

Alzheimer's and Related Diseases Research Award Fund

2019-2020 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 2019-2020 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).

**Carilion
Clinic** **Azizza Bankole, PhD, Martha Anderson, DNP, and John Lach, PhD**
***Implementing a Caregiver-Personalized Automated Non-Pharmacological
Intervention System for Dementia-Associated Agitation (CANIS)***

These investigators previously demonstrated the ability of the Behavioral and Environmental Sensing and Intervention (BESI) system to detect early-stage agitation and provide automated notifications to dementia caregivers, who could then intervene in a timely manner. Expanding work on individualized interventions tailored to each caregiver's unique set of issues, the current study developed a higher level process of agitation classifications and assessments to train the next computer-generated intervention model, called the Caregiver-Personalized Automated Non-Pharmacological Intervention System (CANIS). Based on interviews with caregivers revealed that functionality issues included timeliness in notification of approaching agitation and simplicity in selecting descriptive words on the tablet interface. Case study analyses revealed well received intervention suggestions and a decreased number of agitations, confirming that BESI has good value and acceptability. Helpfulness and usefulness of the invested caregivers were discerned thematically. Results support the use of caregiver knowledge and experience to inform further development of a potentially helpful technology. ***(Dr. Bankole may be contacted at 540/981-7653, aobankole@carilionclinic.org; Dr. Anderson may be contacted at 540-5202761, msaconsulting@mail.com; Dr. Lach may be contacted at 434/924-6086, jlach@virginia.edu)***

UVA **Christopher Deppmann, PhD and John Lukens, PhD**
Receptor Mediated Death Pathways in Alzheimer's Pathogenesis

Neuronal death is a hallmark of Alzheimer's disease (AD). AD pathology spreads from one brain region to another over the course of decades, yet the mechanism underlying this spreading remains unknown. Necroptosis and extrinsic apoptosis are two cell death pathways that have been implicated; however, their precise contributions to AD pathogenesis and spread have not been elucidated. The investigators delineated the role of these signaling receptors in the AD inflammatory response and the promotion of pathology. They confirmed that caspase-8 is a key regulator of the pro-inflammatory cytokine IL-1 β , which induces apoptosis, and a negative regulator of Receptor Interacting Protein Kinase 3 (RIPK3), a key regulator of necroptosis. They also found that loss of caspase-8 led to reductions in neurotoxic amyloid deposition and inflammation via glial cells in AD mouse models. Interestingly, blocking RIPK3 had no comparable influence on AD pathogenesis, suggesting that is likely affecting AD pathogenesis through pathways that do not involve necroptosis. Overall findings suggest that caspase-8 inhibition may offer a therapeutic strategy to limit neurodegeneration and neuroinflammation in AD. ***(Dr. Deppmann may be contacted at deppmann@virginia.edu; Dr. Lukens may be contacted at 434/924-7782, john.lukens@virginia.edu)***

VCU **J. William Kerns, MD, and Jonathan Winter, MD**
Shenandoah ***Evaluation of the Impact of Race, Payer, and Other Factors on the Changing***
Valley Family ***Management of Dementia Symptoms: High and Low Performing Virginia***
Residency ***Nursing Homes Compared***
Practice

Although use of risky antipsychotic drugs is declining in Virginia long-term-care facilities (LTCFs), prescribing of unreported alternative drugs, such as mood-stabilizers, has increased precipitously. The investigators compared LTCFs in the highest and lowest quintiles of antipsychotic use and found that higher antipsychotic use was found more predominantly in African American males, rural areas, locales with poorer social determinants of health (SDH), and predominantly publicly owned facilities. An examination of payers in the three highest antipsychotic use quintiles showed that most were in good SDH locales with greater than 95% Caucasian residents, selective admissions, and enhanced nursing, physician, and psychiatric staffing. Qualitatively, the perspectives of facility managers, key clinical personnel, and medical directors revealed that drug use focused on safety and quality of life in patients with dementia. Yet all LTCFs in these quintiles reported more than 20% antipsychotic use. Successful strategies to positive change included individualized non-pharmacologic management of behaviors and the employment of multiple behavioral modalities. ***(Dr. Kerns may be contacted at 540/636-2028, bkerns@valleyhealthlink.com and Dr. Winter may be contacted at 540/631-3700, jwinter@valleyhealthlink.com***

UVA **Amanda M. Kleiman, MD and colleagues**
Post-operative Electroencephalographic Changes and Effects on the Incidence of Delirium
Following Cardiac Surgery

Sleep impairment, defined as problems falling asleep, staying asleep, reduced rapid eye-movement (REM) sleep and slow wave sleep, and increased non-REM sleep, is prevalent in the post-operative period. It has been implicated in the development of post-operative cognitive dysfunction and delirium, as well as dementia. This study aimed to determine the prevalence and severity of sleep disturbance following cardiac surgery using a single-lead electroencephalograph (EEG) device and sleep questionnaires. Self-reported questionnaire data suggest the post-operative period is associated with a reduction in the perceived amount of sleep. This was associated with post-operative EEG findings of a reduction in sleep quality (reduced deep and REM sleep), as opposed to actual time spent sleeping (light sleep and total sleep) which was increased in the post-operative period. Due to a low sample size and the non-standardized nature of the delirium assessment, poorer self-assessments and lower quality sleep EEG results were only weakly associated with delirium in the intensive care unit. More formalized assessments will be conducted moving forward. This cohort of subjects will ultimately be followed for five years to evaluate the association between EEG changes following surgery and the development of dementia. Results show that sleep is altered post-operatively following cardiac surgery and that this sleep alteration is likely associated with post-operative delirium. They also highlight the potential importance of interventions aimed at reinstating restorative sleep in the post-operative period for cardiac and other surgeries. ***(Dr. Kleimann may be contacted at 434/924-2283, ak8zg@virginia.edu)***

VCU **Faika Zanjani, PhD, Jennifer Inker, PhD, and Joann Richardson, PhD**
Health Coaching to Prevent Alzheimer's Disease

Behavior change health coaching is an underutilized strategy for AD prevention. Targeting AD prevention factors (e.g. alcohol, depression, physical inactivity, smoking, isolation, medication management) is extremely challenging for multiple reasons, including the failure in making the connection between AD and health behaviors, and due to motivational, self-efficacy, and knowledge barriers. Connecting health behaviors to AD can be psychologically beneficial, motivating, and programmatically supportive. To improve AD risk factors, the investigators recruited 20 diverse older adults (aged 60+) with incomes below \$12,000/year who were managing diabetes and/or cardiovascular disease as part of the iCubed Health and Wellness in Aging Population Core. A patient preference behavior change health coaching strategy was used, where the person decides on health goals, and is offered health coaching education, motivation, self-efficacy, and referral support targeting AD risk factors. Nine-five percent of those recruited participated in the health coaching. They all rated their health coaching experience as positive, and reported improvement in health and healthy behaviors. There were also improvements in AD lifestyle risk, AD knowledge and cognitive function. These findings demonstrate that telephone-based health coaching is feasible (based on participant engagement) and beneficial (based on positive trends in reducing AD risk factors). ***(Dr. Zanjani may be contacted at 804/828-0670, fzanjani@vcu.edu; Dr. Inker may be contact at 804/828-0670, inkerjl@vcu.edu; Dr. Richardson may be contacted at 804/828-1948, jtrichar@vcu.edu)***