Sex Differences in the Molecular Determinants of Alzheimer’s Disease Risk: Prodromal Endophenotype project is to determine the complex interaction between chromosomal sex and the major risk factors for late onset Alzheimer’s (LOAD): age, APOE*4 genotype and maternal history of AD. As LOAD accounts for the greatest incidence and prevalence of the disease, determining molecular mechanisms relevant to LOAD has the potential for greatest impact. Further, targeting early stage transitions of risk have the greatest potential for therapeutic efficacy. Thus, research proposed herein focuses on the prodromal / preclinical stage of LOAD and the sex differences that underlie early risks of LOAD progression. Elucidation of sex differences in the mechanisms driving prodromal LOAD will lead to identification of therapeutic targets to change the trajectory of the disease to prevent, delay and potentially reverse course of developing LOAD. Role: PI

NIA T32 AG061897 Brinton (PI) 9/1/18 - 8/31/23

**Translational Research in AD and related Dementias (TRADD)**

The University of Arizona (UA) Training Program to Advance Translational Research on Alzheimer’s Disease and AD Related Dementias is designed to address knowledge and experience gaps in AD therapeutic discovery and preclinical translational development. To meet this challenge, the UA Translational Research in AD and related Dementias (TRADD) training program is designed as a problem based translational learning experience for predoctoral PhD and MD/PhD fellows. In alignment with the 2012, 2015 and 2018 NIH Alzheimer’s Disease Research summits and the National Alzheimer’s Project Act, the goal of the TRADD training program is to fill critical gaps that exist for AD translational research in academic graduate programs. To achieve this goal, the University of Arizona TRADD program will: 1) recruit trainees across multiple scientific disciplines; 2) employ problem-based learning approaches to solve challenges in AD therapeutic development with emerging tools and techniques; and 3) equip TRADD trainees with career development and leadership skills necessary to conduct team science and manage multidisciplinary teams in the 21st century. Role: PI

NIA R37-AG053589 Brinton (PI) 3/15/17 - 2/28/22

**Aging and Estrogenic Control of The Bioenergetic System In Brain**

The proposed program of research is designed to first test estrogentic control of the bioenergetic system in the female brain requires: 1) both nuclear and mitochondrial genomes; 2) integration of gene expression across both genomic compartments and 3) activation of rapid signaling cascades to provide real time feedback on bioenergetic performance. Second, that loss of estrogen in the aging female brain leads to a systematic dis- integration of estrogenic control of nuclear and mitochondrial genomes followed by decline in bioenergetic sensing mechanisms.

*Recipient NIH MERIT (Method to Extend Research in Time) Award, recognizing outstanding scientific contributions and allowing for up to 5 years non-competitive extension.

Role: PI

NIA P01 AG026572 Brinton (PI) 7/1/05 - 5/31/21

**Perimenopause in Brain Aging and Alzheimer’s Disease**

The Perimenopause in Brain Aging and Alzheimer’s Disease Program Project will determine how the brain changes during the perimenopausal transition and how these changes can lead to development of early risk factors for developing Alzheimer’s disease. The goal of these studies is the early identification of those at greatest risk for developing AD and the window of opportunity for
Interestingly, there are interventions to prevent Alzheimer's disease in those at greatest lifetime risk, postmenopausal women.

Role: Program PI; PL Administrative Core A, Project 1 and Project 4

NIA U01 AG047222 Brinton (PI) 6/15/18- 6/30/19

*Allopregnanolone a Regenerative Therapy for Alzheimer's: FDA-Required Toxicology*

This project addresses the urgent need to develop therapeutics to prevent, delay and treat Alzheimer’s disease (AD). A promising regenerative medicine, Allo, is being developed. Allo activates the brain's own regenerative ability while also reducing the pathology of AD. Studies proposed here are required by the FDA to ensure that Allo is safe to use for extended period of time to generate new neurons, restore cognitive function, reduce AD pathology and to regenerate the connective tracts of the brain.

Role: PI

Alzheimer’s Association Brinton (PI) 5/1/17 - 4/30/20

*Perimenopause In ApoE4 Brain: Accelerated Myelin Catabolism for Fuel*

Discovery of at-AD-risk phenotypes in women and the underlying mechanisms could potentially lead to early identification of those at greatest risk of developing AD and interventions to prevent the disease. Having established that the perimenopause is a neurological bioenergetic transition state that shifts the brain from utilizing glucose as its primary fuel to utilizing ketone bodies as an auxiliary fuel and that metabolic compromise is associated with compromised cognitive function in postmenopausal women [3], we advance a program wide three hit hypothesis for women positive for ApoE4: Females positive for ApoE4 gene experience three strikes that result in accelerated bioenergetic aging in brain and concomitant generation of three hallmarks of Alzheimer's disease in brain, hypometabolism, beta amyloid deposition and white matter (WM) degeneration. Strike one for ApoE4 positive females, is the genetic risk conferred by the ApoE4 genotype. Strike two is chronological aging. Strike three is the bioenergetic transformation of the perimenopause. Interestingly, all three of these strikes are independently associated with WM degeneration and we hypothesize that in combination they will lead to an accelerated AD-like WM degeneration phenotype.

NIA R01 AG059093 Kaddurah-Daouk (PI) 8/1/18 - 6/30/23

*Metabolic Networks and Pathways Predictive of Sex Differences in AD Risk and Responsiveness to Treatment*

In this study, we use global metabolomics approach to delineate biochemical differences in men and women across the trajectory of disease. We aim to define biochemical pathways and networks for greater vulnerability of disease in women and men that would enable discovery of more effective therapies for each of the sexes.

Role: Subaward PI
Biographical Sketch

Ying-hui Chou, Ph.D.
Assistant Professor, Psychology

Education/Training

<table>
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<tr>
<th>Institution &amp; Location</th>
<th>Degree</th>
<th>Year(S)</th>
<th>Field Of Study</th>
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<tr>
<td>National Taiwan University, Taipei</td>
<td>B.S.</td>
<td>1994</td>
<td>Occupational Therapy</td>
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<tr>
<td>Boston University, Boston, MA</td>
<td>M.S.</td>
<td>2001</td>
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<tr>
<td>Boston University, Boston, MA</td>
<td>Sc.D.</td>
<td>2005</td>
<td>Movement &amp; Rehab Sci</td>
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<tr>
<td>Brigham and Women's Hospital Boston, MA</td>
<td>Postdoc</td>
<td>2005</td>
<td>Brain Imaging</td>
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<td>Duke University Medical Center, Durham, NC</td>
<td>Postdoc</td>
<td>2012</td>
<td>Gerontology and Brain Imaging</td>
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<td>Duke University Medical Center, Durham, NC</td>
<td>Other training</td>
<td>2012</td>
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<td>Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA</td>
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<td>2013</td>
<td>Transcranial Magnetic Stimulation</td>
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<td>Duke University Medical Center, Durham, NC</td>
<td>Postdoc</td>
<td>2013</td>
<td>Brain Imaging</td>
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<tr>
<td>Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA</td>
<td>Other training</td>
<td>2015</td>
<td>Transcranial Direct Current Stimulation</td>
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Personal Statement

My research has focused primarily on the cognitive and clinical neuroscience of aging and neurodegenerative disorders. Within this framework, my laboratory is particularly interested in integrating brain imaging and transcranial magnetic stimulation (TMS) techniques to 1) develop image-guided therapeutic TMS protocols and 2) explore TMS-derived and image-based biomarkers for early diagnosis and prediction of therapeutic outcomes for individuals with mild cognitive impairment as well as Parkinson’s disease. For the past few years, I have been involved in a number of NIH-funded studies investigating brain function and its relation to cognitive performance. I am currently the Director of Brain Imaging and TMS Laboratory and teach undergraduate and graduate level courses in cognitive neuroscience, brain rehabilitation, and brain connectivity at the University of Arizona.


Positions

1994 – 1995 Occupational Therapist, Department of Psychiatry, Taipei Veterans General Hospital, Taiwan
1995 – 1997  Occupational Therapist, Department of Physical Medicine and Rehabilitation, National Taiwan University Hospital, Taiwan
2001 – 2003  Research Assistant, Center for Neurological Rehabilitation, Boston University, Boston, MA
2001 – 2003  Teaching Assistant of (1) Neurological Systems and (2) Scientific Inquiry, Department of Physical Therapy, Boston University, Boston, MA
2004 – 2005  Postdoctoral Fellow of Radiology, Brigham and Women’s Hospital/Harvard Medical School, Boston, MA
2005 – 2008  Chair and Assistant Professor, Department of Occupational Therapy, Fu-Jen Catholic University, Taiwan
2008 – 2011  Maternity Leave
2011 – 2013  Postdoctoral Fellow, Center for Aging and Human Development and Brain Imaging and Analysis Center, Duke University Medical Center, Durham, NC
2013 – 2016  Medical Instructor, Brain Imaging and Analysis Center, Duke University Medical Center, Durham, NC
2016  Assistant Professor of Psychology, University of Arizona, Tucson, AZ
2016  Director, Brain Imaging and TMS Laboratory, University of Arizona
2017  Research Associate, Arizona Center on Aging
2017  Scholar, CDC Arizona Healthy Brain Research Center

Honors

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

Contribution to Science

Transcranial magnetic stimulation for neurodegenerative disorders. Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive brain stimulation technique that has been closely examined as a possible treatment for neurodegenerative disorders. However, results evaluating the effectiveness of rTMS are mixed, mostly due to low statistical power or variety in individual rTMS protocols. Recently, we published a meta-analysis that included 13 studies with 293 patients with mild cognitive impairment (MCI) and Alzheimer’s disease (AD)\(^5\). The therapeutic effect of rTMS on overall cognitive function was significant (effect size = 0.77, \(p < .0001\)). Subgroup analyses of the 13 studies revealed that 1) high-frequency or excitatory rTMS over the left DLPFC significantly improved memory function (effect size = 0.68, \(p < .005\)), and the effects of 5-30 consecutive rTMS daily sessions were durable for 4-12 weeks. We conducted another meta-analysis examining differences in TMS-induced measures of cortical excitability between AD, MCI and cognitively normal older adults (CN)\(^5\). Findings of this meta-analysis suggest the existence of cortical hyper-excitability in AD and MCI, as well as reduced inhibition in AD. We are currently conducting 2 pilot TMS/MRI studies to 1) investigate differences in cortical excitability, meta-plasticity, and brain connectivity between MCI and CN (current \(N = 44\)); and 2) develop an image-guided rTMS protocol to stimulate the hippocampus in MCI (current \(N = 9\)).

In 2015, we published a meta-analysis of 20 clinical trials in 470 patients with Parkinson’s disease, suggesting a significant medium effect size favoring active rTMS over sham rTMS for reducing motor
symptoms. In the same year, we published another article investigating the effects of high-frequency rTMS over the primary motor cortex on motor function and brain connectivity in individuals with multiple system atrophy. Findings of this clinical trial support the therapeutic effect of 10-session, high-frequency rTMS in improving motor symptoms in multiple system atrophy. Several functional links involving the default mode, cerebellar and limbic networks exhibited positive changes in functional connectivity. The positive changes in functional connectivity were associated with improvement in motor symptoms. The present findings suggest that rTMS may improve motor symptoms by modulating functional links connecting to the default mode, cerebellar and limbic networks, inferring a future therapeutic candidate for patients with multiple system atrophy.


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


Virtual reality and rehabilitation. I was trained as a movement and rehabilitation scientist during my graduate studies investigating gait patterns and how a virtual reality environment would modulate
locomotion in healthy older adults and patients with Parkinson’s disease. We have successfully combined the virtual reality apparatus and three-dimensional motion analysis system to investigate perceptual-motor interaction. These studies demonstrate the usefulness of virtual reality in modulating locomotion and will facilitate the development of systematic approaches for effective preventive and therapeutic intervention for gait dysfunction in older adults and patients with Parkinson’s disease. Virtual reality is compatible with many brain-imaging techniques and has allowed researchers to evaluate typical and atypical brain function when users are immersed in a virtual reality environment. We published a book chapter in 2012 summarizing research findings that combine both virtual reality and brain imaging technologies. This chapter has been downloaded more than 2,000 times from the publisher’s website.


