Abstracts
SCTR Scientific Retreat
on Aging Related Research

October 20, 2017
MUSC Bioengineering Building Auditorium
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Ron Acierno, PhD  
Professor - Nursing - MUSC  

Title: Lesson’s learned from the Florida Hurricanes Study: Older Adult Mental Health  

Objectives:  
Data are limited regarding mental health effects of disasters such as hurricanes. We sought to determine the prevalence of and major risk factors associated with posttraumatic stress disorder (PTSD), generalized anxiety disorder, and major depressive episode 6 to 9 months after the 2004 Florida hurricanes.  

Methods:  
Random-digit dialing was used to recruit a representative population sample of 1452 hurricane-affected adults.  

Results:  
Posthurricane prevalence for PTSD was 3.6%, for generalized anxiety disorder was 5.5%, and for major depressive episode was 6.1%. Risk factors varied somewhat across disorders, with the exception of previous exposure to traumatic events, which increased risk of all negative outcomes.  

Conclusions:  
Storm exposure variables and displacement were associated primarily with PTSD. Notably, high social support in the 6 months preceding the hurricanes protected against all types of disorders.
Andreana Benitez, PhD
Assistant Professor - College of Medicine - Neurology - MUSC

Type: 15 minute talk

Title: Sphingolipids and Brain White Matter in Aging and Mild Cognitive Impairment

Co-Authors:
Samar Hammad, Associate Professor, Department of Regenerative Medicine and Cell Biology, Medical University of South Carolina

Text:
Objectives:
• To describe brain white matter changes in aging and Mild Cognitive Impairment
• To describe a pilot study that is testing whether in vivo measurements of brain white matter (via diffusion MRI) are associated with blood-based lipid biomarkers (via sphingolipidomics)

The prevalence of Alzheimer's disease and related dementias (ADRD) is expected to triple by 2050. As such, there is an urgent need to improve early detection to stall dementia onset through affordable, clinically-feasible procedures, with a focus on novel targets to expand therapeutic development. Significant advances in glial biology have implicated the role of brain myelin in the pathogenesis of ADRDs, but no prior studies have tested the association between in vivo measurements of brain myelin and sphingolipids. This new, collaborative project seeks to address this gap in the literature using sphingolipidomics of blood plasma samples from an ongoing longitudinal study of cognitively intact older adults (Controls) and those with Mild Cognitive Impairment (MCI). Our preliminary data from Controls (N=17) show lower baseline total ceramide and sphingomyelin levels in those who demonstrate cognitive decline at follow-up. We also found that, at baseline, lower sphingosine levels significantly correlate with greater axonal density measured through diffusion MRI. Considerable demographic, clinical, neuropsychological, and neuroimaging data are being collected from Controls and MCI patients to further examine these associations, with the long-term goal of developing sensitive prognostic blood-based biomarkers that can be widely disseminated to detect risk for ADRD.
Federica Del Monte, MD, PhD
Associate Professor - College of Medicine - Medicine - MUSC

Type: 15 minute talk

Title: Mind the Heart. Alzheimers and Cardiomyopathy - A tangled Web

Co-Authors:
Luca Troncone, Marco Luciani

Text:
Heart failure (HF) and Alzheimer Disease (AD) are, individually, severe threats to population health, and their potential coexistence is an alarming perspective. In addition to analogous epidemiological and genetic profiles and common triggers, we recently recognized common molecular and pathological features between the two conditions. We identified in the heart of patients affected by idiopathic dilated cardiomyopathy (iDCM) the pathological hallmark of misfolded protein diseases and aging, namely the accumulation of proteotoxic aggregates in the tissue. Even though numerous studies identified HF as a risk factor for AD, whether, instead, AD affects myocardial function and if the two conditions bear a common pathogenesis, was unknown. In a retrospective cross-sectional study from a cohort of AD patients and age/gender/ethnicity-matched controls we found that patients with AD present an anticipated diastolic dysfunction. By imaging and proteomics approaches we found Aβ40/Aβ42 aggregates are present in the heart, and their expression is increased in AD. Those can directly affect cardiomyocytes function. In conclusion our findings depict a novel biological framework in which AD may be viewed either as a systemic disease or as a metastatic disorder. Importantly our findings bring a new unpredicted etiology for iDCM and heart failure with preserved ejection fraction (HFpEF).
Michael Gower, PhD  
Assistant Professor - College of Engineering and Computing - Chemical and Biomedical Engineering - University of South Carolina

