subprocesses of conflict processing and performance evaluation, respectively. RESULTS/ANTICIPATED RESULTS: Those with higher alexithymia, as measured by the difficulty identifying feelings (DIF) facet of the TAS-20, had lower right anterior cingulate cortex (ACC)-left superior frontal gyrus (SFG) connectivity in the P300 window, suggesting impaired performance evaluation. Further, in females specifically, those with higher DIF had greater right inferior frontal gyrus (rIFG)-bilateral ACC connectivity in the N200 window than those with lower DIF, suggesting greater resources were allocated for conflict processing and inhibition. Right ACC-rIFG connectivity also correlated with better stop accuracy and faster stop-signal reaction time, supporting this network's role in successful inhibition. DISCUSSION/SIGNIFICANCE: Overall, during successful inhibition, higher DIF was associated with reduced performance monitoring efficiency as well as greater resource allocation for conflict processing during motor stopping in women only. Thus, alexithymia (via DIF) may exacerbate age-related EF dysfunction and risk for future cognitive decline, especially for females.

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Addressing the Gaps in Diabetic Foot Ulcer Management: Prediction and Prevention

Shirley Lin and Ronald Sherman
Johns Hopkins University School of Medicine

OBJECTIVES/GOALS: Globally, diabetes affects 537 million people and 15-25% will develop a foot ulcer in their lifetime. Diabetic foot ulcers (DFU) tend to be chronic and non-healing due to the poor wound healing environment, leading to infection or amputation. Our study aims to develop a method to predict and prevent DFU formation. METHODS/STUDY POPULATION: Our preliminary plan is to develop a method to detect high plantar pressures, coupled with the ability to automatically adjust an orthotic device to offload excess pressure. Our current aim is to create a "smart orthotic" which will link with foot mapping technology to automatically offload high pressure areas, reducing the need for a separate clinic visit for orthotic adjustment. We aim to prove that our device will normalize plantar pressure distribution, which will prevent callus and subsequent DFU formation. The current target population includes those with diagnosed diabetes and are ambulatory. RESULTS/ANTICIPATED RESULTS: With our technology, we anticipate normalization of plantar pressure distribution in a more frequent fashion than is currently done. Because annual orthotic fittings, which is current standard of care, do not provide regular enough adjustments to match the rate of diabetic foot structural changes and peak plantar pressure redistribution, our device will address two gaps in management. One, patients will receive near-instantaneous changes in plantar pressure offloading, allowing for near continuous orthotic customization. Secondly, our device would reduce the clinical appointment burden, which would be especially important for patients with multiple medical comorbidities or experience other barriers to accessing healthcare. DISCUSSION/SIGNIFICANCE: While DFUs are commonplace and their complications are well recognized, there still exists a gap in ulcer prevention. Our proposed solution will redistribute pathologic plantar pressures, allow for more frequent monitoring, automatic therapy, and aid in the management of high ulcer risk patients.

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Effects of GLP-1 Agonist on Pediatric Populations in a Real-World Setting

Gabi Barajas and Jessica Schmitt
University of Alabama at Birmingham

OBJECTIVES/GOALS: Compare metabolic health of type 2 diabetics on GLP-1 to those on traditional therapy METHODS/STUDY POPULATION: Outcomes of interest of this study include analyzing GLP-1 agonists on overall metabolic health, focusing primarily on weight loss and ability to wane off insulin without rebounding metabolic health. The data will be collected in a retrospective chart review from medical records of type II diabetics from Children's of Alabama and will follow patients over two years. The charts have been narrowed to those patients prescribed GLP-1 agonists who have been on the medication for at least one year with consistent visits to the endocrinology clinic.The following data will be collected from the charts:race/ethnicity, date of visit, BMI/weight, A1C, insulin therapy, lipids, LFTs (AST/ALT), and insurance coverage RESULTS/ANTICIPATED RESULTS: With these results, we hope to study the metabolic health effects of GLP-1 agonists on type II diabetes in the pediatric population. It is known that obesity is a risk factor for type II diabetes, and that GLP-1 agonists aid in weight-loss in adults. Further research is needed to see the real world health effects, and with these results we hope to assess if GLP-1 agonist have an affect on metabolic health within the pediatric population by collecting data on values aforementioned. We also hope to compare and contrast the different GLP-1 agonists being used based on adherence, insurance coverage, adverse effects, and patient preference. Currently, only Liraglutide and Exetanide are approved for pediatric type II diabetics. DISCUSSION/SIGNIFICANCE: Insulin use can lead to weight gain; metformin does not aidin weight reductions. If GLP-1 agonists aid in weight loss, it could potentially help slow complications of diabetes in the pediatric population. B-cell function in children declines more rapidly; and, as a result, insulin resistance occurs more rapidly.

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Can Exogenous Ketones Prevent the Effects of High Salt Intake on Renal Vascular Resistance During Sympathoexcitation?