Complete list of published work in MyBibliography

Research Support
NIA NIBIB Witte (PI) 9/30/19 – 9/29/20

Transcranial Acoustoelectric Imaging for High Resolution Functional Mapping of Neuronal Currents
Role on Project: Co-Investigator

NIA R56 AG061888 Wilson (PI) 9/30/18 - 8/31/23

Evaluating the Neurocomputational Mechanisms of Explore Exploit Decision Making in Older Adults
Role on Project: Co-Investigator

NIA P30 AG019610 Reiman(PI); Chou (Pilot PI) 7/01/17 - 06/30/19

Use of TMS and fMRI Measures to Assess the Risk of Conversion of MCI to Dementia
In this pilot project, we propose probing cortical excitability and plasticity in individuals with MCI in order to assess the diagnostic potential of TMS-evoked responses.
Role on Project: Pilot Project PI

NIA P30 AG019610 Reiman (PI); (Wilson Pilot PI) 7/1/17 – 6/30/19

The Neural Substrates of Explore-Exploit Decisions in Old Age
The purpose of this pilot study is to understand the neural systems underlying explore-exploit decisions and how these systems change in old age and with cognitive decline.
Role on Project: co-investigator

Arizona Alzheimer’s Consortium, DHS Chen (PI) 7/1/19 – 6/30/20

Transcranial Magnetic Stimulation for Mild Cognitive Impairment
Role on Project: Project PI

Arizona Alzheimer’s Consortium, DHS  Chen (PI)  7/1/18 – 6/30/19
High-resolution MR Imaging Technologies for Mapping Neuronal Connectivity Network to Subfields of Hippocampus and Amygdala: Application to Studies of Alzheimer’s Disease
Role on Project: Project PI

Cancer Center, University of Arizona  Kou (PI)  7/1/18 - 6/30/20
Feasibility Study for the Treatment of Post-Chemotherapy Cognitive Impairment with Transcranial Magnetic Stimulation
Role on Project: Co-Investigator

BIO5 Institute, University of Arizona  Chou (PI)  7/1/18 - 6/30/19
Developing a Non-Invasive Magnetic Brain Stimulation Protocol for Mild Cognitive Impairment
Role on Project: PI
**Biographical Sketch**

Stephen Cowen, Ph.D.
Assistant Professor, Psychology

**Education/Training**

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<th>Year(S)</th>
<th>Field Of Study</th>
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<td>University of Wisconsin, Madison, Wisconsin</td>
<td>B.B.A</td>
<td>1992</td>
<td>Management and Marketing</td>
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<td>University of Arizona, Tucson, Arizona</td>
<td>Ph.D.</td>
<td>2007</td>
<td>Psychology and Neuroscience</td>
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<tr>
<td>The Neurosciences Institute, San Diego, CA</td>
<td>Postdoc</td>
<td>2008</td>
<td>Neuroscience</td>
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**Personal Statement**

A fundamental and unresolved question in neuroscience is how the activities of tens of billions of interconnected neurons become coordinated during learning, decision making, and sleep. Resolving this question is important as dysregulated neural coordination and communication contributes to age-associated cognitive decline, substance abuse, epilepsy, Parkinson’s disease (PD), and depression. My research seeks to understand the mechanisms by which the timing of the activities of ensembles of neurons and dopamine release is organized during learning and sleep. Towards this end, my laboratory and the laboratory of Dr. Heien have developed novel instrumentation that allows, for the first time, the simultaneous measurement of the activities of large groups of neurons and fast changes in dopamine release (Parent et al., 2017). My laboratory is using this tool to investigate the role that dopamine plays in regulating neuronal coordination and plasticity in anesthetized and behaving animals, and we are working towards testing this device in animal models of substance abuse and PD. The advanced sensing technologies described in the Research Enhancement Grant proposal would provide my laboratory with opportunities to directly expand and extend this research and would provide key preliminary data for NIDA R01 applications in the next 2 years.

Beyond technology development and the study of dopamine release, my lab also investigates the roles that brain oscillations play in learning, memory, disease, and aging. For example, we have found that normal aging is associated with a significant decrease in the frequency of oscillations in the hippocampus that are associated with memory formation (Wiegand et al., 2016; Cowen et al., 2018).

With regard to disease, my laboratory is investigating how low to moderate doses of ketamine (a drug of abuse and anesthetic) alter brain oscillations in the dorsal and ventral striatum (Ye et al., 2018). Data collected in my laboratory now suggests that ketamine simultaneously enhances cortico‐striatal coherence at high‐frequencies (~135 Hz) and reduces coherence at theta and beta frequencies (~8‐30 Hz) – frequency ranges associated with Parkinsonian motor symptoms.

Positions

2007 – 2008 Postdoctoral Fellow The Neurosciences Institute, San Diego, CA
2008 – 2010 Research Fellow The Neurosciences Institute, San Diego, CA
2010 – 2012 Associate Fellow The Neurosciences Institute, San Diego, CA
2012 – Present Assistant Professor Department of Psychology, University of Arizona Graduate Interdisciplinary Program in Neuroscience
Graduate Interdisciplinary Program in Cognitive Science
Graduate Interdisciplinary Program in Phys. Sciences

Honors

1998-1999 Recipient of National Science Foundation training grant
2010 Blasker-Rose-Miah Technology Development grant, San Diego Foundation

Contribution to Science

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


Ketamine induces brain-region specific patterns of synchrony and desynchrony. Ketamine has been used as a safe and effective anesthetic for over 50 years, and, in the last decade, the potential therapeutic applications of ketamine have expanded considerably. For example, hour to days-long exposure to sub-anesthetic ketamine can provide weeks-long management of depression, post-traumatic stress disorder (PTSD), chronic pain, and L-DOPA-induced dyskinesias (LID). The neural mechanisms by which the therapeutic effects of ketamine are achieved are unknown. Furthermore, little is known about how ketamine alters neural coordination throughout the brain. Understanding the impact of ketamine on neural coordination is important and neural plasticity and communication between brain regions depends on the precise timing of action potentials within and between brain structures. Consequently, we hypothesized that hours-long exposure to ketamine entrains synchronized activity within corticostriatal and hippocampal circuits. To investigate this question, we measure oscillatory activity in behaving rats following administration of low-dose ketamine. We recorded from motor cortex, ventral striatum, dorsal striatum, and hippocampus and found that ketamine induces unique patterns of neural coordination in each brain region studied. Critically, we found that extended exposure to ketamine hyper-synchronizes corticostriatal circuits at delta (~4 Hz), gamma (~50 Hz), and high-frequency (~140 Hz) bands. In stark contrast, activity in the hippocampus became desynchronized or “noisy”. These data suggest that ketamine facilitates communication and plasticity in corticostriatal circuits and disrupts these processes in the hippocampus. Indeed, desynchronous activity in the hippocampus could reduce the strength of
associative networks encoding memories for negative events. Disrupting such networks could have positive therapeutic effects in depression and PTSD. An important next step is to determine if ketamine alters coordination in these brain regions though single-unit ensemble recordings.


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


Expanding the traditional view of the hippocampal representation of space. The discovery of the hippocampal place cell (O’Keefe and Drostovsky, 1971) provided convincing physiological evidence that the hippocampus creates a cognitive map of the environment. With time, it was found that the response properties of these place cells were more nuanced than expected. For example, “place cells” were found to be sensitive to both location and trajectory and that these neurons coupled their activity to specific phases of the hippocampal theta (7 Hz) oscillation. My research contributed to the expansion of the traditional view of the place cell by challenging the view that spatial coding in the hippocampus is an exclusive property of principal cells. Together with Drew Maurer and Bruce McNaughton, we determined that inhibitory interneurons convey precise information about space, and that this information is only identifiable if the phase of the theta rhythm at which interneurons fire is accounted for. We used this phase-based definition of the place field to improve upon existing measures of place-field sizes, an approach which became useful in quantifying how the spatial scale of the cognitive map changes in different regions of the hippocampus.

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


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

- Ultrasound measurement of electrical brain activity. I am a collaborator on Brain Initiative R24(Lead PI: Russel Witte, UA) to develop a non-invasive ultrasound system for the measurement of electrical activity in the brain. The system capitalizes on the acoustoelectric effect, and my role is to validate the system’s effectiveness by comparing in vivo measurements obtained from the ultrasound system with measurements obtained from traditional electrophysiology.
- Simultaneous dopamine and single-unit/local-field measurement. Awarded a 2014 NSF BRAINEAGER grant to develop technologies for the simultaneous recording of the activities of ensembles of neurons and real-time measurement of dopamine release. Since receiving support, we have produced working versions of this device and successfully tested the device in anesthetized and awake and behaving rats (methods paper under review). The next stage of development will be to improve the hardware and software to improve robustness and ease of use.
- To better characterize fine body movements in animals as they perform decision-making behaviors, I developed a novel 9-axis head-mounted inertial measurement system. Prototypes of this system are being developed for three laboratories for the investigation of brain-body interactions in the hippocampus, parietal cortex, and prefrontal cortex.
- Designed and built numerous automated maze systems for the training and testing of decision-making and memory-driven behaviors. The design and required software is freely available. I helped set up these systems in the laboratories of three collaborators and they continue to be used.
- Produced an interactive graphical system for real-time and off-line spike sorting (Waveform Cutter, Cowen 2002). This tool became an integral part of MClust (David Redish, U. Michigan), one of the most popular open-source spike-sorting systems.

**Complete list of published work in MyBibliography**

**Research Support**
LuMind Foundation
PI: Elgin
1/1/17 - present

*Brain Development, Sleep & Learning in Down Syndrome*
Objective: Identify neural signatures of sleep dysfunction in Down-syndrome subjects (EEG).
Role on Project: Co-Investigator

Michael J. Fox
PI: Cowen
8/1/17 - 7/31/19
Identification of Network and Oscillatory Signatures Of The LRRK2 Mutation
Objective: Identify neural biomarkers that distinguish the LRRK2 genetic form of Parkinson’s disease from healthy controls and idiopathic Parkinson’s disease.
Role on Project: Principal Investigator

R44 MH114776
PI: Hedlin
8/1/19 – 1/1/20
High density, miniaturized, zero switching, stimulation and recording headstage for small animals
Objective: Develop new technologies for simultaneously stimulating and recording brain activity
Role on Project: Co-Investigator

R56 NS109608
PI: Falk
8/1/19 – 8/1/20
Mechanisms of low-dose ketamine treatment for Parkinson's disease
Objective: Identify the circuit and single-neuron properties that drive Parkinson’s disease associated oscillations and determine how ketamine works to reduce pathology associated oscillatory activity
Role on Project: Co-Investigator

NIA NIBIB
Witte (PI)
9/30/19 – 9/29/20
Transcranial Acoustoelectric Imaging for High Resolution Functional Mapping of Neuronal Currents
Role on Project: Co-Investigator
Biographical Sketch

Arne Ekstrom., Ph.D.
Associate Professor, Psychology,

Education/Training

<table>
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<th>Institution &amp; Location</th>
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<td>University of Arizona, Tucson, AZ</td>
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<td>Neuroscience</td>
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<td>Ph.D.</td>
<td>2004</td>
<td>Neuroscience</td>
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Personal Statement

The primary focus of my research is to better understand the neural basis of human memory, with a particular focus on spatial navigation. I employ several different methodologies to better understand spatial memory, including immersive virtual reality, intracranial EEG, fMRI, and scalp EEG. Studies in my lab focus on how neural signals code space vs. time, how we represent different scales of space, how navigation and episodic memory are represented differently in the brain, and how the different recording modalities used tie together or provide complementary information about underlying brain processes.

Positions

1996 – 1997  Research Assistant  Department of Psychology, Harvard University, Cambridge
2004 – 2009  Postdoctoral Fellow  Division of Neurosurgery and Center for Cognitive Neuroscience, Semel Institute of Neuroscience and Human Behavior, University of California, Los Angeles
2009 – 2014  Assistant Professor  Department of Psychology and Center for Neuroscience, University of California, Davis
2014 – 2018  Associate Professor  Department of Psychology and Center for Neuroscience, University of California, Davis
2018 – Present  Associate Professor  Department of Psychology and Evelyn F. McKnight Brain Institute, University of Arizona, Tucson

Honors

1996  B.A., Brandeis University, magna cum laude, High Honors in Neuroscience
1998 – 2000  Flinn Biomathematics Fellow, University of Arizona
2006 – 2009  NIH/NINDS Postdoctoral NRSA fellowship
2008  The Brain Research Institute Distinguished Postdoctoral Fellow in Neuroscience
2011  Hellman Young Investigator Award
2011 – 2012  Alfred P. Sloan Fellow
2012  Kavli Fellow – National Academy of Sciences Kavli Frontiers of Science
2015  Chancellor’s Fellow

Contribution to Science

Multivariate approaches to the fMRI of human episodic memory and navigation. In the work cited below, we demonstrate mechanisms by which hippocampal subfields store and retrieve spatiotemporal memories, helping to resolve how the human hippocampal subfields contribute to episodic memory. Using high-resolution imaging of the hippocampus along with multivariate pattern
analysis, we demonstrate how patterns of activations within hippocampal subfields might be important to memory for details of events. Together, this work has advanced our understanding of how the human hippocampal subfields code spatial and temporal context as part of a more general role in episodic memory.