Type: 15 minute talk

Title: Adipose Tissue Engineering: A therapeutic strategy for aging

Text:
Two objectives of the talk:
1. Discuss the role of adipose tissue in aging.
2. Demonstrate that biomaterial implants can modulate gene expression within the adipose tissue.

Cellular senescence is a significant cause of tissue dysfunction implicated in age-related disease. Senescent cells cause tissue dysfunction through the release of proinflammatory cytokines that act locally and systemically. The adipose tissue contains pre-adipocytes, which are susceptible to senescence. The adipose tissue is a large organ and a substantial depot for senescent cells during aging, making it an attractive therapeutic target for age-related diseases. Our lab develops biomaterials for implant into the adipose tissue. These materials are engineered to deliver small molecules, proteins, and gene therapy vectors allowing us to target a range of cellular processes. Recently, we have studied how porous poly(lactide-co-glycolide) implants affect adipose tissue function. In mice, the implants decrease fat pad weight and adipocyte size and modulate expression of leptin, adiponectin, and IGF-1—all secreted factors that play key roles in metabolic diseases associated with aging. Furthermore, the implants promote glucose tolerance in mice fed a high fat diet. While the lab is currently developing therapies for diabetes, a goal is to seek collaborations to (i) address how biomaterials modulate cellular senescence and (ii) develop biomaterial-based therapies for age-related diseases.
Melba Hernandez-Tejada, DHA
Associate Professor - Nursing - MUSC

Type: 15 minute talk

Title: An Epidemiological Study of the Effects of Elder abuse on Self-Reported Health and Mental Health

Co-Authors: Ron Acierno, PhD. College of Nursing, MUSC

Text:

Objective 1: to learn about the effects of elder abuse in terms of health and mental health 8 years following the event.

Objective 2: to identify potential intervention targets to mitigate these negative effects.

Abstract: Objectives: To conduct an 8-year follow-up of the National Elder Mistreatment Study (NEMS) and specify risk ratios for negative outcomes of elder abuse, including DSM-5 defined depression, generalized anxiety disorder (GAD), posttraumatic stress disorder (PTSD), and poor self-reported health.

Methods: Attempts were made to re-contact all 752 NEMS participants who reported mistreatment since age 60 at Wave I, as well as a randomly selected sample of non-mistreated NEMS participants.

Results: 183 NEMS Wave I elder abuse victims and 591 non-victims provided data. In bivariate analyses, elder mistreatment 8 years earlier increased risk of negative outcomes by 200-700%. However, multivariate analyses revealed that Current (Wave II) social support was highly protective against negative outcomes, and even appeared to nullify effects of mistreatment on GAD and poor self-reported health. Thus, current (Wave II) social support appears to be a prime target for intervention.

Future Collaborative Potential: We must now apply findings insofar as developing and evaluating interventions that target social support and connection. Thus the primary questions to be answered are 1) how can we enhance social connection in community residing older adults; and 2) how can we compile this into a replicable / exportable intervention.
Pai Liu, MLA
Student - Architecture, Arts and Humanities - Planning Design & Environment - Clemson University

Type: 15 minute talk

Title: Independence: American Culture of Elder Care in a Facility Setting

Co-Authors:
Matthew Powers, PhD, Director of Department of Landscape Architecture, CAAH, Clemson University

Text:
Objectives:

1. Presenting American culture of elder care
2. Propose a new topic in the field of aging and the built environment.

Although elder care is a widely discussed topic, the culture of elder care rarely attracts the researchers' attention. Elders tend to live in a familiar cultural environment when they are aged, meaning the elders prefer not to move to new places for their later lives. But an interesting phenomenon is that a growing number of American elders choose to live in retirement communities instead of aging-in-place or living with their families. Moving to retirement communities informs a new culture of elder care for Americans. This project aims to explore the American culture of elder care in a facility setting and how the elders interpret their lives in the facilities. Ethnographic interviews had been conducted with the fifteen residents of independent living from a retirement community in South Carolina. Six key words were generalized from the data as burden, finance, health conditions, assistance, social activities, and family connections, listed in an order of the importance to the informants. The six key words directed to a theme, independence, which is the core of American culture of elder care. The future research is aiming to apply the culture of elder care, independence, into the design and operation of the elder care facilities.
Objectives of the talk:

1.) Highlight the novel discovery of PARP1-dependent up regulation of cellular NAD+.

2.) Highlight our novel approach to exploit the therapeutic potential of PARP1 for aging research.

Abstract:
Nicotinamide adenine dinucleotide (NAD+) emerged as the central player in aging research; SIRTuin research being the major contributor. However, the role of poly-ADP-ribose polymerase 1 (PARP1), the major modulator of NAD+ metabolism and signaling is largely ignored in the area of aging research. PARP1 senses and responds to DNA damage, oxidative, environmental and other stresses through the activation of cellular repair and protective pathways. Nonetheless, counter intuitively, activation of PARP1 has been perceived as detrimental to cellular viability through depletion of cellular NAD+ under chronic degenerative and metabolic disorders. My work established that Tyr-tRNA synthetase (TyrRS) is a nuclear stress-signaling molecule and translocates to the nucleus and activates PARP1 under stress conditions. Human TyrRS thus emerged as a novel regulator of NAD+ metabolism and signaling by virtue of its ability to interact and modulate the activity of PARP1. Contrary to the existing scientific dogma that activation of PARP1 leads to the depletion of cellular NAD+, our work demonstrates that TyrRS-dependent activation of PARP1 up regulates cellular NAD+ levels. Based on these observations, we currently focus on innovative methods to exploit activation of PARP1 for therapeutic purposes with an emphasis on targeting neurodegenerative and metabolic diseases and aging.
Objectives:

1- Learn more about the South Carolina Alzheimer's Disease Registry
2-Learn about racial and ethnic differences among registry cases

Abstract: The shift in age structure associated with population aging is one of the most distinctive and imperative demographic events of our era. In tandem with the shift in age, the US is becoming more diverse. Advancing age is the most well-known risk factor for Alzheimer's disease and related dementias (ADRD). The South Carolina ADRD Registry is currently one of only three population-based registries in the Nation; it provides a unique opportunity to better understand ADRD with data compiled from a range of sources on a racially/ethnically diverse sample of South Carolina residents with ADRD. An analysis of 2013 Registry data showed that Whites were significantly older at the time of ADRD diagnosis that either Hispanics or African Americans (3 and 3.5 years older, respectively) and were also older at the time of death (3 and 1.5 years older, respectively). In addition, African Americans and Hispanics with ADRD were significantly more likely than their White counterparts to live in the community (73% vs. 39%, respectively) and have vascular dementia (OR: 1.9 vs. 1.51). Understanding racial and ethnic differences in ADRD can better inform planning for social and health-related services for the growing and increasingly diverse aging population of South Carolina.
Subina Saini
Student - Business and Behavioral Sciences - Psychology - Clemson University

Type: 15 minute talk

Title: Checking-in with My Friends: Results from an In-situ Deployment of Peer-to-Peer Aging in Place Technologies

