

Alzheimer's and Related Diseases Research Award Fund

2010 – 2011 FINAL PROJECT REPORT SUMMARIES

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 2010-2011 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).

VCU Severn B. Churn, Ph.D. "Neuronal Mechanisms of Trauma-induced Alzheimer's Disease"

Several studies have shown an association between traumatic brain injury (TBI) and the development of AD. Recently, similar mechanisms have been associated with TBI-induced memory loss and the development of AD. This investigation focused on the TBI-induced pathological activation of a neuronally-enriched enzyme, calcineurin. Activation of calcineurin has been shown to result in the loss of dendritic spines, the major communication route between neurons. Through several, carefully controlled studies, the investigator was able to demonstrate a prolonged, pathological activation of calcineurin that resulted in delayed loss of dendritic spines. In cortical, but not hippocampal, structures the spine loss could be prevented by the application of calcineurin antagonists acutely after TBI. These studies are the first to identify a cellular mechanism through which TBI could accelerate the progression of AD. (*Dr. Churn may be contacted at 804/828-0290*)

GMU Vasiliki N. Ikonomidou, Ph.D. and Pamela Greenwood, Ph.D. "Detection of ApoE-related White Matter Degeneration using Tissue Specific Magnetic Resonance Imaging (MRI): Sensitivity and Implications for Cognitive Function"

This study examined whether Tissue Specific Imaging (TSI), a new MRI technique sensitive to the detection of white matter degeneration, and associated T1 quantitative techniques are capable of detecting Alzheimer's Disease associated changes in middle aged adults, thus potentially serving as a early-detection biomarker for AD. It was anticipated that carriers of the ApoE-e4 genetic risk factor for AD would show a larger degree of white matter degeneration as detected by TSI. While using TSI for differentiating between carriers and non-carriers proved not feasible in the selected cohort, the data acquired is currently serving as the basis for further investigations identifying differences between carriers and non-carriers, and the association of such differences with both cognitive performance and brain anatomical changes. The dataset served as a basis for the development of an automated technique for the detection of Virchow-Robin spaces, a marker of potential vascular pathology that is known to have increased incidence in AD. Furthermore, the investigators are currently exploring the use of texture analysis techniques to develop a more robust methodology for white matter characterization.

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VCU Kate Lapane, PhD "Assessment of Factors which Influence Physician Decision-making Regarding Medication Use in Patients with Dementia at the End of Life"

Few studies have examined the importance of rationalization of medications in patients with advanced dementia nearing the end-of-life, and little is known about the impact of non-clinical factors on prescribing decisions. The investigators evaluated the extent to which nursing home placement, family involvement, and advanced directives influence prescribing decision-making in patients with end-stage dementia. A multidisciplinary team developed four vignettes of patients with end-stage dementia with specific questions relating to discontinuation or initiation of specific medications. Using a modified Dillman approach, the investigator invited a sample of primary care physicians with an active Virginia medical license to participate via email. Of the 269 responders, 191 were eligible for the study. They received vignettes that varied with respect to three randomly assigned factors: 1) Place of residence of the patient (community-dwelling, nursing home); 2) Presence/absence of an advance directive; and 3) Family desires active measures, family desires supportive measures, no family involvement. Chi-square analyses were performed and a balance of potential confounds was achieved through randomization. Continuation of therapies not likely conferring benefits (e.g. statins) was commonplace, regardless of randomly assigned factors. Physicians were less likely to initiate antibiotic therapy for patients with advanced directives (e.g. treating pneumonia with fever: 38% with advanced directives vs. 53% without ($p < .05$)). Medication initiation was not influenced by family involvement or nursing home residence. Prescribing decisions for patients with end-stage dementia may be influenced by non-clinical factors. Guidance on strategies to discontinue medications may be warranted. (*Dr. Lapane may be contacted at 804/628-2506*)

**Alzheimer's Association
Southeastern Virginia**

**Patricia Lacey, MBA, Sonya Barsness, MSG and Scott Sautter, PhD
“The Impact of Early Alzheimer’s Support and Education Programs
on Both Diagnosed Participants and Their Care Partners”**

This study investigated the social and psychological impact of EASE (Early Alzheimer’s Support and Education), a program intended to empower diagnosed individuals and their partners to become active participants in their care. The study employed a quasi-experimental (switching replications) research design with validated measures and a wait-listed comparison group. It was hypothesized that, in comparison with those assigned to the delayed intervention group (n = 17), EASE participants (n = 20) would show improvements in personal self-efficacy, mental and physical health status, and the quality of life for those diagnosed with Alzheimer’s disease. No statistically significant group differences were documented between the intervention and wait list groups, but 2 X 2 factorial and repeated measure ANOVAs showed main effects for time of testing on all three outcome measures, and improvements in the intervention group were generally sustained three months after the program. Comparing scores for care partners and those diagnosed revealed statistically significant interaction effects for several of the health status and quality of life indicators. Scores provided by those with the diagnosis decreased (worsened) from the time of pre-testing, while the scores for the care partners increased (improved). However, both care-partners and those with the diagnosis indicated that the overall quality of life for the diagnosed person improved. Given the benefits of the EASE program documented in this study (e.g., lessened depression, improved quality of life, and perceived ability to handle unforeseen situations), it is surprising that the primary hypothesis was not supported. It appears that there was a positive anticipatory effect for the wait-list group in knowing that they would participate. Perhaps simply making the decision to participate in EASE improved their outlook and knowledge of future participation influenced both self-efficacy and quality of life. Although early stage programs have garnered some evidence-based support, additional research is needed to document new models of support and education, and determine the long-term effects of these as the disease progresses.

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EVMS

Serina A. Neumann, Ph.D. and colleagues “Donepezil’s Effect on Cardiac Function in Patients with Alzheimer’s Disease Through an In Vivo, Non Invasive Measure of Peripheral Neuro-cholinergic Function: Relation to Therapeutic Efficacy”

AD is known to affect the nervous system in ways that influence heart function, which may place AD patients at increased risk for cardiovascular-related death. One of the very probable mechanisms of the subtle cardiac autonomic dysfunction in AD is degenerative damage of central nervous structures related to the autonomic nervous system and the influence of these neurodegenerative changes on higher cerebral functions. Involvement of peripheral nervous structures may also play a role. The characterization of changes in cardiac autonomic function in AD patients, however, has been scarcely evaluated. Furthermore, the effectiveness of treatment for AD with standard FDA-approved drugs like donepezil (Aricept®) may be related to the protection of heart function. This investigation measured both cardiac autonomic function (measured by heart rate variability) and mental thinking abilities in four elderly men while taking donepezil for suspected mild AD. The investigators found irregular heart function in two of the four patients; one during the initial evaluation and the other at three months. This study helped to characterize cardiac autonomic function and potential relations to neuropsychological function in AD patients in the early phase of treatment with donepezil, and adds to the understanding of donepezil’s effect on cardiac autonomic function in these patients.