The brain as a network: Graph theory reveals medial temporal lobe and neocortical interactions during successful memory retrieval. Multiple brain regions are important to spatiotemporal memory yet how these interact at a “systems” level in the brain is not clear. In Watrous et al. 2013 Nature Neuroscience, using multi-lobar recordings from patients undergoing clinical monitoring, we reported that the medial temporal lobe showed elevated levels of low-frequency coherence with neocortical nodes during correct retrieval of recently encoded events. In Schedlbauer et al. 2013 Scientific Reports, We demonstrated a similar finding using fMRI in healthy human participants (specifically, that connectivity was higher across multiple nodes, specifically to the hippocampus, during correct memory retrieval). In two additional papers we outline and test models in which neural specific interactions at specific hubs are critical to both encoding and retrieval of navigation and episodic memories. These findings advance our understanding of how networks of brain areas contribute to human navigation and episodic memory both empirically and theoretically.


Behavioral and neural correlates of human spatial navigation. In the work cited below, we employ patients with focal lesions, fMRI, and behavioral methods to better understand the neural basis of human spatial navigation. Prior to this work, the exact contribution of the human hippocampus versus extra-hippocampal cortical areas to encoding and retrieval spatial locations was unclear. Based on our findings, we propose that allocentric spatial memory (memory for object locations referenced to external cues in the environment rather than the self) depends primarily on extra-hippocampal network contributions, with the hippocampus primarily contributing to the precision of such spatial memories. Together, these findings argue for the importance of hippocampal and extra-hippocampal cortical areas to spatial navigation and provide novel paradigms for understanding human spatial navigation.


Direct recordings from epilepsy patients undergoing seizure monitoring reveal the cellular and oscillatory basis of human spatial navigation. The work summarized below addresses the critical issue of how and in what manner cellular and oscillatory coding mechanisms in the rodent are conserved in humans. In Ekstrom et al. 2003, we establish the presence of both place and view responsive neurons in the hippocampus and parahippocampal cortex, respectively, using direct recordings in patients undergoing surgical monitoring. By demonstrating both place and view coding in the human medial temporal lobe, we helped resolve decades of debate on whether place coding or view coding mechanisms were present in the primate temporal lobes. This paper has been cited more than 1,000 times and forms the foundation of other studies that investigated cellular responses in humans during navigation. Watrous et al. (2011, 2013) establish the presence of low-frequency oscillations during movement and spatial navigation in the human hippocampus. Vass et al. (2016) establish that low frequency oscillations in the human hippocampus code spatial distance by removing sensory and vestibular cues during virtual teleportation. Together, these findings advance our understanding of the extent to which rodent cellular coding mechanisms are both similar and different in the human hippocampus.


High-resolution imaging of the human hippocampus and the neural basis of the human hippocampal BOLD signal. Another focus of the lab has been developing ways to better image the human hippocampus using fMRI and to relate these hippocampal BOLD-specific changes to underlying neural activity. Our work has developed novel BOLD sequences for imaging the human hippocampus in-plane with 1.5 mm x 1.5 voxels, which provides functional resolution sufficient to image changes in the neural activity at specific subfields (Ekstrom et al. 2009 Neuroimage). Together, these findings advance current methods in the field for imaging and recording from the human hippocampus.

Research Support

NINDS R01 NS076856  PI: Ekstrom  7/1/12 – 6/30/22
Representation of Spatiotemporal Information in Human Episodic Memory and Navigation
The human hippocampus is critical for both episodic memory and navigation, as indicated by the devastating consequences of neural diseases such as stroke and ischemia. This proposal seeks to leverage functional magnetic resonance imaging and intracranial electrode recordings in patients to address these gaps in knowledge, with potential outcomes providing a more complete framework for understanding how the hippocampal circuitry underlies memory and navigation and how cortical circuits might partially compensate for lost function following hippocampal damage.
Role on Project: PI

NSF BCS-1630296  PI: Ekstrom  9/1/16 – 8/31/20
The Neural Basis of Human Spatial Navigation in Large-scale Virtual Spaces with Vestibular Input
A major gap in our knowledge about human spatial navigation regards the importance of vestibular and other proprioceptive cues (termed “body-based” cues). We propose to cross this barrier in our knowledge by developing a novel set-up in which participants freely ambulate on a 2-D treadmill with a head-mounted display, allowing for full range of motion during navigation. The expected outcomes from this project are a better understanding of how we represent large-scale spaces during free ambulation and the neural basis of direction and distance codes during enriched vs. impoverished body-based cues.
Role on Project: PI

NIA R01 AG003376  PI: Barnes  10/1/15 – 9/30/20
Neurobehavioral Relations in Senescent Hippocampus
The objective of this research program is to understand the basis of memory impairments that result from normal aging in rhesus macaques.
Role on Project: Co-investigator

NINDS R01 NS08402  PI: Gurkoff  2/1/14 – 1/30/19
Restoring Connectivity Following Traumatic Brain Injury
The goal of this grant is to assess how traumatic brain injury alters oscillations, particularly phase coherence across distal neural networks, during performance of cognitive tasks and to determine whether deep brain stimulation can be utilized to improve coherence and restore function. Role on Project: Co-investigator

NIMH R01 MH113855  PI: Geng  6/1/18 – 5/31/23
Quantifying the Attentional Template
Problems of attentional control are a core deficit in many mental health disorders, most notably the attention deficit disorders. The proposed work investigates why the quality of attentional control varies between people and situations.
Role on Project: Consultant
Biographical Sketch

Fabian Fernandez, Ph.D.
Assistant Professor, Psychology and Neurology

Education/Training

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<td>2002</td>
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<tr>
<td>Stanford University, Palo Alto, CA</td>
<td>Ph.D.</td>
<td>2008</td>
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<td>University of Colorado, Denver, CO</td>
<td>Postdoctoral</td>
<td>2009</td>
<td>Neuropharmacology</td>
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<td>Johns Hopkins University, Baltimore, MD</td>
<td>Postdoctoral</td>
<td>2015</td>
<td>Translational Neurosci</td>
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Personal Statement

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

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

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

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

1999 – 2002  University Scholars undergraduate research fellow with Dr. Darragh P. Devine, University of Florida, Gainesville
2002 – 2008  PhD research in neuroscience with Dr. Craig C. Garner, Stanford University, Palo Alto, CA
2008 – 2009  Fondation Jérôme-Lejeune fellow with Dr. Alberto C.S. Costa, University of Colorado, Denver
2009 – 2012  Senior Scientist and Consultant, Intellimet LLC.
2012 – 2015  Research Associate with Dr. Roger H. Reeves, Johns Hopkins University, Baltimore, MD
2015  Assistant Professor, Department of Psychology and Neurology, Bio5 Fellow, University of Arizona, Tucson

**Honors**

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

**Contribution to Science**

My early publications were concerned with therapeutics research in animal models of intellectual disability. While at Stanford University, I spearheaded efforts to “cure” memory problems in Ts65Dn mice, animals with a genetic background similar to individuals with Down syndrome (DS). For decades, it was assumed that nothing could be done to improve cognitive function in the DS population. The condition results from the over-expression of ~200 categorically diverse genes that steer development of the brain in a completely different direction from that of the typical one. By 2004, it became clear, however, that the Ts65Dn DS model showed one central difference in brain signaling that could contribute to the animal’s difficulties with learning and memory: an increase in the signaling of a neurotransmitter called GABA. I established that higher-than-normal GABA was a key therapeutic target—drugs that reduced this transmitter in the brain also restored the ability of these mice to remember novel objects and navigate mazes.

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

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


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


Research Support
Velux Stiftung PI: Fernandez 2019 - 2021
Programming the Circadian Clock with Precision Flashes of LED Light Role on Project: Project PI
Biographical Sketch

Elizabeth L. Glisky., Ph.D.
Professor, Psychology

Education/Training

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<td>University of Toronto</td>
<td>Post-doc</td>
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Personal Statement

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

Positions
1987 – 1989 Visiting Assistant Professor, Department of Psychology, University of Arizona
1989 – 1995 Assistant Professor, Department of Psychology, University of Arizona
1995 – 1999 Associate Professor, Department of Psychology, University of Arizona
1999 Professor, Department of Psychology, University of Arizona
2000 – 2002 Head, Interdisciplinary Program in Gerontology, University of Arizona
2004 – 2008 Associate Head and Director of Graduate Studies, Dept. of Psychology, UA
2006 – 2019 Professor, Evelyn F. McKnight Brain Institute
2008 – 2009 Acting Head, Department of Psychology, University of Arizona
2010 – 2015 Head, Department of Psychology, University of Arizona
2019 Professor Emerita, University of Arizona

Honors and Awards
1981 – 1982 University of Toronto Open Fellowship
1982 – 1983 Ontario Government Scholarship
1983 – 1986 University of Toronto Postdoctoral Award to Research Fellow
1989 – 1990 University of Arizona, Provost’s Teaching Award
2003 Social and Behavioral Sciences Research Professorship
2006 Fellow of the Association for Psychological Science
2011 Elizabeth Hurlock Beckman Award for Educational Leadership and Translational Work in Cognitive Rehabilitation

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


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


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

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


Research Support
Arizona Alzheimer’s Consortium, DHS PI: Glisky 7/1/18 -6/30/19

Memory and executive function in normally-aging older adults: Completion, analyses, and publication of two projects
The goals are to document changes over time in episodic memory and executive function in normally aging older adults aged 65+; identify specific demographic, health, genetic, and neurocognitive variables that are associated with differential change; and validate an executive function test battery for older adults incorporating specific sub-components of executive function.
Role on Project: PI
Biographical Sketch

Matthew D. Grilli, Ph.D.
Assistant Professor Psychology

Education/Training

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<td>Brandeis University, Waltham, MA</td>
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<td>2013</td>
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<td>VA Boston Healthcare System, Boston, MA</td>
<td>Postdoc</td>
<td>2015</td>
<td>Clinical Neuropsychology</td>
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Personal Statement

I am an Early Stage Investigator and Assistant Professor in the Departments of Psychology and Neurology at University of Arizona. I am also Director of neuropsychology training for our clinical psychology PhD program and a licensed psychologist. As Principal Investigator of the Human Memory Lab at University of Arizona, my team’s research is broadly focused on the clinical and cognitive neuroscience of autobiographical memory, which is memory for real world events. I utilize a combination of cognitive, neuropsychological, neuroimaging (magnetic resonance imaging), and genetic methods. For the past 10 years, I have studied young and older adults, as well as individuals with medial temporal lobe lesions, to gain insights into the cognitive and neural bases of our ability to form and retrieve long-term memories. In the past 4 years, my lab has focused intensively on the relationship between Alzheimer’s disease (AD) risk and autobiographical memory, combining novel cognitive testing with genetics and brain imaging. Much of this work has been done in collaboration with Dr. Jessica Andrews-Hanna, Director of the Neuroscience of Emotion and Thought Lab. My initial work in this area has gained national attention, as I was recently recognized as an Alzheimer’s Disease Core Center Junior Investigator. This R01 application, which builds on our currently funded R03 from NIH/NIA (PI: Grilli, Co-I: Andrews-Hanna) and a grant from the Arizona Alzheimer’s Consortium (PI: Andrews-Hanna, Co-I: Grilli), extends our theoretical and empirical approach to studying autobiographical thought and the default network as cognitive and neural markers of Alzheimer’s disease risk among cognitively unimpaired adults. In addition to the invaluable expertise of MPI Andrews-Hanna (see Biosketch), I believe that my expertise in clinical neuropsychology, aging, and AD risk ensures that the proposed research has the potential to be translated to improved assessment and intervention, and potentially new cognitive tests for neuropsychologists. Our active collaboration and experience executing studies of this magnitude and complexity demonstrates that we are prepared for this R01, especially given our support from Co-I’s Dr. Matthias Mehl and Dr. Matthew Huentelemen, Other Significant Contributor Dr. Eric Reiman, Other Significant Contributor Dr. Edward Bedrick, and the unique resources of GeneMatch and MindCrowd (see Facilities and Resources).