Co-Presenter:
Yifang Li

Co-Authors:
Yifang Li, Subina Saini, Kelly Caine, Kay Connelly

Text:
Many older adults in need of care are not able to afford formal caregivers or assisted living facilities, and prefer to age in place in their own home. We propose a new model of peer-care facilitated by a suite of four, in-home, technologies that enable older adults to provide some elements of care for each other. We investigate older adults' experiences with the technology suite that we designed specifically to address the needs of urban, low socio-economic status (SES) older adults. We deployed the technologies - Activity Clock, Community Window, Check-In Tree, and Trip Coordinator - in participants' homes for eight weeks with the aim of enabling an interactive, peer-to-peer support system within the community. We explored older adults' technology-related privacy concerns with a privacy-enhancing feature - DigiSwitch - that allowed participants to control which peers in their peer network could view activity information. We conducted weekly surveys to assess loneliness, quality of life, interpersonal support, perceived burden, usability, satisfaction with the technologies, and privacy perception.
Objective 1: Introduce optical clearing methods as a new way to study vascular structure in post-mortem tissues.

Objective 2: Discuss the goals of our pilot project.

Cerebral small vessel disease (SVD) is a major contributor to dementia in the US. The goal of this project is to visualize (for the first time) the 3-D structure of cerebral microvessels in human tissue using novel optical clearing and imaging technology. We will define the structure of abnormal vessels that arise during arteriolosclerosis, and use computational methods to simulate blood flow through these vessels. This project is innovative because it is a major advance from conventional neuropathological examination of thin tissue sections, which preclude visualization of vascular networks. This project is significant because it may provide new information on how small vessel disease contributes to impaired brain perfusion during dementia, a disease with enormous impact on the aging population in the US.
Title: Cognitive persistence explains speech recognition in noise variability across older adults

Co-Authors:
Susan Teubner-Rhodes, PhD, Department of Otolaryngology-Head and Neck Surgery, College of Medicine, MUSC, Kenneth I. Vaden, PhD, Department of Otolaryngology-Head and Neck Surgery, College of Medicine, MUSC, Lois J. Matthews, MS, Department of Otolaryngology-Head and Neck Surgery, College of Medicine, MUSC, Judy R. Dubno, PhD, Department of Otolaryngology-Head and Neck Surgery, College of Medicine, MUSC, Mark A. Eckert, PhD, Department of Otolaryngology-Head and Neck Surgery, College of Medicine, MUSC

Text:

Two objectives of the talk:

1) To understand the role of cognitive persistence in overcoming age-related speech recognition difficulties.

2) To foster collaborations with researchers investigating motivation and effort in age-related neurological disorders.

Abstract:
Older adults exhibit poorer speech recognition in noise than younger adults after controlling for audibility, perhaps partly due to declining attentional control. We propose that "cognitive persistence," applying effort to overcome difficulty, may also be important for understanding speech in noise.

We developed a novel measure of cognitive persistence from the classic Wisconsin Card Sorting-64 test and used it to predict performance on the revised Speech Perception in Noise (SPIN) test after adjusting for audibility. We find that persistence significantly predicted word recognition in older adults but not in younger adults. In contrast, attentional control significantly predicted word recognition in younger adults but not in older adults. This suggests that persistence is important for successful communication as speech recognition difficulty increases with age.

Future plans include testing the extent to which cognitive persistence predicts hearing health behaviors, such as hearing-aid use and satisfaction. We also plan to examine the effect of cognitive persistence on treatment and recovery in age-related neurological disorders. We're particularly interested in collaborating with researchers who study disorders that may affect motivation and effort, such as Parkinson's or frontal stroke.
Caitlin Torrence, MA  
Student - Behavioral, Social and Health Sciences - Public Health Sciences - Clemson University

Type: 15 minute talk AND/OR 3 minute data blitz

Title: Targeting rural dementia caregivers: An innovative group-based approach.

Co-Author:
Cheryl Dye, PhD, Public Health Sciences, Clemson University

Text:
Two objectives of the talk:

1. To share experiences translating an individual dementia caregiver intervention into a group-based intervention.

2. To discuss how dementia uniquely impacts rural caregivers and garner feedback from the audience about reaching and meeting the needs of rural caregivers.

