Alzheimer's and Related Diseases Research Award Fund

FINAL PROJECT REPORTS FROM THE 1999-2000 ALZHEIMER'S RESEARCH AWARD FUND

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 along a variety of avenues, such as the causes, diagnosis, and treatment of the disorder; public policy and financing of care; and the social and psychological impacts of the disease upon the individual, family and community. ARDRAF conducts an annual competition for pilot study awards (currently $25,000 each), administered by the Virginia Center on Aging at Virginia Commonwealth University.

GMU Giorgio Ascoli, Ph.D. (Krasnow Institute), "Effect of Dendritic Morphology on Neuronal Electrophysiology in a Lesion Model of Alzheimer's Disease"

An important neurobiological marker of Alzheimer's disease (AD) is the loss of neuronal cells and connections in the hippocampus. Because this brain structure is involved in memory formation, hippocampal damage has been the focus of animal models of AD. In particular, kainate lesions in the rat have been shown to reproduce anatomical (dendritic elongation and branch loss) and biochemical (spread receptor distribution) correlates of AD. This proposal explored the hypothesis that altered dendritic morphology, in itself, causes the drastically impaired electrophysiological behavior of nerve cells that is fundamental to memory loss and dementia. The investigator adopted an identical biophysical model to examine the potential interaction between the anatomical and physiological effects of kainate lesions in hippocampal neurons, characterizing the kainate-induced modifications of pyramidal cell dendritic morphology as well as the electrophysiological changes induced by these anatomical modifications. Results indicated that, although the kainate-lesioned neurons are structurally different from both young and aged control neurons, the electrophysiological behavior emerging from these three groups is much less differentiated. In other words, changes in dendritic morphology similar to those observed in AD are sufficient to induce only minimal quantitative (and no qualitative) alterations of neuronal activity. The researchers concluded that the electrophysiological impairment observed in AD and kainate-lesioned neurons requires both anatomical and biochemical changes to be fully explained. The results indicate a need for more extensive studies and larger pools of neurons to shed light on the mutual interactions between morphological and biochemical influences on neuronal activity. **(Dr. Ascoli can be reached at 703/993-4383)**

UVA Suzanne Holroyd, M.D. (Dept. of Psychiatric Medicine) & Andrew Wolf, M.D. (Dept. of Internal Medicine), "Attitudes on Whether Physicians Should Tell Alzheimer's Disease Patients Their Diagnosis"

There is no established protocol to guide physicians who diagnose dementing illnesses such as Alzheimer's disease (AD) about informing patients of their diagnosis. There are multiple dilemmas and difficulties related to when and how to deliver the diagnosis that pose challenges for both clinicians and families. This study surveyed two groups regarding their attitudes towards being given the diagnosis of AD, elderly clinic outpatients without dementing illness and family members of patients with AD in the community. Responses from the clinic outpatients, who represent diverse racial and socioeconomic backgrounds, were compared to earlier data from predominantly white older adults residing in an upscale retirement community. Here, a significantly greater proportion of respondents in the more diverse sample indicated that they would prefer to be informed of the diagnosis (92% vs. 79.5%), even though significantly fewer of them reported having relatives or close friends with AD or a similar illness (21.5% vs. 48.7%). Surveys of the family members of patients with AD indicated that while the vast majority of caregivers had been told of the diagnosis, only half of the patients had been informed. More than three-quarters of respondents agreed that patients should be told when they are diagnosed with a disease that affects memory and thinking. The level of their care recipients' cognitive impairment distinguished between those who agreed and disagreed. The results of this study lend support to the guidelines recently released by the American Medical Association advocating that patients be directly informed when a dementing illness is diagnosed. **(Drs. Holroyd and Wolf can be reached at 804/924-2241)**

VA Tech Shannon E. Jarrott, Ph.D. (Dept. of Human Development), "The Effects of Instrumental Assistance on Family Caregivers of Patients with Dementia"