**Positions**

2012 – 2013 Psychology Intern, Boston Consortium in Clinical Psychology, Boston, MA
2012 – 2014 Teaching Fellow in Psychiatry, Boston University School of Medicine, Boston, MA
2012 – 2015 Clinical Fellow in Psychology, Harvard Medical School, Boston, MA
2014 – 2015 Assistant Professor, Boston University School of Medicine, Boston, MA (Promoted while completing postdoctoral fellowship)
2015 – Present Assistant Professor, University of Arizona, Tucson, AZ
2015 – Present Director of Neuropsychology Track for the Clinical Psychology PhD Program
2015 – Present Director of the Neuropsychology Clinic, Evelyn F. McKnight Brain Institute
2015 – Present Affiliate, Department of Neurology, Evelyn F. McKnight Brain Institute, Graduate Interdisciplinary Program – Cognitive Sciences

**Honors**

2007 Summa Cum Laude, University of California, Irvine
2007 Undergraduate Investigator Spotlight, University of California, Irvine
2007 Order of Merit Scholar-Athlete of the Year, University of California, Irvine
2007 Undergraduate Research Fellowship, University of California, Irvine
2008 Community Outreach Fellowship, University of Arizona, Tucson
2010 Human Development and Aging Fellowship, Heidelberg University, Germany
2012 College of Science Scholar of the Year, University of Arizona, Tucson
2008 Council of Graduate Schools Dissertation Nominee, Univ of Arizona, Tucson
2019 Junior Investigator Recognition, Arizona Alzheimer’s Disease Core Center

**Contribution to Science**

Introduced the episodic autobiographical memory hypothesis of preclinical AD cognitive detection. My colleagues and I recently proposed that disrupted retrieval of detailed episodic autobiographical memories may be a sensitive indicator of subtle cognitive decline from AD, because this type of memory taxes a neural network associated with this disease. Our initial findings support the notion that disrupted episodic autobiographical memory may be a marker of AD risk. In regard to my role, with my collaborator MPI Andrews-Hanna’s, we have since extended our hypothesis to include other forms of autobiographical thought and to propose a more refined connection between autobiographical thought patterns and integrity of the default network. I have also served as a Co-I on Dr. Andrews-Hanna’s work on depressive symptoms, autobiographical thought, and the default network, and I collaborated on a review paper that Dr. Andrews-Hanna led on normal and abnormal aging, autobiographical thought, and the default network. I was the lead researcher and first author for the first publication on our novel hypothesis, and I was the PI of several small grants that supported this work.

Developed a novel cognitive neuroscience model of how personal semantics are stored and retrieved. Much of one’s autobiographical memory is composed of personal semantics, which is knowledge about the self that contextualizes experiences and adds meaning to the life story. Despite the importance of personal semantics to one’s sense of self, how such knowledge is organized and retrieved remains underspecified. I have attempted to close this gap in knowledge by studying personal semantics in individuals with lesions to core regions of the autobiographical memory neural network. I have proposed that personal semantics can be viewed as consisting of subtypes of content that place distinct computational demands on regions in the autobiographical memory network. Personal semantics can be bound to events, in which case they are supported by bilateral medial temporal lobe structures (Grilli & Verfaellie, 2014; 2016). They also can be associated with personally known people, places, and objects and critically depend on the left anterior ventrolateral temporal lobe (Grilli et al., 2018). Or, they can represent categorical knowledge about the self, such as personality traits or social roles, in which case they are supported by neural regions that are implicated in basic level categorical knowledge or schema-like knowledge, including the medial prefrontal cortex (Marquine, Grilli, et al., 2016). This cognitive neuroscience model reflects a comprehensive attempt to explain the neural bases of personal semantics. For my role, I was the lead researcher and first author (or co-first author) of the publications that have come from my work on this topic, including key theory pieces (Grilli & Verfaellie, 2016; Grilli et al., 2018).


Advanced understanding of how autobiographical memory is necessary for maintaining the self-concept. Autobiographical memory, which is the repository of experiences and facts that are unique to each person, has long been thought to ground one’s conceptualization of the self. My research has supported this idea. First, in a neuropsychological study, I demonstrated that MTL amnesics rely entirely on abstract personal semantic memories to ground their identity, which comes at a cost: they cannot retrieve as many self-defining traits as healthy controls do. This indicates that episodic autobiographical memories serve a necessary role in grounding the self-concept. Second, I showed that the relative importance of episodic autobiographical memory and personal semantic memory depends on the stability of one’s traits and roles. Specifically, I found that whereas healthy adults primarily rely on episodic and episodic-like autobiographical memories to ground recently formed traits and roles, they tend to ground remotely formed traits and roles with abstract personal semantic memories more than other autobiographical contents. These studies provide important insight into the self-supporting function of autobiographical memory.

Developed a novel cognitive strategy for improving memory. Although much of my research has focused on advancing cognitive neuroscience models, I always consider how insights from basic research can inform new interventions for memory disorders. My first line of research merged two largely separate literatures on self-referential processing and imagination to establish a new cognitive strategy for improving episodic memory in individuals with acquired brain injury, which I referred to as self-imagination. In a series of studies, I have demonstrated that self-imagination is a highly effective cognitive intervention for individuals with traumatic brain injury, capable of enhancing recognition, cued recall, free recall, and prospective memory across various delays and over and above a variety of cognitive strategies. In regard to my role, I was the lead researcher and first-author on most of this work.

Complete list of published work in MyBibliography

Research Support
RO3 AG060271 Grilli (PI) 4/15/19 – 3/31/21
NIH/NIA
The episodic autobiographical memory (EAM) hypothesis of preclinical Alzheimer's disease: Developing a new approach for early cognitive detection and measurement of Alzheimer's disease
The specific aims of this projects are to 1) To reveal that core EAM sub-components are disrupted in cognitively normal older ε4 carriers. 2) To demonstrate that EAM disruption is associated with altered RSFC in the DMN, indicating that disrupted EAM detects mild and/or severe preclinical AD.

McKnight Brain Research Foundation Grilli (MPI) 4/6/18 – 9/1/20
Uncovering Risk Profiles of Deception and Mitigating Susceptibility to Scamming in Midlife and Older Age: A Novel Intervention Tool
The specific aims of this project are to: 1) develop a prototype of MERLIN, an automated warning tool to support decision-making online; 2) develop the in-lab Scam Identification Task (SIT), a new
behavioral task to effectively “scam people in the lab” and allow validation of the efficacy of MERLIN under controlled conditions; and 3) quantify the cognitive, physical, and socio-affective correlates of scam susceptibility to tailor MERLIN to age-specific user profiles.

Role on Project: PI (multi-PI)

Arizona Alzheimer’s Consortium, DHS  Grilli (PI)  7/1/19 -6/30/20

*Improving clinical neuropsychological assessment of subtle cognitive decline and mild cognitive impairment.*

The specific aims of this project are to 1) To test everyday cognition in the context of subtle cognitive decline and mild cognitive impairment. 2) to begin longitudinal assessment of everyday cognition in these populations.

Arizona Alzheimer’s Consortium, DHS  Grilli (PI)  7/1/18 -6/30/19

*The Status of Personal Semantic Memory Among Cognitively Healthy Older Adults and Individuals with Mild Cognitive Impairment.*

The specific aims of this project are: 1) to identify patterns of spared versus impaired personal semantic memory (PSM) among cognitively normal older adults relative to young adults, as well as in comparison to individuals with mild cognitive impairment (MCI), and 2) to reveal that PSM status is related to neural markers of the integrity of the medial temporal and ventrolateral temporal lobes, as measured with MRI methods.

NIA P30 AG019610  Reiman(PI); Andrews-Hanna (Pilot PI)  7/1/17 - 6/30/19

*Uncovering Neurocognitive Links between Alzheimer’s Disease and Depression in Mid-Life to Early Aging*

The specific aims of this project are: 1) to compare symptoms of depression and characteristics of internally oriented thought across middle-aged adults with and without a first-degree family history of late-onset AD, and 2) to develop novel, dynamic neurocognitive markers of depressive symptoms in cognitively healthy middle aged to early older-aged adults.

Role on Project: co-investigator
Biographical Sketch

Matthew J. Huentelman, Ph.D.
Professor of Neurogenomics

Education/Training

<table>
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<td>University of Florida, Gainesville, FL</td>
<td>Postdoc</td>
<td>2004</td>
<td>Physiology &amp; Genomics</td>
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<tr>
<td>Translational Genomics Res. Inst., Phoenix, AZ</td>
<td>Postdoc</td>
<td>2006</td>
<td>Neuroscience &amp; Genomics</td>
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Personal Statement

I have researched traits and diseases of the central nervous system for over twenty years, and I have extensive training in the physiology, live cell imaging, and molecular dissection of neuronal and glial cells. During the past fifteen years I have focused on the application of molecular genetic “-omics” technologies in the study of the basic characteristics of the aging brain as well as Alzheimer’s disease. The focus of my lab is on the molecular genetic association and biomarker discoveries linked to neurodegenerative diseases as well as cognitive performance in healthy aging individuals.

During my time at TGen, my laboratory has grown significant experience in the wet laboratory generation and bioinformatics assessment of next generation DNA and RNA sequencing data. My laboratory is split approximately 60:40 between wet laboratory (5 full-time employees; 2 postdoctoral fellows, 1 graduate student, 1 Masters-level lab technician, and 1 Bachelors-level lab technician totaling over 15 years of experience in my laboratory) and bioinformatics (3 full-time employees; 1 Research Assistant Professor, 1 Masters-level, and 1 Bachelors-level totaling over 13 years of experience in my laboratory) personnel and I have a demonstrable publication track record in both general areas of research. My laboratory has current expertise in the techniques and approaches required for successful execution of the proposed work as well as experience in multidisciplinary team-based science.

Positions

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<td>Visiting Researcher, MV Lomonosov Moscow State University, Moscow, Russia</td>
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<td>Visiting Postdoctoral Research Fellow, University of Bristol, United Kingdom</td>
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<td>11/03 – 06/04</td>
<td>Postdoctoral Research Fellow, University of Florida, Gainesville, FL</td>
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<td>07/04 – 08/06</td>
<td>Postdoctoral Research Fellow, Translational Genomics Research Institute, Phoenix, AZ</td>
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<td>08/06 – 12/08</td>
<td>Assistant Professor, Translational Genomics Research Institute, Phoenix, AZ</td>
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<td>12/08 – 02/16</td>
<td>Associate Professor, Translational Genomics Research Institute, Phoenix, AZ</td>
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<td>06/10 – Present</td>
<td>Affiliate, Evelyn F. McKnight Brain Institute, University of Arizona, Tucson, AZ</td>
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<tr>
<td>08/11 – Present</td>
<td>Adjunct Faculty Member, Arizona State University SoLS, Tempe, Arizona</td>
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<tr>
<td>10/13 – Present</td>
<td>Scientific Director, Center for Rare Childhood Disorders, TGen, Phoenix, Arizona</td>
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<td>05/14 – Present</td>
<td>Research Affiliate, Mayo Clinic, Scottsdale, Arizona</td>
</tr>
<tr>
<td>07/14 – Present</td>
<td>Research Associate Professor, Dept of Basic Medical Sciences, University of Arizona, Phoenix, AZ</td>
</tr>
<tr>
<td>-02/16 – Present</td>
<td>Professor, Translational Genomics Research Institute, Phoenix, AZ</td>
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Honors

1994  Richard Eddy Service Award, Dept. of Chemistry, Ohio University, Athens, OH
1994  Hiram & Florence Wilson Scholarship, Dept. of Chemistry, Ohio Univ, Athens, OH
1998  Hamilton Community Foundation Award, Hamilton, OH
1998  Jeanette Grasseli-Brown Undergrad Research Award, Ohio Univ, Athens, OH
2000-2002  American Heart Assoc Predoctoral Fellowship, Florida/Puerto Rico Affiliate
2001  Proctor & Gamble Professional Opportunity Award, American Physiological Soc
2008  Young Investigator Award, The Arizona Alzheimer’s Consortium, Phoenix, AZ
2009  Award for Research Excellence (nominee), Arizona Bioindustry Association
2013  40 Under 40 Awardee, Phoenix Business Journal
2014-2016  Board Member, Alzheimer’s Association / Desert Southwest Chapter

Contribution to Science

Identification of the Genetic Basis of Human Disease – Rare Diseases in Children and Alzheimer’s Disease: During the last 15 years my laboratory has focused on the use of multi-omics approaches [DNA, RNA, and protein analyses] to identify the genetic basis of rare and common human neurological diseases. Typically, these studies involve either a long-distance collaboration with other clinics and sequencing laboratories or large multi-laboratory collaborative efforts (this is especially true for our Alzheimer’s disease work). In the last five years, we have reported on the identification of a new genetic basis for over 8 different neurological disorders.

In TGen’s Center for Rare Childhood Disorders (C4RCD) clinic we have sequenced over 1,500 DNA samples in our attempts to identify the basis of disease in pediatric patients with neurological symptoms. Due to our focused efforts and extremely close collaboration with each treating neurologist we have identified the genetic cause in ~35% of our families. A particular focus of our Center is in the study of underserved individuals including over 60% of our families who are on Arizona’s medical public assistance program (AHCCCS) and a partnership with a medical clinic in Hermosillo, Mexico in the cross-border Arizona-neighboring state of Sonora.

For Alzheimer’s disease, we collaborate openly with the national and international efforts focused on the disease including the ADGC, ADSP, ADNI, and IGAP. We were one of the first groups to openly share the genetic data resulting from our neuropathologically characterized AD cohort (an autopsy-based case/control series collected by John Hardy and Amanda Myers when they were at the National Institute on Aging at the NIH, known by the field as “TGen II”). These efforts have helped to greatly expand our collaborative network and we have been honored to play a role in the collective better understanding of AD genetic risk and protection.