Alzheimer's disease (AD) is the sixth leading cause of death in the United States, and the incidence of AD is expected to increase. The healthcare system is ill-equipped to provide care; therefore, most care is provided by unpaid family members. AD family caregivers report higher levels of stress and burden and poorer health outcomes than non-AD caregivers. Rosalynn Carter Institute for Caregiving Resources Enhancing Alzheimer's Caregiver Health (REACH), an evidenced based one-on-one caregiver intervention, has resulted in significant reductions in caregiver stress and burden; however, it is timely and costly to implement. As an extension of a traditional REACH program in Greenville, SC, the research team adapted the program into a group-based format. Group REACH was offered in Seneca, SC, a rural community, as a companion training to an AD respite program. All REACH pre- and post-outcomes were obtained to allow for comparisons between the traditional and group programs. The researchers plan to continue offering and refining the group based program to assess compatibility and effectiveness within rural communities where a lack of social support and elevated levels of stigma associated with AD are common. The researchers are interested in garnering feedback about appropriate methods of targeting rural communities.

*(If more appropriate, will do a 3 minute data blitz instead)*
Naren Vyavahare, PhD
Hunter Endowed Chair and Professor - Engineering - Bioengineering - Clemson University

Type: 15 minute talk

Title: Age related vascular calcification- New therapies for an age old problem

Co-Authors:
Saketh Karamched, Vaideesh Parasaram

Text:

Two objectives of the talk-

1) Describe the problem of elastin degradation and calcification with age that is a significant cause of cardiovascular diseases and mortality in elderly patients.

2) Show data on newly developed targeted nanomedicine that removes vascular calcification and repair of vascular elastin.

Abstract-

Medial arterial calcification (MAC) is a common outcome in diseases like the chronic kidney disease (CKD), and aging. It occurs as linear mineral deposits along the elastin lamellae and is responsible for increased aortic stiffness. There are no therapies to reverse calcification. Ethylene diamine tetraacetic acid (EDTA), a chelating agent may provide an alternative treatment strategy by directly interfering with the mineral deposition. In the current study, renal failure was induced in rats by a customized high adenine diet that led to vascular calcification seen in aging. We developed albumin based nanoparticles (NPs) with attached elastin antibody that only targets calcification sites. The NPs were loaded with EDTA. Systemic administration of NPs led to the reversal of vascular calcification without any untoward effects. We believe that targeted NP therapy will provide an attractive option to reverse vascular calcification and has the high potential for clinical translation.
Lingling Zhang, ScD
Assistant Professor - Behavioral, Social and Health Sciences - Public Health Sciences - Clemson University

Type: 15 minute talk

Title: Needs Assessment of a Community-based Social Engagement Program for Family Caregivers of Those with Dementia

Co-Authors:
Cheryl Dye, PhD, Professor, Clemson University, Department of Public Health Sciences, College of Behavioral, Social and Health Sciences, Institute for Engaged Aging; Caitlin Torrence, PhD Student, Clemson University, Department of Public Health Sciences, College of Behavioral, Social and Health Sciences

Text:
Purpose: The purpose of this study was to assess the needs for a social program among old community dwellers who are caregivers for their family members with Alzheimer's disease and related disorders (ADRD). There are a variety of community-based programs to support the role of family caregivers (CGs), but not every program conducted a needs assessment.

Methods: A purposive sample of 20 CGs was recruited to our structured interview based on the Spearman-Brown Prophesy Formula assuming the agreement obtained is 0.55 and reliability is 98%. All CGs were asked open-ended questions with probes for clarification and additional details. The recorded interviews were transcribed and processed through thematic and coding analyses and word counts and consensus analysis will be particularly used to analyze data from the interviews to identify the important aspects of a social engagement program and quantify them for discovering patterns and degree of agreement/disagreement among CGs.

Results: The major finding is that CGs’ needs varies by the status of their CRs. The CGs who articulated a higher needs of a social engagement program are more likely to be either those with less experience and knowledge in caring for ADRD, or those with more severe ADRD patients and perceived a bigger burden. The important factors indicated by CGs, to name a few, include information, time, CR watch, etc..

