

Alzheimer's and Related Diseases Research Award Fund

2013-2014 ALZHEIMER'S RESEARCH AWARD FUND RECIPIENTS ANNOUNCED

The Alzheimer's and Related Diseases Research Award Fund (ARDRAF) was established by the Virginia General Assembly in 1982 to stimulate innovative investigations into Alzheimer's disease (AD) and related disorders along a variety of avenues, such as the causes, epidemiology, diagnosis, and treatment of the disorder; public policy and the financing of care, and the social and psychological impacts of the disease upon the individual, family, and community. The ARDRAF competition is administered by the Virginia Center on Aging at Virginia Commonwealth University. Questions about the projects may be directed to the investigators or the ARDRAF administrator, Dr. Constance Coogle (ccoogle@vcu.edu).

UVA **Matthew J. Barrett, M.D., M.Sc., Bradford B. Worrall, M.D., M.Sc., and Robert D. Abbott, M.A., M.P.H., Ph.D.**

Assessment of Whether Genetic Risk Factors for Alzheimer's Disease and Vascular Dementia are Associated with Cognitive Impairment in Parkinson Disease

Cognitive impairment is common in Parkinson's disease (PD). However, there is significant variability in the onset of cognitive impairment during the course of disease. At this time the pathophysiology of cognitive impairment in PD is incompletely understood, and it is not possible to predict when patients will develop significant cognitive impairment. A few genetic factors have been found to influence the onset of cognitive impairment in PD. One of these is the APOE ε4 allele, an important risk factor for Alzheimer's disease (AD). The presence of Alzheimer's pathology in individuals with PD and dementia suggests that genetic risk factors for AD may contribute to cognitive impairment in PD. In addition to Alzheimer's pathology, cerebrovascular pathology has also been associated with dementia in PD. Recently, genome wide association studies have identified two alleles associated with increased risk of vascular dementia. The objective of this study is to evaluate whether alleles associated with increased risk of AD and vascular dementia are also associated with increased risk of cognitive impairment in PD. This study takes advantage of two large existing PD datasets with single nucleotide polymorphism arrays and Mini-Mental State Exam scores. Determining genetic risk factors for cognitive impairment in PD will provide insight into disease pathophysiology, improve prognostication, and inform personalized treatment strategies.

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ODU **Christianne Fowler DNP, RN, GNP-BC and colleagues**

The Impact of an Interdisciplinary Virtual Healthcare Neighborhood on Sleep, Healthcare/Social Support, and Self-Efficacy among Caregivers of Elderly Persons with Dementia

Patients with Alzheimer's and other forms of dementia and their caregivers (i.e., patient/caregiver dyads) often suffer from sleep disturbances. These sleep disturbances have been linked to poor health outcomes and impaired quality of life for these patient/caregiver dyads. This study evaluates a Virtual Healthcare Neighborhood (VHN) as an intervention for improving patient/caregiver dyads' sleep quality, self-efficacy, provider support, and social support. Bandura's Theory of Self-Efficacy provides the conceptual framework for developing the VHN based on the following four constructs: performance accomplishments, vicarious experiences, social persuasion, and physiological and emotional states. The VHN will provide caregivers with home access to: 1) a team of allied healthcare professionals in the fields of nursing, physical therapy, counseling, dental hygiene, and biomedical technology, 2) peer support, and 3) relevant healthcare information and resources. The Telehealth intervention will result in a virtual patient-centered home. The investigators anticipate that this will prove to be an effective, low-cost method for improving both caregiver and patient sleep, as well as related outcomes, while ultimately preventing or delaying the institutionalization of patients. *(Dr. Fowler may be contacted at 757/683-6869, cfowler@odu.edu)*

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Liberty Gary D. Isaacs, Ph.D.

University *Remodeling of DNA Methylation Associated with Increased Beta Amyloid Deposition in Mice*

Although several mutations have been associated with patients suffering from AD, several lines of evidence suggest that AD development might be caused by chemical modifications of the base DNA sequence (e.g., cytosine methylation, cytosine hydroxymethylation). Our project seeks to identify regions of the genome that become epigenetically altered as cells progress toward an AD-like state. To this end, the investigators plan to use DNA microarrays to map the locations of both cytosine methylation and cytosine hydroxymethylation in an AD mouse model system. Mice expressing two AD-related transgenes will serve as our AD-like condition, while mice lacking the transgenes will serve as our AD control group. The transgene positive mice produce more beta amyloid plaques than control mice, they do significantly worse on cognitive function experiments, and die at a younger age. This model is by far better than human cell culture models that utilize immortalized cell lines and exogenous treatment of purified amyloid beta. Our approach to identify AD-related epigenetic changes on a genomic scale represents a novel application of current technology to the realm of AD biology.

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CCAL Karen Love, B.S., Elia Femia, Ph.D., and Sonya Barsness, M.S.G.