Listed below are some of our published works related to rare neurological disease. Not shown are the several dozen publications with the Alzheimer’s community at large that include work with ADNI, ADGC,IGAP, and others.


Technology Development – Lentiviral Vectors / SNP Genotyping / Bioinformatics: During my career I have demonstrated a significant impact on technology development in the fields I work in. This initiated during the early days of my graduate studies. I was working in the newly emerging field of lentiviral vector development (late 1998). At the time the field was struggling to make high quality viral vector in high concentrations. I co-developed a standardized transfection and purification approach that yielded industry leading titers approaching 1 X 10^10 infectious units on a routine basis. This was an important advance for the field because high titer stocks of virus are critical for brain and cardiovascular system injections of the vector. Innovation in tech development has continued throughout my career including the development of an improved SNP genotyping calling algorithm which generated additional usable data from some of the early human microarrays, the development of a pooled genotyping approach on the microarray which permitted rapid screening of samples for “low hanging fruit” associated with disease, the reduction to practice of bar-coded next generation sequencing on the Illumina equipment which ushered in the beginning of our ability to optimize sequencing design and depth per sample, and the demonstration that iPSC can be generated from autopsy donor derived fibroblasts. In short, I have demonstrated an ability to innovate, as necessary, to both advance my specific scientific goals as well as others in the field.


Fluid Biomarker Discovery: Since 2010 my laboratory has investigated biomarkers for human disease in fluid biological samples including blood, urine, saliva, and CSF. Our major area of focus has been on cell-free molecular investigations (biomarkers in exosomes and other freely circulating microvesicles) of RNA species and their use as biomarkers (“exRNA”). We were funded as part of NIH’s inaugural
extracellular RNA communication consortium (ERCC) to further this work. Our expertise includes both the development of wet laboratory methods and informatics approaches for biomarker discovery and characterization.


Complete list of published work in MyBibliography
https://www.ncbi.nlm.nih.gov/myncbi/1nmZZMm8R79/bibliography/public/

Research Support
Aging Foundation Grant 20170175 Padilla (PI) 9/1/17-11/20/19

Early Onset Alzheimer’s Disease Genomic Study
Clinical genomic analysis will be conducted on blood samples from patients who have been diagnosed with early onset Alzheimer’s Disease and are “outliers” with no risk factors or family history of the disease.
Role: Co-Principal Investigator

NIA R01 AG031581 Reiman (PI) 5/1/28-3/31/19

Brain Imaging, APOE & Preclinical Course of Alzheimer’s Disease
Dr. Huentelman will lead a team for this grant that will perform generation and analysis of exome sequencing and hypothesis-driven SNP genotyping data.
Role: Co-Investigator

NIA R01 AG049465 Barnes (PI) 8/1/14-3/31/20

Neural System Dynamics and Gene Expression Supporting Successful Cognitive Aging
The major goal of this project is to understand the basis of differing cognitive trajectories that occur even over the lifespan of inbred rat strains.
Role: Co-Investigator

R01 AG049464 Coleman/Barnes/Alexander (MPI) 8/1/14-7/31/20

Epigenetic, Neuroimaging and Behavioral Effects of Hypertension in the Aging Brain
The major goals of this project are to determine what hypertension-induced epigenetic changes occur in a transgenic rat model of hypertension.
Role: Co-Investigator

NIA P30 AG019610    Reiman (PI)    7/1/16-6/30/21

Arizona Alzheimer’s Disease Core Center
This grant supports the clinical and research investigation of Alzheimer’s disease. Dr. Huentelman will contribute his expertise regarding aspects of next generation sequencing data generation, quality control, statistical analysis, storage/dissemination, and general project and personnel management.
Role: Co-Investigator

NIH UG30D023313    Deoni (PI)    9/21/16-8/31/21

The Developing Brain: Influences and Outcomes
Dr. Huentelman will advise the research team on the collection and analysis of DAN samples collected from all participants. In addition to overseeing the specific analysis described in this proposal, he will also work closely with the ECHO Core on implementing and performed required standardized analyses and contributing this data back to the overall consortium.
Role: Co-Investigator

NIA R01 1AG054180    Kaczorowski (PI)    5/15/17-4/30/22

Systems Genetics of Cognitive Aging and Alzheimer’s Disease
Dr. Huentelman will contribute his expertise in the curation, interpretation, and analysis of his own – as well as publicly available data – for Alzheimer’s disease and aging.
Role: Co-Investigator

NIH R56HL141165    Hale (PI)    9/20/18-8/31/23

Identifying a Pathogenic Fibroblast Subpopulation to Target for Protection Against Cardiac Fibrosis
Dr. Huentelman will lead a team for this grant that will perform generation and analysis of single cell RNA sequencing data.
Role: Co-Investigator

AZ Alzheimer Consortium (ADHS)    Huentelman/Reiman    7/1/18-6/30/20

AARC FY 19 & 20: Alzheimer’s Projects
This grant is a collection of collaborative research projects focused on the better understanding and earlier diagnosis of Alzheimer’s disease.
Role: Principal Investigator

Necroptosis as a novel mechanism of neurodegeneration in Alzheimer’s disease
The ultimate aim of this project is the discovery of novel candidate risk factor genes using a multi-omic approach, determining relationships among genetic epigenetic modifications, and expression of specific transcripts Alzheimer's disease.
Role: Co-Investigator

FA8650-11-C-6159    Broderick (PI)    7/1/18-12/31/19

Wright State Applied Research Corporation
RFP WSARC-17-00751 Revolutionary Intelligence
Role: Co-Investigator

1UH2/UH3TR000891    Huentelman/Jensen (PI)    8/1/13-7/31/19

exRNA signatures Predict Outcomes after brain injury
Role: Principal Investigator (Multi
Biographical Sketch

Matthias R. Mehl, Ph.D.
Professor, Psychology

Education/Training

<table>
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<th>Institution &amp; Location</th>
<th>Degree</th>
<th>Year(S)</th>
<th>Field Of Study</th>
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<td>University of Erlangen, Germany</td>
<td>B.A./M.A.</td>
<td>1998</td>
<td>Psychology</td>
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<tr>
<td>University of Texas, Austin, TX</td>
<td>Ph.D.</td>
<td>2004</td>
<td>Psychology</td>
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Personal Statement

I am a social, personality, and health psychologist with broad interest and expertise in the conceptualization and measurement of how social processes affect health. Methodologically, I use subjective and objective ambulatory assessment methods to study social processes and have helped to pioneer novel methods of ecologically valid data collection. One of these methods involves the collection and coding of ambient sounds via a recording device called the Electronically Activated Recorder (EAR). As the developer of the EAR method, a naturalistic observation sampling method, I have extensive experience in the administration of the EAR, the coding of the sound files, and the management and analysis of the EAR data. Further, I have extensively published about and given workshops on the method. I joined the faculty of the Psychology Department of the University of Arizona in 2004 and I am now a tenured full professor. I am also an adjunct faculty in Family Studies and Human Development and the Department of Communication and an affiliated investigator at the Arizona Cancer Center and the Evelyn F. McKnight Brain Institute. My prior collaborative EAR research has been funded by, among other sources, the American Cancer Society and the NIH (National Institute of Mental Health, National Cancer Institute, National Center for Complementary and Integrative Health, National Institute for Child Health and Human Development).

Positions

1998 – 1999 Visiting Scholar, Department of Psychology, University of Texas at Austin
1999 – 2000 Research Assistant, Institute for Physiological Psychology, University of Düsseldorf
2004 – 2010 Assistant Professor, Department of Psychology, University of Arizona
2010 – 2016 Associate Professor, Department of Psychology, University of Arizona
2007 – Present Adjunct Faculty, Department of Communication, University of Arizona
2007 – Present Associate Investigator, Arizona Cancer Center, University of Arizona
2010 – Present Affiliate Faculty, Department of Communication, University of Arizona
2011 – Present Affiliate Faculty, Evelyn F. McKnight Brain Institute, University of Arizona
2016 – Present Professor, Department of Psychology, University of Arizona
2017 – Present Affiliate Faculty, Div of Family Studies & Human Development, Univ of Arizona
2017 – Present Affiliate Faculty, Institute of Place, Wellbeing & Performance, Univ of Arizona

Honors

1996 – 1998 Undergraduate Fellowship, German National Academic Foundation
1998 – 1999 Postgraduate Fellowship for Studying Abroad, German National Academic Foundation
2003 – 2004 University Continuing Fellowship, University of Texas at Austin
2011 Rising Star Award, Association for Psychological Science
Contribution to Science

Development of a Methodology for Naturalistic Observation of Daily Social Behavior and Interactions. Despite the fact that psychology is the study of human behavior, naturalistic observation of social behavior has a remarkably thin history in the field. I have (co-)developed and psychometrically validated the Electronically Activated Recorder as an ecological momentary assessment method for tracking people’s naturally occurring (acoustic) social lives. Technically, the EAR is a digital audio recorder that intermittently records snippets of ambient sounds while participants go about their normal lives. Conceptually, it is a naturalistic observation method that produces an acoustic log of a person’s day as it unfolds. With the EAR, researchers can study how subtle yet objective aspects of people’s daily behaviors and interactions are related to core psychological processes. The EAR app is freely available on iTunes and the Google Playstore and is currently being used in research studies by more than two dozen investigator groups on three continents.


Natural Word Use as Linguistic Marker of Psychological Processes. Despite the fact that verbal behavior is by far the most frequent human behavior (apart from sleep), verbal data sources, until recently, have been surprisingly neglected. We have found that computerized text analysis programs, despite their relative conceptual simplicity, can provide highly valuable information about patterns of word use. People’s natural (written or spoken) word use shows clear associations with their personalities, social status, well-being and even mental and physical health. In my research, I have studied word use mostly in the context of personality and coping-related couple and family interactions.

The Role of Everyday Social Interactions in Coping and Health. Critical life events can cause serious disruptions to people’s social lives. In my research, I explore the role that people’s daily social lives play in coping with and adjustment to personal and collective upheavals. Because self-reports are particularly susceptible to bias when material of high personal relevance and emotional intensity is assessed—the very material in which coping researchers are interested—I have pursued this question primarily from a behavioral observation perspective. This choice of method has led to a theoretical focus on the role that people’s mundane, ordinary, everyday conversations play for coping and health (in contrast to direct coping conversations about the focal illness or critical life event).


Behavioral Manifestations of Personality in Everyday Life. Personality is an important predictor of personal and relational life outcomes. However, for a long time, the field of personality was largely built on questionnaire responses and was lacking an empirical grounding in observable social behavior which, conceptually, is the variable that should “carry” or mediate personality’s effects on life outcomes. My research in this area has been aimed at identifying such behavioral manifestations of personality and other individual differences in daily life. Importantly, to really understand how personality can affect life outcomes through variability in daily behavior, shared method variance should be minimized and therefore daily behavior be assessed through direct observation rather than indirect (self-)reporting. Over the last years, we have made critical contributions to this field by identifying clear, observable behavioral markers of the Big Five personality domain, subclinical depression, and psychological well-being.


Complete list of published work in MyBibliography
Research Support

NIMH RO1 MD008940  Stone: PI  9/25/14 – 5/31/19
Reducing Implicit Verbal and Nonverbal Bias toward Hispanic Patients
The goal of this project is to test (a) how doctor's implicit bias is related to how they talk to Hispanic patients, and (b) how an intervention aimed at reducing implicit bias changes the way doctors talk to Hispanic patients.
Role on Project: Co-Investigator

Biomarkers, Social, and Affective Predictors of Suicidal Thoughts and Behaviors in Adolescents
The goal of this project is to examine adolescent in vivo emotion reactivity as related to social context in the real world during the high-risk post-discharge period.
Role on Project: Investigator

NIMH RO1 MH108641  Nugent: PI  7/1/16 – 6/30/21
Understanding the Interplay of Social Context and Physiology on Psychological Outcomes in Trauma-Exposed Adolescents
The goal of this project is to examine real-world emotion and social context as risk and protective factors for adjustment in trauma-exposed adolescents.
Role on Project: Co-Investigator

IARPA MOSAIC  Ziegler (LM-ATL; PI)  8/1/17 – 6/30/20
Rapid Automatic & Adaptive Model of Performance Prediction (RAAMP2)
The goal of this project is to design and evaluate a multimodal mobile sensing system for the assessment of psychological traits and states traits (e.g., personality, stress, affect, performance) in the workplace.
Role: Co-Investigator
Biographical Sketch

Mary-Frances O’Connor, Ph.D.
Associate Professor, Psychology

Education/Training

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<td>Clinical Psychology</td>
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<td>Ph.D.</td>
<td>2004</td>
<td>Clinical Psychology</td>
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<td>University of California, Los Angeles, CA</td>
<td>Postdoc</td>
<td>2007</td>
<td>Psychoneuroimmunology</td>
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Personal Statement

I am an Associate Professor of Clinical Psychology at the University of Arizona, and I began in Fall, 2019 as Director of Clinical Training. My research focuses on the physiological correlates of emotion, in particular the wide range of physical and emotional responses during bereavement. I investigate the failure to adapt following the death of a loved one, termed Complicated Grief, included as an area of research in the DSM-5. To that end, I have studied the neurobiological, immune and autonomic parameters that vary between individual grief responses. Currently, I mentor or co-mentor 7 graduate students, 3 international MD/PhDs, and 1 postdoctoral scholar in my lab. I serve as the mentor an F31 NRSA award to my graduate student, and as co-mentor for several NIA K awards (subsequent to my own prior K award). Service to my academic department, as well as national and international professional societies, has been largely focused on mentoring and training. I recently served on the Council for the American Psychosomatic Society (APS), where I inaugurated the annual Health and Behavior International Collaborative Award, to enable trainees (graduate students, residents, post-doctoral fellows) to attend international laboratories and gain skills not available at their home institution. Additionally, I organize the Cousin's Center Global Outreach Award, which assists an applicant residing in a developing nation to attend the APS Annual Meeting each year. In addition to pending grant funding (see below), I am author of a forthcoming popular press book by HarperCollins, The Grieving Brain.

