Mechanisms and the Impact of Dietary PUFAs

Vascular Cognitive Impairment: Novel Endothelial

underlying the benefits of PUFA-enriched diets are unknown. However, dietary intervention alongside increased blood brain barrier integrity and altered vasotrophic uncoupling, impairing endothelial integrity. Additionally, we believe that a preventative PUFA-enriched dietary intervention 1 month prior to hypoxic injury blocks this uncoupling and subsequently prevents/delays neurovascular dysfunction and cognitive decline. Male and female mice will be administered a control or novel PUFA-enriched dietary intervention 1 month prior to hypoxic injury using the bilateral carotid artery stenosis model. Mice will continue their diet and be assessed for cerebral blood flow, cognitive function, and motor function at 1- & 3-month time points. Following euthanasia, tissue samples from deep cortical regions and microvasculature will be examined for endothelial- & neuronal-specific P-tau accumulation, inflammation, and cell death.

RESULTS/ANTICIPATED RESULTS: Preliminary data in our lab indicate that hypoxia leads to a two-fold increase in endothelial P-tau accumulation and lowered mature BDNF (mBDNF) in brain microvascular endothelial cells (BMECs) compared to controls. Further, BMECs cultured in media with the PUFA docasahexaenoic acid (DHA) had lowered P-tau and increased mBDNF after hypoxia compared to controls. Based on this data and past research, we anticipate that mice on the PUFA-enriched diet will have enhanced cognitive and motor function alongside improved cerebral blood flow compared to controls. Also, we expect that mice on our PUFA-enriched diet will have lowered tau pathology, cell death, and neuroinflammation alongside increased blood brain barrier integrity and altered fatty acid composition in brain and vascular tissue samples.

DISCUSSION/SIGNIFICANCE: An AHA Presidential Advisory identified cognitive function as modifiable through the management of cardiovascular risk factors, like diet. However, the mechanisms underlying the benefits of PUFA-enriched diets are unknown. Successful completion of these studies will provide insight into the vaso-neuronal protective effects of PUFAs in VCI.

Brain pathophysiology in SARS-CoV-2 disease

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OBJECTIVES/GOALS: The SARS-CoV-2 (Severe Acute Respiratory Syndrome CoronaVirus-2), which underlies the current COVID-19 pandemic, among other tissues, also targets the central nervous system (CNS). The goal of this study is to investigate mechanisms of neuroinflammation in Lipopolysaccharides (LPS)-treated mouse model and SARS-CoV-2-infected hamsters. METHODS/STUDY POPULATION: In this research I will assay vascular reactivity of cerebral vessels to assess vascular dysfunction within the microcirculation. I will determine expression of proinflammatory cytokines, coagulation factors and AT1 receptors (AT1R) in isolated microvessels from the circle of Willis to assess inflammation, thrombosis and RAS activity in the microvasculature. LPS and SARS-CoV-2, are both associated with coagulopathies and because of that I will measure concentration of PAI-1, von Willebrand Factor, thrombin and D-dimer to assess the thrombotic pathway in the circulation. Histology and immunohistochemistry will assess immune cell type infiltration into the brain parenchyma, microglia activation and severity of neuroinflammation and neural injury.

RESULTS/ANTICIPATED RESULTS: We hypothesize that under conditions of reduced ACE2 (e.g., SARS-CoV-2 infection), AT1R activity is upregulated in the microvasculature. In the presence of an inflammatory insult, these AT1Rs promote endothelialitis and immunothrombosis through pro-thrombotic pathways and pro-inflammatory cytokine production leading to endothelial dysfunction in the microvasculature, blood brain barrier (BBB) injury, deficits in cognition and increased anxiety. We will test this hypothesis through 2 aims: Aim 1: Determine the role of the pro-inflammatory arm of the RAS in the pathophysiology of the brain in animal models of neuroinflammation and COVID-19. Aim 1: Determine the role of the protective arm of the RAS in the pathophysiology of the brain in animal models of neuroinflammation and COVID-19.

DISCUSSION/SIGNIFICANCE: This study will provide insights that will complement ongoing clinical trials on angiotensin type 1 receptor (AT1R) blockers (ARBs) in COVID-19. This research is a necessary first step.
Factors needing attention to implement effective drug treatment in community correctional in Puerto Rico
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OBJECTIVES/GOALS: The complex health profile of those supervised by community corrections places them at a greater risk of morbidity and mortality from social disruption, infection, and of substance misuse, relapse, and overdose. This study aims to explore individual and social determinants of SUD and treatment utilization for this population. METHODS/STUDY POPULATION: A secondary data analysis was conducted using an administrative database from the Department of Corrections of Puerto Rico (DoC-PR) that included individuals under community supervision between 2015 and 2018 (N=13,163). Two logistic regression analysis were performed to predict SUD and SUD treatment utilization. The predictors included in the models were: a) age, b) gender, c) civil status, d) education level, e) employment status, f) income, g) number of dependents, h) housing zone, i) type of crime, j) offender classification k) community sentence classification, and k) sentence duration. RESULTS/ANTICIPATED RESULTS: A total of 4,531 cases (34.4%) were identified with an SUD and of these 79.2% were enrolled in treatment. Significant predictors of SUD included a parole sentence (vs probation), commission of felony, decreasing sentence duration and recidivism. Significant demographic variables include, male, single, younger age, unemployed, residing in an urban zone and decreasing income. Significant predictors for SUD treatment utilization were a probation sentence, older age and residing in a rural zone. Mandated treatment may explain a higher likelihood of treatment utilization, yet prevalent modalities consist of residential abstinence based, non-professionalized services known to have poor treatment outcomes. The current data set does not include follow up data to assess changes in treatment utilization. DISCUSSION/SIGNIFICANCE: We should aim to prevent health and social disparities and risk of sentence revocation associated with interventions that lack evidence to support their effectiveness. Next steps should address challenges and opportunities for the adoption of EBPPs for individuals with an SUD under community corrections supervision.

Advanced Practice Provider Perspectives on Advanced Care Planning
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OBJECTIVES/GOALS: Perioperative surgical care is team-based with close partnership between surgeons, residents, advanced practice professionals (APPs), and others. The objective is to develop an understanding of the current state and implementation needs required for APPs to engage surgical patients in advanced care planning (ACP) to promote goal concordant care. METHODS/STUDY POPULATION: We will conduct a mixed methods evaluation of ACP knowledge, attitudes, and beliefs amongst surgical APPs to identify barriers and facilitators of APPs engaging in a team-based approach to engaging surgical patients in ACP. We will conduct an online survey and qualitative interviews in the following 4 domains: 1) knowledge, skills, and attitudes about engaging in ACP with a patient or their surrogate decision maker during their perioperative care; 2) prior ACP-specific education; 3) experiences conducting ACP discussions with patients; and 4) perceived training needs to increase ACP uptake and documentation. The findings will provide the foundations to design team-based interventions focused on addressing the barriers and inform training and coaching needs to develop expertise and comfort in the ACP process. RESULTS/ANTICIPATED RESULTS: We expect variability in the knowledge, skills, attitudes, and experiences with the ACP process. We anticipate gaining a better understanding of the educational materials best suited to support APPs as they begin engaging patients in ACP. Possible barriers to APP-led ACP discussions include inconsistent role delineation, uncertainty about the value of pre-operative vs. post-operative ACP discussions, lack of experience engaging in ACP discussion, and lack of familiarity with electronic health records ACP tools. Possible facilitators of APP-led ACP discussions may be related to past work experience settings, exposure to ACP in....