Alzheimer's and Related Diseases Research Award Fund

FINAL PROJECT REPORT SUMMARIES FROM THE 2009-2010 ALZHEIMER'S RESEARCH AWARD FUND

The Alzheimer's and Related Diseases Research Award Fund (ARDRAF) was established by the Virginia General Assembly in 1982 and is administered by the Virginia Center on Aging at Virginia Commonwealth University. Summaries of the final project reports submitted by investigators funded during the 2009-2010 round of competition are given below. To receive the full reports, please contact the investigators or the ARDRAF administrator, Dr. Constance Coogle (ccoogle@vcu.edu).

Alzheimer's Association Central and Western Virginia — **Ellen Phipps, C.T.R.S., and Barbara Braddock, Ph.D. "Home-based activity intervention program in dementia"**

This study investigated and promoted 'partnered volunteering' by pairing University students with individuals who have dementia and their family caregivers to examine an eight-week home-based activity engagement program. The twice weekly intervention provided opportunities for participants to complete activities that were once meaningful in their lives using Montessori-based instruction, therapeutic recreational principles, and environmental modifications. The program was designed to provide an opportunity for successful engagement in life among persons with a diagnosis, to offer respite and support to caregivers, and to foster positive inter-generational relationships. Participants in the intervention group (n = 16) were matched to those with dementia in the comparison group (n = 16) on the basis of sex, age, education, and cognitive screening scores. Comparison group participants selected activities in consultation with the students who implemented the set up, but did not receive regular student visits. Pre- and post-intervention data indicated that activity set up and in-home environmental supports promoted high levels of physical and verbal engagement among participants enrolled in both groups. In contrast to those that did not receive regularly scheduled student visits, caregivers with student support reported statistically significant reductions in burden between program initiation and end. Partnered volunteering may be most beneficial to the caregiver as a supportive intervention to reduce general caregiving stress while sustaining home activity for the individual with dementia.

(Ms. Phipps may be contacted at 434/ 973-6122; Dr. Braddock may be contacted at 434/924-4000)

UVA — **Karen M. Rose, Ph.D., R.N., and Ishan C. Williams, Ph.D. "Family quality of life in dementia"**

Because a diagnosis of dementia has implications for the overall functioning and well-being of the family unit involved, a reliable and valid instrument to assess the impact of interventions and services provided, or not provided, on family quality of life is needed. The goal of this project was to develop a Family Quality of Life in Dementia (FQOL-D) instrument that can be used in clinical and service settings to measure the impact on *families* dealing with dementia. An expert consensus panel of 12 representatives from medicine, neuropsychology, nursing, and gerontology completed three Delphi survey rounds to determine the face validity of items. Approximately 40 items were retained, representing five overall domains: family interactions; direct care/activities of daily living support; emotional/behavioral well-being; physical and cognitive well-being; and disease-related support/medical care. In addition, interviews with persons diagnosed as having mild-moderate dementia and their family members were conducted to pilot-test the instrument and collect qualitative data on their individual family quality of life perspectives. The investigators partnered with local Area Agencies on Aging and the Virginia Caregiver Coalition to distribute the FQOL-D across the state. Imminently pending results will confirm the psychometric properties of this clinically-meaningful instrument. ***(Dr. Rose may be contacted at 434/ 924-5627; Dr. Williams may be contacted at 434/924-0480)***

VCU **H. Tonie Wright, Ph.D. "Alzheimer's Aβ amyloid peptide interactions with inflammatory chaperone molecules"**

Research suggests that certain aggregated states of the β-amyloid (Aβ) peptide are toxic to brain cells and may also disrupt communication between neurons in the brain. This project hypothesized that the pathophysiological effects of Alzheimer's Aβ amyloid peptides are modulated by interaction of the peptide with chaperone-like inflammatory molecules in a way that alters the pool of biologically active Aβ oligomer forms. Reciprocal to the effects of Aβ on these molecules, which are also linked to the neuronal damage associated with AD, is the question of how the interacting proteins affect distribution of the different forms of Aβ. Study results showed that the incubation of dissolved Aβ with these proteins changed how the Aβ molecules assembled into aggregates and altered the distribution by resulting in the significant loss of some forms of Aβ. In addition, Aβ peptide and its combination with two of the inflammatory proteins were tested for their effects on brain cells that produce the inflammatory response. Findings show that these proteins diminish the release of neuron-damaging molecules from the activated inflammatory brain cells, and may therefore serve a protective function. Mobilization or stabilization of these proteins, and/or disruption of pathways that lead to immune cell activation, offer possible paths to suppressing brain inflammation and thereby delaying or interdicting the symptoms associated with Alzheimer's disease. ***(Dr. Wright may be contacted at 804/828-6139)***

UVA **J. Julius Zhu, Ph.D., and Lei Zhang, Ph.D. "Mechanisms for Cdk5-mediated synaptic depression."**

This project investigates the central hypothesis that Cdk5 is a novel rapid homeostatic transmission regulator and aberrant Cdk5 signaling causes the synaptic depression associated with Alzheimer's disease. Preliminary evidence indicated that synaptic activity regulates Cdk5 signaling, which in turns induces a beta-amyloid-independent synaptic depression. The activity-stimulated Cdk5 signaling rapidly depresses transmission independent of transcription and translation, and it depresses NMDA responses prior to AMPA responses, distinguishing itself from beta amyloid (Aβ) and other homeostatic transmission regulators. This suggests that Cdk5 imposes a new type of fast and fine homeostatic regulation on synaptic transmission and dysfunction of Cdk5 signaling is responsible for the early pathogenesis of Alzheimer's disease. Although a number of molecules, including Aβ and a specific Cdk5 activator p25, have been implicated in Alzheimer's disease, it remains unclear which molecule(s) are responsible for the early synaptic pathogenesis. This study has identified p25 as the first molecule responsible for the early pathogenesis of Alzheimer's disease. The results explain the lack of correlation between Aβ deposition and cognitive impairment observed in AD patients and may also account for the failed clinical trials blocking Aβ, which should complementarily stimulate more homeostatic Cdk5 signaling and synaptic depression. The findings suggest additional molecular targets and provide the scientific foundation for developing new detection and treatment strategies for Alzheimer's patients.

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2009-2010 ARDRAF Awards Committee