Positions

2007 – 2011  Assistant Professor, Cousins Center for Psychoneuroimmunology, Semel Institute for Neuroscience and Human Behavior, UCLA
2012 – 2017  Assistant Professor, Department of Psychology, University of Arizona, Tucson
2013 – Present  Affiliated Faculty, Evelyn F. McKnight Brain Institute, Univ of Arizona, Tucson
2017 – Present  Associate Professor, Department of Psychology, University of Arizona, Tucson

Honors

2005  NIH Loan Repayment Program Award
2006  UCLA Semel Institute for Neuroscience Research Fellow
2008  NIA and OBSSR invitation to “Opportunities for Advancing Behavioral and Social Science Research on Aging” Workshop
2009  UCLA School of Medicine John H. Walsh Young Investigator Research Prize Nominee
2010  NSF/University of Arizona ADVANCE Junior Scientist Award
2011  RAND Summer Institute Workshop on Aging Invitee
Contribution to Science

Neuroimaging correlates of grief. Scientific contributions from my research investigate the way the brain processing the changing reality after the death of a loved one. Notably, my research was the first to using neuroimaging to investigate typical grief (5), and has now been cited nearly 200 times. Later work demonstrated that those with Complicated Grief show differential activation from to those with Non-Complicated Grief (4), highlighting the uniqueness of the disorder. This latter article, from 2008, has been cited nearly 150 times. My work investigates the relationship between both brain and peripheral physiology (3), because of the impact of grief (recursively) on these systems. From my K award, I have recently published on the cognitive-affective dysregulation of Complicated Grief during the emotional Stroop task (2), and hallmark symptoms of the clinical disorder (1).


Bereavement: Immune system and stress physiology. Additional work from my laboratory has investigated the biomarkers of adaptation during grief, primarily in the stress response systems (sympathetic nervous system(3) and hypothalamic pituitary adrenal axis(2d)) and the immune system (1,2). Supporting the hypothesis that Complicated Grief is the clinical outcome of concern in bereavement, I have demonstrated the flattened diurnal slope of cortisol in Complicated compared to Non-Complicated Grief groups (4). In addition, I have extensively reviewed the work in this subfield (a).

Psychological outcomes in bereavement. A third area of my work includes the study of psychological outcomes in patient families after the death of a loved one. Specifically, I have contributed to understanding the psychological reaction to interpersonal loss, how adaptation happens in typical grief, and what factors lead to poor adaptation. These psychological factors include cognitive functioning, yearning and repetitive thought, and quality of life.


Development of criteria for disordered grief. As part of a group of leaders in the fields of psychology and psychiatry, I contributed to the argument that under specific extreme conditions, poor adaptation should be considered a disorder. This argument persuaded the committee developing the DSM 5, and Persistent Complex Bereavement Disorder was included as a disorder for further research. This article has been cited almost 600 times.


Complete list of published work in MyBibliography

Research Support
R13 AG066368 O’Connor(PI) 9/1/19 – 8/31/21
**Social Neuroscience of Grief: 2020 Vision and Social Neuroscience of Grief: Early Adversity and Later Life Reversibility**
The major goal of this conference grant is to give researchers an opportunity to 1) obtain knowledge about state-of-the-art animal and human research on grief, and 2) interact with like-minded investigators and trainees to foster collaborations and develop a translational model of the social neuroscience of grief.
Role on Project: PI

R13 AG066393 O’Connor(PI) 9/1/19 – 8/31/21
**Conference Grant to support American Psychosomatic Society’s 78th and 79th Annual Scientific Meetings**
The major goals of this conference grant to support for pre- and post-doctoral trainees to attend the 78th and 79th Annual Scientific Meeting of the American Psychosomatic Society (APS).
Role on Project: PI
Biographical Sketch

Naomi Rance, M.D., Ph.D.
Professor, Pathology

Education/Training

<table>
<thead>
<tr>
<th>Institution &amp; Location</th>
<th>Degree</th>
<th>Year(S)</th>
<th>Field Of Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>University of Maryland, College Park</td>
<td>B.S.</td>
<td>1973</td>
<td>Psychology</td>
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<tr>
<td>University of Maryland, Baltimore</td>
<td>Ph.D.</td>
<td>1981</td>
<td>Physiology</td>
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<tr>
<td>University of Maryland, Baltimore</td>
<td>M.D.</td>
<td>1983</td>
<td>Medicine</td>
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<td>The Johns Hopkins Hospital</td>
<td>Fellowship</td>
<td>1989</td>
<td>Neuropathology</td>
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<tr>
<td>The Johns Hopkins Hospital</td>
<td>Residency</td>
<td>1983 – 1987</td>
<td>Pathology</td>
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Personal Statement

For more than 25 years, our overall goal has been to characterize and understand the physiological significance of the changes that occur in the hypothalamus secondary to menopause. We observed hypertrophy and increased gene expression in a subpopulation of estrogen receptor expressing neurons in the hypothalamic infundibular nucleus of postmenopausal women. These neurons are called KNDy neurons, based on the co-expression of kisspeptin, neurokinin B (NKB), and dynorphin. For many years, our goal was to understand the role of NKB in reproductive regulation. The significance of these studies became widely recognized with the observation that mutations in either the gene encoding NKB or its receptor (NK3R) result in hypogonadotropic hypogonadism. In the last 10 years, we have focused on studying the role of KNDy neurons in the estrogen modulation of body temperature. The results of these studies allowed us to propose that KNDy neurons play a role in the generation of hot flushes via NKB signaling in the hypothalamic median preoptic nucleus. Recent clinical trials in have shown that NK3R antagonists effectively reduce the number and severity of hot flushes, thus providing strong support for our hypothesis.


Positions

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

**Honors**

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

**Contribution to Science**

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


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


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


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


Research Support
NIA RO1 AG047887 Rance (PI) 8/15/14 – 4/30/19

Role of Preoptic NK3R Neurons in the Estrogen Modulation of Body Temperature
This grant explores how preoptic neurons that express the neurokinin 3 receptor participate in the neural circuits regulating body temperature. Our goal is to provide information related to mechanism of menopausal flushes. $1.5 million total award.
Role on Project: PI

NIA R21 NS099468 Teske (PI) 2017 - 2019

Pre-clinic model for sleep deprivation-induced obesity and hedonic intake due to noise exposure
Role on Project: co-investigator
Biographical Sketch

Lee Ryan, Ph.D.
Professor, Psychology, Neurology and Neuroscience Program

Education/Training

<table>
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<tr>
<th>Institution &amp; Location</th>
<th>Degree</th>
<th>Year(S)</th>
<th>Field Of Study</th>
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<td>University of Toronto, Canada</td>
<td>B.Mus.</td>
<td>1979</td>
<td>Music</td>
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<td>University of Toronto, Canada</td>
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<tr>
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<td>1988</td>
<td>Psychology/Neuroscience</td>
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<td>University of British Colombia,</td>
<td>Ph.D.</td>
<td>1992</td>
<td>Clinical/Cognitive Psych</td>
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<td>Vancouver, Canada</td>
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<tr>
<td>University of California, San Diego, CA</td>
<td>Postdoc</td>
<td>1993 - 1995</td>
<td>Neuropsychology</td>
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Personal Statement

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

Positions and Honors

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

Contribution to Science

Recently, my colleagues and I published a theoretical article that combines evidence from human cognitive neuroscience and animal models to build an integrative model of age-related memory changes. The model describes the impact of aging on neural circuitry across subregions of the medial temporal lobe, and how these changes are responsible for the specific types of memory impairments associated with normal aging. In addition, the model makes strong predictions regarding the neuropathological changes associated with normal aging versus those that may provide early pre-clinical markers of Alzheimer’s disease.


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

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


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


Complete list of published work in MyBibliography

Research Support
Arizona Alzheimer’s Consortium, ADHS Ryan (PI) 7/1/19 – 6/30/20
Contextual retrieval impairment in self-defining autobiographical memories as an early indicator of risk for AD
This project studies medial temporal lobe functions in a group of older adults using functional MRI. Role on Project: PI

Arizona Alzheimer’s Consortium, ADHS Ryan (PI) 7/1/18 – 6/30/19
A Novel Model of Medial Temporal Lobe Functions: Implications for Aging and Memory
This grant studies medial temporal lobe functions in a group of older adults using functional MRI. Role on Project: PI
Biographical Sketch

Robert C. Wilson, Ph.D.
Assistant Professor, Psychology and Cognitive Science

Education/Training

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<th>Field Of Study</th>
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<td>University of Cambridge</td>
<td>B.A.</td>
<td>2002</td>
<td>Natural Sciences</td>
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<td>University of Cambridge</td>
<td>M.Sci.</td>
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<td>Chemistry</td>
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<td>University of Pennsylvania</td>
<td>M.S.E.</td>
<td>2003</td>
<td>Bioengineering</td>
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<tr>
<td>University of Pennsylvania</td>
<td>Ph.D.</td>
<td>2009</td>
<td>Bioengineering</td>
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<tr>
<td>Princeton University</td>
<td>Postdoc</td>
<td>2014</td>
<td>Psychology and Neuroscience</td>
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Personal Statement

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


Positions

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

Contribution to Science

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


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


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

**Research Support**

**Thinking About Sweat: Sweat biomarker correlates of physical and mental effort**
This grant uses infrared imaging of sweat pores in combination with mass spectroscopy of sweat to probe the effect of physical and mental effort on sweat processes.
Role on Project: co-PI

**Evaluating the Neurocomputational Mechanisms of Explore-Exploit Decision Making in Older Adults**
This grant uses behavioral, neuroimaging, and neurostimulation experiments to investigate explore-exploit behavior in younger and older adults.
Role on Project: PI

**The Neural Substrates of Explore-Exploit Decisions in Old Age**
The purpose of this pilot study is to understand the neural systems underlying explore-exploit decisions and how these systems change in old age and with cognitive decline.
Role on Project: PI
Trainees

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

Alexander Danvers, Ph.D. (Mehl)
Area of Interest: Mobile-phone and wearable sensor-based assessment of social and emotional processes in daily life; dynamic systems modeling of emotion dynamics

Yu (Karen) Du, Ph.D. (Ekstrom)
Area of Interest: Virtual reality, scalp EEG, and fMR

Daniel Gray, Ph.D. (Barnes)
Area of Interest: Circuits involved in working memory and their decline with age in a non-human primate model of aging

Derek Huffman, Ph.D. (Ekstrom)
Area of Interest: Decoding body-based neural codes underlying human spatial navigation using fMRI

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

Adam Lester, Ph.D. (Barnes)
Area of Interest: Spatial computations made by the entorhinal cortex and how this changes in aging rats (Ph.D. received fall 2018)

Candice Lewis, Ph.D. (Huentelman)
Area of Interest: Understanding how genetics and epigenetics is associated with differential human development from the aspect of behavior and cognition.

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

Erin Maresh, Ph.D. (Andrews-Hanna)
Area of Interest: Neural underpinnings and health relevance of social cognition

Joshua Talboom, Ph.D. (Huentelman)
Area of Interest: Massive internet-based cohort recruitment for a better understanding of factors associated with cognitive performance across the aging spectrum.

Li Zheng, Ph.D. (Ekstrom)
Area of Interest: Temporal interval representation during human episodic memory and navigation using high-resolution fMRI.

