



GRECCs: VA's Network of Aging Centers of Excellence Explores Aging, Age-related Diseases and Promising Interventions.

...what follows is a small sampling from among the hundreds of research investigations currently underway in VHA's Geriatric Research, Education and Clinical Centers (GRECCs).

Ann Arbor GRECC: Antipsychotic Use in Parkinson's disease patients.

Use of antipsychotics (APs) in Parkinson's disease (PD) is common. Noting the high rate at which persons with PD experience psychosis and dementia, investigators at the **Ann Arbor GRECC** hypothesized that use of APs placed patients at elevated risk for mortality. Multivariate analysis of a Veterans Health Administration database of PD patients revealed that antipsychotic users had more than twice the risk of death as observed in a matched group of non-users. The commonly used atypical antipsychotics identified during the study were olanzapine, risperidone, and quetiapine. This work highlights the need for caution when prescribing atypical antipsychotics to PD patients and the importance of always considering non-pharmacologic strategies in managing psychosis. To learn more about this research, contact Dr. Helen C. Kales at helen.kales@va.gov.

Little Rock GRECC: Nutrient Intake and Hospitalization.

Older Veterans often become severely malnourished during hospitalization, leading to a range of complications and a higher risk of mortality. To prevent this from happening, inpatient programs need to closely monitor each patient's nutrient intake. Yet most hospitals are not adequately staffed to do this. The **Little Rock GRECC** developed and studied a novel means for completing daily patient nutrient intake assessments in less than one-third the time required by traditional methods, and the new approach was found to be more accurate as well. The greater ease and improved accuracy facilitates identification of patients at elevated risk for becoming malnourished. Anyone interested in this new approach to assessing nutrient intake can contact Dennis H. Sullivan, MD at dennis.sullivan@va.gov.

San Antonio GRECC: Proteins Block Neuronal Death. A number of aging-related neurological diseases such as stroke, Lou Gehrig's disease, and Alzheimer's disease, involve the death of neurons in the brain. The **San Antonio GRECC** recently described ferroptosis, a previously unrecognized mechanism of neuronal death. Even more exciting, the investigators identified a protein that disrupts this mechanism. Enhancing the activity and delivery of this protein might be a new approach for supporting healthy brain aging. To find out more about this work, contact Dr. Nicolas Musi at Nicolas.musi@va.gov.

Minneapolis GRECC Research Highlights: Dr. Cathy Kotz, PhD and Dr. Michael Lee, PhD, of the Minneapolis VA Medical Center GRECC are exploring ways to improve learning and memory in an animal model of Parkinson's disease. Their focus is on manipulation of the neuropeptide orexin, the activity of which is significantly reduced or even lost during progression of many forms of dementia. Orexin is known to improve learning and memory, and thus the investigators propose that if orexin activity is restored and/or enhanced in Parkinson's disease, there will be improvement in learning and memory. To date, the investigators have shown that animals made deficient in orexin by genetic manipulation have impairments in learning and memory tasks, and that infusions of orexin into memory centers of the brain in these animals reverses these deficits. The investigators are now moving these findings into a genetic model of Parkinson's disease, to test whether infusions of orexin in these animals can improve deficits in their learning and memory profile. Instead of infusion of orexin into the brain, they plan to stimulate remaining orexin neurons "remotely" through the use of Designer Receptors Exclusively Activated by Designer Drugs (DREADD) approach. With this method, a designer receptor is introduced into the cell surface of the orexin neurons. This receptor is then activated by a designer drug that binds exclusively to that receptor, stimulating the orexin neurons. It is hoped that by stimulating the remaining orexin neurons with the designer drug, learning and memory will improve in these mice. This work was funded by VA BLRD in 2016. Dr. Kotz is also collaborating with Dr. Patricia Bunney, PhD, a recent career development awardee in the GRECC at the Minneapolis VA Medical Center. Their work focuses on the biological basis for reductions in physical activity with aging, and looking at ways to improve physical activity levels in aged mice. They are using the DREADD approach to understand how declines in various central nervous system pathways can lead to reductions in physical activity, and whether stimulation of these pathways using designer drugs can improve physical activity in normally aging mice. They are hoping to identify new therapeutic targets for age-induced obesity. To learn more about this research, contact Dr. Cathy Kotz at kotz004@umn.edu.
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