Caring for an elderly relative with a dementing illness has consistently been associated with increased levels of overload and decreased well-being. Caregivers may turn to informal (family and friends) and formal (paid) sources for assistance with the care of their relative, but often with mixed results. The present study examined how the amount and types of help dementia family caregivers receive affected caregiver stress and well-being (e.g., depression, anger, overload, and worry). Rather than relying on subjective caregiver evaluations, this study utilized multiple objective measures of the nature and extent of assistance that urban and rural caregivers receive. Results indicated that higher baseline levels of formal, but not informal, help were associated with lower caregiver distress. Greater formal assistance with the activities of daily living (ADLs) was the type of help most strongly associated with lower distress. Although gains in informal help across time were associated with lower depression, changes in the levels of formal help were not related to caregiver distress. Higher levels of conflict associated with formal helpers buffered the effects of increased formal assistance and resulted in higher caregiver distress. It is suggested that even mild conflict has an important negative effect on caregivers. Support programs that provide appropriate and acceptable assistance are warranted. **(Dr. Jarrott can be reached at 540/231-5434)**

UVA Virginia Simnad, M.D. (Dept. of Neurology), "Alteration in Proton Spectra of the Hippocampus to Oral Ingestion of Glucose in Alzheimer's Disease"

Alzheimer's disease is accompanied by atrophy or a decrease in brain tissue particularly in the hippocampus. Neurochemical changes also take place, although, until recently, it has been difficult to view these changes in living individuals. Magnetic Resonance Spectroscopy (MRS) is a new technology which identifies chemical activity in the brain in a safe non-invasive manner. This is accomplished using the same magnet that is used for magnetic resonance imaging (MRI) which identifies brain structures. This study examined chemical activity in the hippocampus, a brain area critically affected by Alzheimer's disease. Significant differences were observed in the brain patterns exhibited by Alzheimer's patients, healthy elderly, and healthy young people. N-acetyl-aspartate, a chemical associated with energy production and neuronal viability, was lowest in the Alzheimer's patients, followed by somewhat higher levels among the healthy elderly, with highest levels of the compound in the healthy young participants. Current investigations are examining the relationship between cognitive functioning and chemical concentrations in the hippocampus. **(Dr. Simnad can be reached at 804/243-5931)**

VCU Patricia W. Slattum, Pharm.D., Ph.D. & Vivien E. James, Pharm.D. (Dept. of Pharmacy and Pharmaceutics), "Anticholinergic Medication Use in Elderly Patients Diagnosed with Dementia or Taking Acetylcholinesterase Inhibitors"

Age- and disease-related changes in the cholinergic nervous system contribute to the functional decline, memory impairment and worsening quality of life observed in Alzheimer's (AD) patients. Administration of anticholinergic medications could result in further adverse consequences in these patients. A wide variety of anticholinergic medications are used to treat conditions comorbid with AD, including Parkinson's disease, incontinence, depression, abdominal cramps, and allergies. Acetylcholinesterase inhibitors, such as donepezil (Aricept®) and tacrine (Cognex®), increase levels of acetylcholine in the central nervous system and improve cognition in some patients with AD. Co-administration of central anticholinergic agents should counteract these effects, reducing the potential benefit of either agent. This study assessed the use of prescribed anticholinergic medications in a Medicare Supplemental insured population and in elderly patients treated in a large group family physician practice. Patients were evaluated for anticholinergic medication use and presence of AD or other dementia. Concurrent use of anticholinergics and acetylcholinesterase inhibitors was also determined. Review of insurance claims revealed that 12.0% of patients with dementia and 13.4% of patients taking acetylcholinesterase inhibitors received anticholinergic medications known to have significant effects in the central nervous system, compared to 10.0% of elderly patients without dementia. Review of charts in the group family practice showed that 41% of dementia patients and 56% of patients taking acetylcholinesterase inhibitors received a medication with some degree of anticholinergic effects, compared to 19% of elderly patients without dementia. Results of this study suggest that patients at high risk for anticholinergic adverse events, particularly those with dementia, continue to receive anticholinergic drugs inappropriately. Drug-drug interactions may be lessening the intended therapeutic effect of the Alzheimer's medication. Increased attention to this problem is needed. **(Drs. Slattum and James can be reached at 804/828-6355)**

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