Promoting Change and Action in Person-Centered Care Practices Using a Multi-Media Approach

A paradigm shift is occurring in the way we provide care and support to people living with dementia. Moving away from a purely medically-driven practice, the person-centered model of care is one that offers individualized approaches and considers the values and preferences of the person living with dementia. Recently, there has been much effort in developing practice guidelines and measurement tools to address the "What" and "How" of person-centered care. Missing, however, is the "Why." What influences a person or organization to adopt and maintain person-centered dementia practice? This project will explore the motivation for key stakeholders to adopt person-centered practices, and then develop multi-media tools that help define the "Why." These tools will be targeted to care professionals, family care partners, and people who have early stage dementia. A two-part motivational video will be produced: A primer segment will provide awareness of person-centered practices and a follow-up segment will illustrate the values of such practices. Printed materials based on the theory of planned behavior will also convey that the experience of people living with dementia and their care partners can be improved through simple yet significant daily actions. The impact of these multi-media tools will be evaluated experimentally to determine the extent to which project participants will positively change their practices to improve the quality of life for people living with dementia and those who care for them. *(The investigators may be contacted: Ms. Love, 703/ 533-3225. karenlove4@verizon.net ; Dr. Femia, 703/532-5133, Elia.Femia@verizon.net; Ms. Barsness, 757/773-7841,*

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Radford Lisa L. Onega, Ph.D., R.N.

University *Bright Light Therapy for Individuals with Dementia*

Many older adults with dementia living in long-term care facilities experience depression and agitation. Current treatments for depression and agitation are primarily behavioral and pharmacological. While research results to date are still inconclusive, bright light exposure appears to reduce depression and agitation in these residents. This experimental study seeks to determine whether or not bright light therapy is an effective treatment that can be added to the available repertoire of strategies used to treat these conditions. If bright light therapy, a safe, low-cost intervention, reduces depression and agitation in older adults with dementia, benefits would include improved quality of life, reduced use of medications for depression and agitation, and reduced personal and societal costs.

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GMU **Maren Strenziok, Ph.D. and Pamela Greenwood, Ph.D.**
The Impact of Auditory Perception Training on Brain Activation and Connectivity in Attention Networks, Reasoning Ability, and Everyday Cognitive Function in Patients with Mild Cognitive Impairment

Given the new evidence that cognitive training can improve general cognitive ability, there is a critical need to understand the neural mechanisms that promote transfer effects of cognitive training to everyday cognitive function in patients with Mild Cognitive Impairment (MCI). In the proposed study, the investigators will use auditory perception training in combination with pre- and post-training assessments of brain activation, brain connectivity, reasoning, memory, and everyday problem solving to assess an attentional mechanism that is dependent on functioning of the parietal cortex of the human brain. This attentional mechanism appears to be important for transfer of auditory perception training to general cognitive ability, including everyday problem solving and reasoning. This research is significant for its potential to reveal a critical role of parietal cortex-dependent attentional control in the transfer of training to everyday cognitive function in patients with MCI. Understanding training-related changes would advance understanding of diagnostic brain markers and target points for intervention.

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VCU **Dexian Ye, Ph.D. and Joseph Reiner, Ph.D.**
The Multiple Molecular Appearances of Amyloid- β Aggregates in Alzheimer's Disease

Amyloid-beta ($A\beta$) proteins undergo structural changes in patients with AD. The proteins become misfolded and aggregate to form larger structures which cause dysfunction in the brain. How the structures are formed is not clear due to the lack of suitable detection techniques. In this project, the investigators will study the structure of $A\beta$ assemblies by combining two nanotechnology methodologies. Extremely small holes and metallic needles will be engineered for the detection of these assemblies. The combined methodology will be used to examine $A\beta$ aggregates *in situ* during their misfolding and aggregation processes. The success of this project could offer an ultrasensitive diagnosis of Alzheimer's disease at very early stages.

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VCU **Shijun Zhang, Ph.D. and Hyoung-gon Lee, Ph.D.**
Development of Curcumin/Melatonin Hybrids as Neuroprotective Agents for AD

The multifaceted nature of AD may indicate the therapeutic potential of multifunctional ligands that tackle various risk factors simultaneously as effective AD-modifying agents. While numerous AD-modifying agents targeting one single risk factor have been developed, and a number have entered clinical trials, none of them have been successfully approved by the FDA. Curcumin and melatonin are natural products that have demonstrated multifunctional properties including antioxidant, anti-inflammatory, metal chelating, and anti- $A\beta$ activities. However, certain properties associated with these two compounds have limited their further development as neuroprotective agents. Recently the hybrid molecule strategy has received increased attention in drug design and development. Conceptually, a hybrid strategy incorporates structural features that are essential to the biological activities from different drug structures into one single molecule. The investigators have successfully designed five hybrid molecules based on the structures of curcumin and melatonin. The *overall goal* of this study is to validate the *in vivo* activity of one lead compound in an AD mouse model, and structurally optimize the lead compound to develop more potent analogs. The results are expected to produce a novel and validated hybrid strategy for designing effective neuroprotective agents and ultimately benefiting pharmacotherapy for AD.

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2012-2013 ARDRAF Awards Committee

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