Conclusions: There are a variety of programs to support the role of family caregivers, but not every program conducted a needs assessment before its implementation. Our study has shown that tailored approaches are needed to address different needs of family CGs for patients with ADRD. It is especially critical to identify CGs with high perceived stress burden and recruit them to social engagement programs offered on a large scale.
The freshwater microcrustacean Daphnia has many attractive qualities as a model for aging including a fully sequenced genome, adult tissue regeneration, a form of clonal reproduction that allows generating large populations of isogenic individuals, and substantial genetic variation within and among natural populations leading to significant differences in their lifespans. In order to lay some groundwork for this model, we studied the heat shock responses as well as telomere maintenance in both short- and long-lived ecotypes. In addition, we developed a new method for fast and effective RNA interference (RNAi) for Daphnia. This method is expected to be widely useful for all Daphnia biologists, as no method was yet available for RNAi in adult Daphnia. Our studies also include the characterization of Daphnia Sir2 mRNA levels and activity during life span and examine the effects of RNA interference mediated Sir2 knockdown on the lifespan and survival following proteotoxic stress. Currently we are studying the contribution of mitochondrial genome variations in generating varying extents of reactive oxygen species (ROS) leading to differences in aging and lifespans. Overall, we establish Daphnia as a new model organism for research on aging and offer novel insights into mechanisms related to longevity and aging.

Funding: National Institutes of Health grant 1R01AG037969 awarded to RCP and JLD.
**Mara Steedley**  
Community Health Worker - College of Nursing - MUSC

Type: 3 minute data blitz

Title: Data review of first year achievements of a training program to increase elder abuse screening: The Elder Abuse Identification and Referral Program

Co-Authors:  
Melba Hernandez-Tejada, DHA, MUSC College of Nursing

Text:

Objectives:  
In addition to our mission of continuing to train all service providers in the tri-county, we hope to collect data on actual screens once a clinic has been trained. We hope to improve the recommendation of mandatory screening from all service providers, especially MDs.

Abstract: The growth in the older population is dramatically increasing the number of potential elder abuse victims. To combat this epidemic, the 2015 White House Conference on Aging (WHCOA) justified focus on "elder financial exploitation, abuse and neglect" as one of four priority topics. Under this umbrella falls three Key Areas of Action: a) Research b) Services and c) Policy through which we will create a comprehensive network of elder mistreatment services and training opportunities. To expand training opportunities, the Elder Abuse Identification and Referral Program was created to train free community clinics, non-profits, home health, and other agencies in the tri-county area. Training consists of materials on the signs, symptoms, risk factors, and screening of elder abuse in community residing older adults lasting about 30-45 minutes. Since January, we have trained over 600 current and future healthcare providers on how to identify and refer case of elder abuse. Our program gives community members resources within their county that are often low- to no-cost. In addition, we have consulted with 8 older adults in need of resources and referred 4 for other services. By continuing to train, this program aims to bridge the gap between screening, identification, and referrals for service.
Identifying biomolecules responsive to cochlear injury in cochlear cells

• Develop sample preparation method for proteomic imaging of cochlear samples
• Combine proteomic imaging with transcriptomic analysis to identify responsive biomolecules

Exposure to noise or ototoxic-drugs often results in degeneration of cells in the sensory epithelium, auditory nerve, and supporting cells of the cochlear lateral wall. However, the molecular mechanisms underlying this pathology remain unclear. Global transcriptomic analysis with gene arrays can determine molecular changes in the cochlea after injury, but does not provide precise spatial localization or specify changes in protein levels. Coupling gene arrays with matrix-assisted laser desorption/ionization-time of flight imaging mass spectrometry (MALDI-TOF IMS) offers high resolution spatial signatures of the molecular responses to cellular alterations. Thus, the purpose of this study is to identify and characterize regulatory proteins in the cochlea responsive to noise or ototoxic-drug exposure using this complementary proteo-transcriptomics approach. Gene expression results indicate 394 genes are significantly upregulated in response to injury in both models. MALDI imaging of cochlear sections revealed 14 proteins exhibiting spatially distinct patterns localizing to various cochlear regions. Convergent analysis of the mRNA and protein data yielded 15 candidates, including molecules related to chemotaxis, apoptosis and protein processing. The preparation protocol preserves cochlear structures facilitating analysis of warehoused tissue specimens, therefore representing an approach that can be applied for investigation of pathological alterations in postmortem human temporal bones.
Objective:
• To describe the association between serum BDNF and brain volumes of regions relevant to the development of neurodegenerative disease

