

Alzheimer's and Related Diseases Research Award Fund

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**FINAL PROJECT REPORTS FROM THE  
2000-2001 ALZHEIMER'S RESEARCH AWARD FUND**

**UVA James P. Bennett, Jr., M.D., Ph.D. & Christine Thiffault, Ph.D. (Dept. of Neurology)  
"Mitochondria Membrane Potential in Alzheimer's Disease"**

It has been hypothesized that AD derives from dysfunctioning mitochondria in neurons, and that abnormal mitochondrial genes are ultimately responsible for these defects. The investigators utilized a reliable cell model (known as a "cybrid") that enables the abnormal mitochondrial genes of AD patients to be examined in an intact cell, and studied the biophysiology of mitochondria in these cell models. Cybrid mitochondria from non-AD subjects exhibit a cyclical loss and restoration of their membrane charge. In the presence of a fluorescent dye, this appears under the microscope like blinking lights and is called "flickering." Mitochondria inside cybrid cells made from AD patients do not flicker normally, and this funded study showed that flickering is coupled to the flow of electrons in mitochondria, down what is referred to as the electron transport chain. This is a complex group of proteins that mitochondria use to synthesize ATP, a general source of cell energy. The investigators now believe that AD mitochondria have defective coupling of electron flow to ATP formation, and this is why they fail to flicker normally. The results of this study show that mitochondrial genes in AD produce defective energetics in mitochondria. They also provide a potential means for identifying drug development targets: a drug that could restore flickering to AD mitochondria would be expected to improve this coupling of energy production. *(Drs. Bennett and Thiffault may be contacted at 434/924-8374)*

**Goodwin House Sheila Caswell, Mary A. Corcoran, Ph.D, O.T.R., & Karen Love, B.S.  
"A Staff-Developed Program to Enhance Care Quality for Residents with Dementia"**

This project engaged 39 nursing home staff in designing high quality care for residents with dementia. Staff were taught to use principles of care based on the Montessori educational approach for cognitive development in children. These principles guided the staff to simplify both the physical environment and everyday activities to match the abilities of each resident. By empowering facility staff to direct an aspect of daily care, the investigators anticipated positive outcomes related to staff retention, quality of care, and caregiving self-efficacy in comparison with nine control group participants at a separate but similar facility who did not receive the intervention training. The results of inferential statistical analyses using repeated measures are discussed as they relate to administrative cooperation and commitment, a factor that is emerging in the literature to be crucial for successful staff programs. *(Ms. Caswell and colleagues may be contacted at 703/824-1167)*

**EVMS Barbara Freund, Ph.D., R.N. (Glennan Center for Geriatrics and Gerontology)  
"Use of the Clock Drawing Test as a Screen for Declining Driving Competency in Cognitively Impaired Older Adults"**

The primary purpose of this study was to determine if the onset of declining driving ability can be predicted by the Clock Drawing Test (CDT), a rapid, simple clinical measure of executive functioning in older adults with cognitive impairment. A secondary purpose was to compare simulated driving performance with actual on-road driving performance. Twenty nine men and women, aged 65 and older, completed the CDT and a simulated driving test. In addition, nine of these subjects were randomly selected to complete an on-road driving test. The findings demonstrate that the CDT is a useful screen for driving competency, even among participants with only mild cognitive impairment. Results further suggest that high fidelity driving simulation is a sensitive method to objectively evaluate driving performance and may be a valid alternative to on-road testing. The results support the use of the CDT by clinicians interested in determining when patients should be referred for driving evaluation. *(Dr. Freund may be contacted at 757/446-7040)*

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**VCU/MCV Mohammed Kalimi, Ph.D. (Dept. of Physiology)**