Predoctoral
Mónica Acevedo-Molina (Grilli)
Area of Interest: Self-referential cognition and emotional changes associated with normal aging and Alzheimer’s disease

Eric Andrews (Andrews-Hanna and Allen)
Area of Interest: Brain network underpinnings of emotion and cognition, and relevance to aging and mental health

Pradyumna Bharadwaj (Alexander)
Area of Interest: Applications of multimodal brain imaging in the study of cognitive aging
Yu-Chin Chen (Chou)
Area of Interest: Repetitive TMS treatment for people with MCI

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

Andrea Coppola (Andrews-Hanna, Sbarra)
Area of Interest: Intersection between healthy relationships and healthy minds

Lindsey Crown (Cowen)
Area of Interest: Neural basis of Parkinson’s disease and Neural synchrony involved in memory functions

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

Nathaniel Gallegos (Ryan)
Area of Interest: Genetic family history in ad

Dan Hill (Cowen)
Area of Interest: How the frontal cortex alters dopamine release in aging (PhD received January 2019)

Deanna Kaplan (Mehl and O’Connor)
Area of Interest: Naturalistic study of how everyday behaviors and social interactions impact health and well-being.

Wayne Jepsen (Huentelman)
Area of Interest: Genomics of Alzheimer’s disease and normative aging with a focus on interesting or unique families our cognitive performance outliers.

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

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

Mingli Liang (Ekstrom)
Area of Interest: Human spatial navigation and wireless scalp EEG

Yilin Liu (Chou)
Area of Interest: Brain Imaging and Transcardial Magnetic Stimulations

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

Mairead McConnell (O’Conner)
Area of Interest: The impact of emotion on physical health, mediated through brain mechanisms, and clinical interventions improving emotional expression

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

Alana Muller (Ekstrom)
Area of Interest: understanding the cognitive processes involved in spatial navigation using EEG and virtual reality

David Negelshpach (Fernandez)
Area of Interest: Scaling circadian responses to millisecond administration of FED light
Justin Palmer (Ryan)
Area of Interest: Cognitive and neurobiological changes with normal and abnormal aging trajectories

Quentin Raffaelli (Andrews-Hanna)
Area of Interest: Cognitive neuroscience of memory, creativity, and spontaneous thought

Eva Robinson (Ekstrom)
Area of Interest: Neural basis or navigation and decision making.

Saren Seeley (O’Conner)
Area of Interest: Relationships between cognition and emotion, and neural and psychophysiological mechanisms through which these factors give rise to distress and impairment

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

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

Sahana Srivaths (Barnes)
Area of Interest: Age-related changes of signals involved in spatial memory and decision making

Michael Starrett (Ekstrom)
Area of interest: Human spatial navigation and scales of space

Eva-Maria Stelzer (O’Conner)
Area of Interest: The cultural (collectivist vs. individualist) effects of major life stressors, such as bereavement, on mental and physical health

Ariana Stickel (Ryan)
Area of Interest: Brain imaging, genetics, and cognitive changes in normal older adults (Ph.D received 2019)

Mark Sundman (Chou)
Area of Interest: Development of image-guided rTMS protocols

Alma Tejeda (Mehl)
Area of Interest: Psychological aspects of natural language use; linguistic markers of aging

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

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

Aubrey Wank (Grilli)
Area of Interest: Brain and autobiographical memory changes associated with normal aging and Alzheimer’s disease (Master’s degree received 2018)

Da’Mere Wilson (O’Conner)
Area of Interest: The role of discrimination, grief, and other stressors on the development of cardiovascular disease within the African American and Latinx community

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

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

Dr. Roberta Brinton (EMBI Affiliate Faculty) has been conducting studies to evaluate allopregnanolone as a therapeutic agent to treat age-associated memory deficits. Part of the goal is to complete collecting data in a translational therapeutic development project, required for an Investigational New Drug application to the FDA. The goal is to determine the efficacy of allopregnanolone as a neurogenic regenerative and disease modifying agent, first for Alzheimer’s disease, and then potentially for normal aging brain health.

Dr. Brinton recently received notification that The University of Arizona Center for Innovation in Brain Science has received a $37.5 million federal grant to research a potential regenerative therapy for Alzheimer’s disease. With the initiation of this five-year grant from the National Institute on Aging, Dr. Brinton will lead a nationwide Phase 2 clinical trial that will study the effectiveness of allopregnanolone in early-stage patients, rather than late stage, and hope to determine whether allopregnanolone will be effective as a therapy. She is taking a precision medicine approach for Alzheimer’s disease, designed to treat the right person at the right time.

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

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

2018-2019 A Randomized, Double-Blind, Placebo-Controlled, Two-Cohort Parallel Group Study to Evaluate the Efficacy of CAD106 and CNP520 in Participants at Risk for the Onset of Clinical Symptoms of Alzheimer’s Disease. (Generation 1) Protocol # CAPI015A2201J. Novartis. Total grant: $100,702 / patient. 2% salary support, 2% effort.

2018-2019 A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study to Evaluate the Efficacy and Safety of CNP520 in Participants at Risk for the Onset of Clinical Symptoms of Alzheimer’s Disease. (Generation 2) Protocol # CCNP520A2202J. Novartis. Total grant: $95,456 / patient. 2% salary support, 2% effort.


**Budget update**

**Extramural funding**

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

- **Subcontract PI:** Alexander, Gene E. (Multi-PI: Alexander, Bowers, Woods)
  - **Project:** Revitalizing Cognition in Older Adults at Risk for Alzheimer’s Disease with Near-Infrared Photobiomodulation (R01 AG064587)
  - **Sponsor:** National Institute on Aging
  - **Project Dates:** August 2019 – April 2024
  - **Subaward Amount:** $378,525 (current year)

- **Subcontract PI:** Alexander, Gene E. (PI: Reiman)
  - **Project:** Brain Imaging and Fluid Biomarkers Core (R01 AG019610)
  - **Sponsor:** National Institute on Aging
  - **Project Dates:** August 2018 – June 2021
  - **Subaward Amount:** $304,037 (current year)

- **Subcontract PI:** Alexander, Gene E. (PI’s: Reiman, Caselli)
  - **Project:** Brain Imaging, APOE & the Preclinical Course of Alzheimer’s Disease (RO1 AG031581)
  - **Sponsor:** National Institute on Aging
  - **Project Dates:** May 2014 – March 2020
  - **Subaward Amount:** $14,630 (current year)

- **PI:** Alexander, Gene E. (Multi-PI: Cohen, Woods, Marsaki, Alexander)
  - **Project:** Augmenting Cognitive Training in Older Adults – The ACT Grant (RO1 AG054077)
  - **Sponsor:** National Institute on Aging
  - **Project Dates:** July 2016 – June 2021
  - **Subaward Amount:** $255,352 (current year)

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

- **Co-Investigator:** Alexander, Gene E. (PI: Su)
  - **Project:** Ultra-sensitive and Label-free Detection of Alzheimer’s Disease Biomarkers (R03 AG055020)
  - **Sponsor:** National Institute on Aging
  - **Project Dates:** August 2017 – April 2020
  - **Award Amount:** $85,653 (current year)
Project: A Pilot Intervention with Near Infrared Stimulation: Revitalizing Cognition in Older Adults
Sponsor: McKnight Brain Research Foundation
Project Dates: October 2019 – September 2021

Subaward Amount: $60,000 (project period)

Univ Arizona PI: Alexander, Gene E. (PI: Williamson)
Project: Transcutaneous Vagal Nerve Stimulation and Cognitive Training to Enhance Cognitive Performance in Healthy Older Adults
Sponsor: McKnight Brain Research Foundation
Project Dates: May 2018 – April 2020
Subaward Amount: $60,000 (project period)

PI: Barnes, Carol A. (co-I: Ekstrom)
Project: Neurobehavioral Relations in Senescent Hippocampus (R01 AG003376)
Sponsor: National Institute on Aging
Project Dates: January 2016 – November 2020
Award Amount: $736,431 (current year)

PI: Barnes, Carol A.
Project: Cell Assemblies, Brain Adaptation and Cognitive Aging (R01 AG050548)
Sponsor: National Institute on Aging
Project Dates: September 2015 – May 2020
Award Amount: $516,626 (current year)

PI: Barnes, Carol A. (co-I’s: Alexander, Billheimer, Huentelman, Trouard)
Project: Neural System Dynamics & Gene Expression Supporting Successful Cognitive Aging (RO1 AG049465)
Sponsor: National Institute on Aging
Project Dates: August 2014 – March 2020
Award Amount: $734,165 (current year)

PI’s: Barnes, Carol A. and Huentelman, Matt J. (co-I: Okuno)
Project: CATT: Development and Application of a Neuronal Cell Activity-Tagging Toolbox (RO1 AG049464)
Sponsor: National Institute on Aging
Project Dates: September 2014 – May 2019
Award Amount: $300,969 (current year)
Subcontract PI: Barnes, Carol A. (PI: Stern)
Project: Collaboratory on Research for Cognitive Reserve and Resilience (P30 AG061421)
Sponsor: National Institute on Aging
Project Dates: October 2018 – September 2021
Subaward Amount: $18,945 (current year)

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

PI: Barnes, Carol A. (co-I’s: Bimonte-Nelson, Coleman, Huentelman, Reiman)
Project: Postdoctoral Training, Neurobiology of Aging and Alzheimer’s Disease (T32 AG044402)
Sponsor: National Institute on Aging
Project Dates: May 2016 – April 2021
Award Amount: $260,293 (current year)

PI: Brinton, Roberta
Project: Sex Differences in the Molecular Determinants of Alzheimer’s Disease Risk: Prodromal Endophenotype (R01 AG057931)
Sponsor: National Institute on Aging
Project Dates: September 2018 – August 2023
Award Amount: $1,192,861 (current year)

PI: Brinton, Roberta
Project: Translational Research in AD and related Dementias (TRADD) (T32 AG057931)
Sponsor: National Institute on Aging
Project Dates: September 2018 – August 2023
Award Amount: $146,898 (current year)

PI: Brinton, Roberta
Project: Aging & Estrogenic Control of the Bioenergetic System in Brain (R01 AG053589)
Sponsor: National Institute on Aging
Project Dates: March 2017 – February 2022
Award Amount: $309,287 (current year)

PI: Brinton, Roberta
Project: Perimenopause in Brain Aging and Alzheimer’s Disease (R01 AG026572)
Sponsor: National Institute on Aging
Project Dates: September 2016 – May 2021
Award Amount: $2,070,810 (current year)

PI: Brinton, Roberta
Project: Metabolic Networks and Pathways Predictive of Sex Differences in AD Risk and Responsiveness to Treatment (R01 AG059093)
Sponsor: National Institute on Aging
Project Dates: August 2018 – June 2023
Award Amount: $153,500 (current year)
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<tr>
<th>PI:</th>
<th>Brinton, Roberta</th>
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<tbody>
<tr>
<td>Project:</td>
<td>Allopregnanolone a Regenerative Therapy for Alzheimer’s: FDA-Required Toxicology (U01 AG047222)</td>
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<td>National Institute on Aging</td>
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<td>Project Dates:</td>
<td>June 2018 – June 2019</td>
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<tr>
<td>Award Amount:</td>
<td>$215,348 (current year)</td>
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<th>PI:</th>
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<tbody>
<tr>
<td>Project:</td>
<td>Perimenopause in APoE4 Brain: Accelerated Myelin Catabolism for Fuel</td>
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<tr>
<td>Sponsor:</td>
<td>Alzheimer’s Association</td>
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<td>Project Dates:</td>
<td>May 2017 – April 2020</td>
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<td>Award Amount:</td>
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<tr>
<th>PI:</th>
<th>Chou, Ying-hui</th>
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<tbody>
<tr>
<td>Project:</td>
<td>Use of TMS and fMRI Measures to Assess the Risk of Conversion of MCI to Dementia (P30 AG019610)</td>
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<tr>
<td>Sponsor:</td>
<td>National Institute on Aging (ADC Pilot Award)</td>
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<td>Project Dates:</td>
<td>July 2017 – June 2019</td>
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<td>Subaward Amount:</td>
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<th>Co-Investigator:</th>
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<tr>
<td>Project:</td>
<td>Transcranial Acoustoelectric Imaging for High Resolution Functional Mapping of Neuronal Currents (R56 AG061888)</td>
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<td>Sponsor:</td>
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<td>Project Dates:</td>
<td>September 2019 – September 2020</td>
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<td>Amount:</td>
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<tr>
<th>PI’s:</th>
<th>Coleman, Paul D., Barnes, Carol A., and Alexander G.E. (co-I’s: Billheimer, Huentelman, Trouard)</th>
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<tbody>
<tr>
<td>Project:</td>
<td>Epigenetic, Neuroimaging &amp; Behavioral Effects of Hypertension in the Aging Brain (RO1 AG049464)</td>
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<tr>
<td>Sponsor:</td>
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<td>Project Dates:</td>
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<tr>
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<td>Transcranial Acoustoelectric Imaging for High Resolution Functional Mapping of Neuronal Currents (R56 AG061888)</td>
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<tr>
<td>Project Dates:</td>
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<td>Amount:</td>
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<tr>
<td>Project:</td>
<td>Mechanisms of Low-Dose Ketamine Treatment for Parkinson's Disease (R56 NS109608)</td>
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<td>Sponsor:</td>
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<td>Project Dates:</td>
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<tr>
<td>Amount:</td>
<td>$115,541 (Cowen component)</td>
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Subcontract PI: Cowen, Stephen, L.
Project: Restoring Functional Connectivity Following TBI (R01 NS084026)
Sponsor: National Institute of Neurological Disorders and Stroke
Project Dates: February 2014 – January 2019
Award Amount: $20,413 (current year)