Abstract:
Brain-derived neurotrophic factor (BDNF) biosynthesis and expression have been shown in both animal and human studies to be implicated in aging and neurodegenerative diseases. We sought to demonstrate that, in a study of cognitively intact older adults (N=39), lower baseline serum BDNF levels would be associated with indicators of cognitive/brain aging: worse performance on a test of overall cognition (Montreal Cognitive Assessment [MoCA]) and lower bilateral hippocampal and cortical white matter (WM) volumes (measured via brain MRI/NeuroQuant), and changes in these measures over time. These data were collected at baseline and approximately 15 months later (in a subset of 24 participants). As hypothesized, we found that at baseline, lower serum BDNF was associated with lower left hippocampal (rs=0.33, p=0.05) and bilateral cortical WM (rs=0.32-0.33, p=0.04) volumes. Unexpectedly, lower baseline serum BDNF was associated with an increase in right cortical WM volumes over time (rs=-0.43, p=0.03) but no other volume changes. Baseline serum BDNF was not associated with baseline or change in MoCA scores. These findings indicate that serum BDNF is a modest indicator of brain volumes (but not overall cognition) in aging, with an intriguing possibility that it may also be associated with compensatory brain changes (i.e. WM volume increase).
Title: Vagus nerve stimulation activates TrkB-ERK signaling in a Parkinson's disease model

Co-Authors:
Ariana Farrand, Department of Neurosciences and Center on Aging, MUSC, Rebecca Gregory, MS, Department of Neurosciences and Department of Comparative Medicine, MUSC, Vanessa Hinson, MD, PhD, Department of Neurology, MUSC, Kristi Helke, PhD, Department of Pathology and Department of Comparative Medicine, MUSC, Heather Boger, PhD, Department of Neurosciences and Center on Aging, MUSC

Text:

Talk Objectives:
VNS has therapeutic potential in a preclinical PD model. VNS activates TrkB signaling to mediate its beneficial effects in this model.

Abstract:
Vagus nerve stimulation (VNS) improves noradrenergic (NE) innervation in locus coeruleus (LC) targets. This makes VNS a potential treatment for Parkinson's disease (PD) since LC-NE neurons degenerate prior to substantia nigra dopamine (SN-DA) neurons. Therefore, we propose that VNS activates TrkB-ERK signaling to improve behavior and neuronal populations in a PD model. To test this, we lesioned the LC-NE neurons in rats with DSP-4 (50mg/kg, ip), followed by intrastriatal 6-OHDA (5µg/µL) to lesion nigrostriatal DA neurons. A subset of rats also received a cuff implant and headcap for VNS. After lesion development, rats underwent two daily sessions of VNS at predetermined parameters, and daily injections of either the TrkB inhibitor ANA-12 (0.5mg/kg, ip) or vehicle for ten days. Locomotor activity was measured daily during the afternoon session. Daily TrkB inhibition prevents improvements of VNS on locomotor activity and striatal DA innervation for lesion rats. Additionally, VNS rats had increased TH-positive cells in the SN and LC, and increased BDNF compared to lesion rats. Studies are ongoing to determine the effects of VNS on ERK and CREB activation downstream of TrkB. These data indicate that VNS activates TrkB-ERK signaling to improve behavior and DA innervation in a preclinical PD model.

This work is supported by a Pilot Project from the MUSC Barmore Foundation and NIH/NIGMS 5P20GM103542 (HAB).