**"Amyloid Beta Protein-Induced Hippocampal Cell Death: Mechanism of Action"**

Amyloid beta protein (A beta) is a major constituent of plaques in AD and has toxic properties. The precise cellular and molecular mechanisms by which amyloid beta protein may induce neuronal cell death and injury have yet to be determined. The results of this study suggest that pretreatment with the neurosteroid, pregnenolone, or the estrogen antagonist drug, tamoxifen, protects HT-22 cells against A beta-induced cell death. Second, treatment with A beta resulted in enhanced nuclear localization of glucocorticoid receptors (GR) in clonal mouse hippocampal HT-22 cells as compared to control untreated cells (or pregnenolone- or tamoxifen-alone treated cells). Interestingly, prior pregnenolone or tamoxifen treatment followed by A beta resulted in dramatic reduction in GR nuclear localization. In addition, using pharmacological and biochemical approaches, the investigators showed that under in vitro conditions, A beta-induced cell death is mediated, in part, by the activation of protein kinase C (PKC), activation of mitogen-activated protein kinase (p38 MAPK), and modulation of inducible nitric oxide synthase (iNOS). *(Dr. Kalimi may be reached at 804/828-9500)*

**VCU/MCV Elizabeth O'Keefe, M.D., Pamela Parsons, G.N.P., & Peter Boling, M.D.**

**(Department of Internal Medicine) "Percutaneous Endoscopic Gastrostomy (PEG) for Nutritional Support in Persons with Advanced Dementia and Feeding Difficulties: Do the Outcomes Fulfill the Expectations of the Decision-Maker?"**

Eating difficulties are common in advanced dementia and family members may be faced with the difficult decision of whether to artificially maintain nutrition, which is usually done through a tube placed directly into the stomach by means of a PEG. Recent literature suggests that tube feeding rarely prolongs life, improves nutrition, or makes the patient any more comfortable, yet advanced dementia is still a major indication for PEG placement in Virginia. This study was designed to gain further insight into why the decision is made to place a PEG by interviewing the responsible family member (decision-maker) at the time of PEG placement and three months later. Results indicate that the majority of decision-makers expected tube feeding to prolong life, improve nutrition, decrease aspiration and improve comfort, and most hoped it would improve quality of life (QOL). Although the overwhelming reason given for PEG placement was to keep the patient alive, only 50% of patients survived three months. The decision-makers of the survivors stated that their expectations had largely been met. Subjective improvement in QOL was reported, but little evidence was offered to substantiate this. The investigators conclude that PEG placement in advanced dementia is largely a matter of treating the family, rather than the patient, and raise questions about whether this is ethically justified. *(Dr. O'Keefe and colleagues can be reached at 804/828-5323)*

**VA Tech Sherry Schofield-Tomschin, Ph.D. & Anna Marshall-Baker, Ph.D. (Dept. of Near Environments) "Tactile and Visual Stimuli in Alzheimer's Care Units: Incorporating Quilts in the Living Environment"**

Careful design planning in facilities for individuals with Alzheimer's disease and other forms of dementia can provide environments beneficial to the well-being of residents. Important components in therapeutic settings are objects that provide cultural meaning, are stimulating to the touch, or reminiscent of things familiar in their previous homes. The purpose of this study was to examine the behavioral impact of hanging quilts in the public areas of Alzheimer's care facilities. The investigators were interested in determining if residents with AD would interact physically with the quilts or exhibit altered wandering behavior because of their interest and engagement with them. A modified behavioral mapping technique was employed in two facilities that differed in the amount of visual and textile stimuli available to the residents. The addition of quilts had little impact at the environmentally rich site, but had a dramatic affect in the facility that was previously poor in visual and tactile stimuli. The quilts needed to be vertically lowered to be in the viewing plane, however, in order to achieve significant interest and interaction. Wandering behaviors were only modified to include the quilt manipulations into normal wandering patterns, and exiting behaviors were not diminished. This study, the first in a series to identify more fully appropriate components of the physical environment that can enhance quality of life, has implications for other types of stimulating or culturally meaningful objects in long-term care facilities. *(Drs. Schofield-Tomschin & Marshall-Baker may be contacted at 540/231-3250)*