Subcontract PI: Cowen, Stephen, L.
Project: High Density, Miniaturized, Zero Switching, Stimulation and Recording Headstage for Small Animals (R44 MH114776)
Sponsor: National Institute of Neurological Disorders and Stroke
Project Dates: August 2019 – February 2020
Award Amount: $50,683 (current year)

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

Subcontract PI: Ekstrom, Arne
Project: Representation of Spatiotemporal Information in Human Episodic Memory and Navigation (R01 NS07856)
Sponsor: National Institute of Neurological Disorders and Stroke
Project Dates: July 2012 – June 2022
Award Amount: $347,985 (current year)

PI: Ekstrom, Arne
Project: The Neural Basis of Human Spatial Navigation in Large-scale Virtual Spaces with Vestibular Input (NSF BCS-1630296)
Sponsor: National Science Foundation
Project Dates: July 2016 – August 2020
Award Amount: $347,985 (current year)

PI: Fernandez, Fabian
Project: Programming the Aged Circadian Clock with Flashes of Precision Light
Sponsor: Science Foundation Arizona
Project Dates: November 2019 – November 2022
Award Amount: $297,000 (project period)

PI: Grilli, Matthew (co-I’s: Andrews-Hanna, Ryan)
Project: The Episodic Autobiographical Memory Hypothesis of Preclinical Alzheimer’s Disease: Developing a New Approach for Early Cognitive Detection and Measurement of Alzheimer’s Disease (R03 AG06027)
Sponsor: National Institute on Aging
Project Dates: April 2019 – March 2021
Award Amount: $76,750 (project period)
Co-investigator: Mehl, Matthias (PI: Stone)
Project: Reducing Implicit Verbal and Nonverbal Bias toward Hispanic Patients (R01 MD008940)
Sponsor: National Institute on Minority Health and Health Disparities
Project Dates: September 2014 – May 2019
Award Amount: $90,000 (current year)

Subcontract PI: Mehl, Matthias (PI: Nugent)
Project: Reducing Implicit Verbal and Nonverbal Bias toward Hispanic Patients (R01 MD008940)
Sponsor: National Institute on Minority Health and Health Disparities
Project Dates: September 2014 – May 2019
Award Amount: $90,000 (current year)

Subcontract PI: Mehl, Matthias (PI: Nugent)
Project: Understanding the Interplay of Social Context and Physiology on Psychological Outcomes in Trauma-Exposed Adolescents (R01 MH108641)
Sponsor: National Institutes of Mental Health
Project Dates: July 2016 – June 2021
Award Amount: $59,078 (current year)

PI: O’Connor, Mary-Francis
Sponsor: National Institute on Aging
Project Dates: September 2019 – August 2021
Award Amount: $14,100 (current year)

Co-investigator: O’Connor, Mary-Francis (PI: Palitsky)
Project: Untangling the Health Influence of Religion in Bereavement: The Role of Affect (R13 AG066368)
Sponsor: Society for Scientific Study of Religion
Project Dates: July 2018 – September 2019
Award Amount: $3,000 (project period)

PI: Rance, Naomi E.
Project: Role of Preoptic NK3R Neurons in the Estrogen Modulation of Body Temperature (RO1 AAG047887)
Sponsor: National Institute on Aging
Project Dates: August 2014 – April 2019
Award Amount: $302,094 (current year)

Co-I: Rance, Naomi E. (PI: Teske)
Project: Pre-Clinical Model for Sleep Deprivation-Induced Obesity and Hedonic Intake Due to Noise Exposure
Sponsor: National Institute of Neurological Disorders and Stroke
Project Dates: July 2017 – June 2019
Award Amount: $169,601 (current year)
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<th>Ryan, Lee (PI: Sweitzer; co-I’s: Bedrick, Hay, Khalpey, Konhilas, Ryan)</th>
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<tr>
<td>Project:</td>
<td>Evaluation of the Safety and Efficacy of Angiotensin 1-7 to Enhance Cognitive Function in Participants Undergoing Coronary Artery Bypass Graft (CABG) Surgery (U01 HL131014)</td>
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<td>Sponsor:</td>
<td>National Heart, Lung, and Blood Institute</td>
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<td>Project Dates:</td>
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<td>Project:</td>
<td>Arizona Alzheimer’s Consortium State-Funded Projects</td>
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<td>State of Arizona, DHS</td>
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<tr>
<td>Date:</td>
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<tr>
<td>Amount:</td>
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<td>Project:</td>
<td>Arizona Alzheimer’s Consortium State-Funded Projects</td>
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<tr>
<th>PI:</th>
<th>Wilson, Robert C. (co-I’s Alexander, Andrews-Hanna, Chou)</th>
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<tr>
<td>Project:</td>
<td>Evaluating the Neurocomputational Mechanisms of Explore-Exploit Decision Making in Older Adults (R01 AG061888)</td>
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<td>Sponsor:</td>
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<tr>
<td>Project:</td>
<td>Vulnerability of Older Adults to Financial Deception Schemes</td>
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<tr>
<td>Sponsor:</td>
<td>McKnight Brain Research Foundation</td>
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<td>Date:</td>
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<td>Amount:</td>
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<td>Project:</td>
<td>The Neural Substrates of Explore-Exploit Decisions in Old Age (P30 AG019610)</td>
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<tr>
<td>Sponsor:</td>
<td>National Institute on Aging (ADC Pilot Award)</td>
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<td>Date:</td>
<td>7/1/17 – 6/30/19</td>
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<tr>
<td>Award Amount:</td>
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Educational programs focusing on age-related memory loss

Barnes was probably the first person in the United States (and the world) to develop a ‘true Gerontology’ course that covered the entire spectrum of this discipline. The course was designed for senior undergraduates and graduate students from many disciplines – with the first class being taught when she was at the University of Colorado, Boulder in 1984. Barnes has taught this course almost yearly since then, and still teaches this course at the University of Arizona – it has had the same name for these 35 years – “Gerontology: A Multidisciplinary Perspective”.

Barnes, together with other University of Arizona faculty in the Department of Psychology began to develop in 2018 an on-line on Gerontology Certificate program focused on “Best Practices for Caregivers: Providing Quality Care and quality of Life for Older Adults”. The Fundamental “first course” in this program will be fashioned after Barnes’ upper level course in terms of content areas covered, and then there will be a number of other courses to follow, to allow students to customize their learning experience to best suit their interests, or professional specialty.

Graduate Certificate Program: The graduate certificate in Gerontology is designed to provide a broad overview of the field of aging, while offering targeted information directly applicable to individuals working with an aging population. In this series of courses, the University of Arizona’s renowned scientists and clinicians will discuss research-supported principles and information that are translated into practical applications for anyone working with older adults, in order to enhance the quality of life for older adults and caregivers alike.

The certificate program consists of a minimum of five courses taught in an enhanced interactive online format that gives students an exceptional educational experience with the freedom to work from anywhere, on your own schedule. Each course requires approximately 40 hours to complete. Students begin the program with an introductory core course, Fundamentals of Gerontology. The remaining four courses can be selected from the list of available options listed below.

Fundamentals of Gerontology
This course provides a broad overview of the social, cultural, psychological, cognitive, and biological aspects of aging, as well as a look into the challenges faced by aging adults, their families, their caregivers, and their communities.

Cognitive and Psychological Aspects of Healthy Aging
This course explores healthy aging with an emphasis on understanding how aging affects the quality of life for older adults through changes in cognitive functioning, mental health, personality, and adjustment. Students will learn facts and myths about aging and how caregivers can help optimize well-being among older adults.

Relationships and Aging in a Social-Cultural Context
In this course, students will discuss social and cultural influences on aging, including social support, sexuality, and family dynamics, as well as the impact of an increasingly older population for society.

Dementias and Chronic Conditions in Older Adults
This course focuses on dementias and other chronic conditions commonly experienced by older adults, how these disorders impact daily functioning, and the warning signs that an individual may need additional care. Students will learn about the most recent advances in the assessment and treatment of cognitive and mental health disorders among the elderly.

Caring for Aging Adults and their Caregivers
This course covers basic concepts in the therapeutic care of aging adults with an emphasis on self-care and stress-management for older adults and caregivers alike. Topics include therapeutic
communication, managing depression and stress, and coping with death and loss.

**Elder Care: Law, Policy, and Elder Mistreatment**
The course explores the intersection of law, policy, and elder abuse and neglect. Students will discuss legal and ethical issues relating to older adults. They will also learn about risk factors of abuse, perpetrator profiles, current approaches to elder abuse prevention, and legal responsibilities for reporting suspected abuse.

**Collaborative programs**
with McKnight institutions and research programs and non-McKnight institutions and research programs
The Director, Associate Director, and Affiliate Faculty of the Evelyn F. McKnight Brain Institute at the University of Arizona have many collaborative interactions among themselves and other Institute faculty in Tucson and with other McKnight Brain Institutes. In addition, we have extensive collaborations with faculty inside the University of Arizona, across the state, across the country, and around the world. Some of these interactions have resulted in publications. These are listed in the summary of scientific achievements since last year section at the beginning of this report. I have explicitly included only those publications that have direct or potential relevance to the aging brain and memory. From the review of our progress in that section, it is evident that we are extremely collaborative, as well as extremely productive. We will resubmit the U19 Precision Aging Network grant to NIA in the coming year. If funded, the Miami EMBI (Rundek, Levin, Sacco) is directly involved as an important experimental site in the project, and we hope to eventually engage the other two EMBI sites to participate in our efforts towards making a Precision Aging Network a reality.

**Most important scientific achievements this year**
There were many significant findings published this year, each of which contributes to our understanding of the aging brain and memory loss that occurs during the aging process. I have reviewed a selection of the accomplishments of the Director and Associate Director’s laboratories, as well as those of our affiliate members in the synopsis found under the section “Summary of scientific achievements since last report”.

**Plans for future research**
The Director of the Evelyn F. McKnight Brain Institute at the University of Arizona is in a strong position in the coming year to conduct significant research on memory in the aging brain. In addition to support from the McKnight Brain Research Foundation, her work is supported through five RO1 grants and one postdoctoral training grant. She submitted two new RO1s last year and is submitting two competitive renewals in the coming year that will support her rodent and nonhuman primate work on the biological basis of memory decline in aging.

During the past year Barnes submitted a proposal for a U19 grant entitled “Precision Aging Network: Closing the Cognitive Healthspan, Human Lifespan Gap” for the submission deadline. The proposal was an enormous undertaking, with ~40 individuals participating. It did get reviewed, but it did not quite meet the pay line. Barnes is the PI of this U19 grant, and the Associate Directors of the grant are all Tucson EMBI Affiliate Faculty (Brinton, Hay, Huentelman and Ryan). The five of us, plus Paul Worley (our collaborator from Johns Hopkins) met with Molly Wagster, Jonathan King and Dallas Anderson at NIA last November to discuss strategies for a resubmission. They encouraged us to go forward with the revision and have helped us focus on areas that were of concern to the reviewers.
The most challenging issue was one of feasibility of recruiting the diverse set of participants into the face-to-face experiments – it was simply not possible to conduct pilot experiments on the main study before we received funding.

We received extremely exciting news from the University of Arizona President’s office last summer that notified us that we could apply for pilot support from his Strategic Initiative fund to mount a study to collect preliminary data for our U19 resubmission. Our proposal was positively reviewed last year, the funds are just now being released, and we have begun to hire Program and Project coordinators, get our protocols finalized and IRB approvals in place to begin recruiting participants in Tucson beginning February 1, 2020. Barnes has also applied to the McKnight Brain Research Foundation to request support for a pilot study at the Miami U19 site, that is under consideration. If we had preliminary data from two locations, the resubmission will be even stronger.

The U19 resubmission date is September 25, 2020. We are already working very hard on revisions, and this will continue over the next year as we collect the preliminary data necessary to prove feasibility and improve the clarify of our written document. We are anticipating a positive outcome for this important effort.
Additional notes

Were any funds used for a Prohibited Purpose during the report period?
No

Do you recommend any modification to the Purpose or mandates in the Gift Agreement?
No

Did all activities during the report period further the Purpose?
Yes

Negative Events
N/A

Technology transfer
Nothing to report

Respectfully Submitted,

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