Soolim Jeong[1], Braxton A. Linder[1], Meral N. Culver[1], Nina L. Stute[1], Sofia O. Sanchez[1], Zachary J. Schlader[2], Orlando M. Gutierrez[3] and Austin T. Robinson[1]
[1]Auburn University; [2]Indiana University and [3]University of Alabama at Birmingham

OBJECTIVES/GOALS: Renal vascular resistance (RVR) is the opposition to blood flow by renal arteries. At the population level, dietary salt increases RVR and blood pressure (BP), which are associated with cardiovascular disease. Recent data indicate exogenous ketones may offset adverse cardiorenal effects of salt. METHODS/STUDY POPULATION: Our registered clinical trial (NCT05545501) is a double-blinded, placebo-controlled, crossover study. Participants are being randomized to three 10-day conditions: A) control; B) high salt; C) high salt and ketone

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supplementation. Ten participants are enrolled (target 30 participants). Renal blood velocity (RBV) in the renal and segmental arteries will be measured in the decubitus position using Doppler ultrasound during a 3-minute baseline and 3-minute cold pressor test. We will measure brachial BP with an automated oscillometric BP monitor. RVR will be calculated as mean BP divided by RBV. Statistical analyses will include ANOVA and correlations with α set at ≤ 0.05. RESULTS/ANTICIPATED RESULTS: We anticipate attenuated RBV and increased BP during the cold pressor test, particularly following high salt loading, leading to greater RVR. We hypothesize ketone supplementation will attenuate the high salt induced increase in RVR during the cold pressor test. In addition to RVR we will examine renal vascular conductance which is the ease with which blood flows through arteries, calculated as RBV divided by mean BP. Additional hemodynamics such as heart rate and systolic and diastolic BP will be reported and correlated with primary outcomes. DISCUSSION/SIGNIFICANCE: Dietary salt plays a role in hypertension, cardiovascular disease, and chronic kidney disease, which are leading causes of death. Ketone supplementation may be a promising approach to counteract the detrimental effects of high dietary salt and improve cardiovascular health in adults.

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Microglial Behavior and Iba-1 Expression: Evaluating the Cognitive Impact of Vascular Dementia and Long COVID

Grant McGee Talkington, Saifudeen Ismael, Timothy Gressett and Gregory Bix
Tulane University

OBJECTIVES/GOALS: The study aims to explore the role of microglial behavior in cognitive impairment associated with vascular dementia (VaD) and long COVID. Using immunohistochemistry (IHC) and quantitative PCR (qPCR), we will assess the expression of Iba-1, a microglial activation marker, in subjects with VaD and SARS-CoV-2 infection. METHODS/STUDY POPULATION: Out of 48 female C57BL/6 mice, 24 had surgical intervention in the form of bilateral carotid artery stenosis (BCAS) for experimental induction of vascular dementia. After 2 weeks, 12 BCAS and 12 non-BCAS were infected with 1E4 PFU of mouse-adapted 10 (MA10) strain of SARS-CoV-2. 2 weeks post-infection, 4 weeks post-operatively, all animals were euthanized and tissues were processed for cDNA and histology. Immunofluorescence and RT-qPCR used to quantify microglia via Iba-1, BBB integrity via claudin-5 as well as occludin, GFAP, and integrin a5. RESULTS/ANTICIPATED RESULTS: We anticipate observing distinct patterns of microglial behavior in subjects with vascular dementia (VaD) and those with long COVID. Through immunohistochemistry (IHC), we expect to see increased Iba-1 expression, indicative of microglial activation. Quantitative PCR (qPCR) will likely corroborate these findings, showing elevated levels of Iba-1 mRNA. Lastly, we anticipate that the data will reveal interactions between microglia and the blood-brain barrier (BBB). These interactions could provide insights into how microglial behavior influences BBB integrity and, consequently, cognitive function in VaD and long COVID. DISCUSSION/SIGNIFICANCE: This study aims to clarify the role of microglia in cognitive decline linked to vascular dementia and long COVID. By categorizing patients based on microglial activation, we can better tailor treatments. The findings could lead to targeted therapies that address cognitive impairment in these conditions.

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Eph/Ephrin Signaling Influences Innervation of Outer Hair Cells in Cochlea

Deborah Jane George[1], Aileen Cui[1], Shankar Thiru[1], Michael Deans[2] and Thomas M. Coate[1]
[1]Georgetown University and [2]University of Utah

OBJECTIVES/GOALS: 48,000,000 people in the U.S. have hearing loss, negatively impacting quality of life and work. Unveiling axon guidance for auditory type II spiral ganglia neurons (SGNs) will aid development of new therapies. I study the role of Eph/Ephrin and planar cell polarity (PCP) signaling during type II SGN turning and outer hair cell (OHC) innervation. METHODS/STUDY POPULATION: This quantitative study was conducted on Efna3 and Vangl2 null mice possessing Neurog1CreERT2 and R26RtdTomato mutations. Spontaneous Cre activity within the Neurogenin1CreERT2 line causes recombination and expression of fluorescent Rosa26 Reporter (R26R)tdTomatoin a restricted number of SGNs, including type IIs. Together, these lines permit SGN sparse labeling. Immunostaining and confocal imaging were used to analyze dsRed in Efna3 and Vangl2 mice and quantify type II SGN turning. In combination, Imaris 3D renderings were used to quantify type II SGN turning, branching, navigation features and temporal effects of EPHRIN-A3-Fc on type IIs via cochlear cultures (a gain-of-function manipulation). For both sexes, 5-6 cochleae per genotype were analyzed and compared by t-test to wildtype (WT) controls. RESULTS/ANTICIPATED RESULTS: Efna3 nulls showed a small rise in type II SGNs incorrectly turning toward the apex at an error rate of 16.0% compared to WTs (n=6; p=0.05). P0 Efna3 nulls had reduced branch number compared to WTs, 4.1 and 7.2, respectively (n=129; p=<0.0001), suggesting EPHRIN-A3 acts as a positive growth cue. In cochlear cultures, EPHRIN-A3-Fc led to type II SGN collapse at E15.5, indicating a repulsive function. However, at P0, EPHRIN-A3-Fc treatment led to type II SGNs with elevated branch numbers compared to Control-Fc treatment: 18.1 and 11.4, respectively (n=116; p=<0.0001). This indicates a positive growth function. At E16.5, EPHRIN-A3 protein immunoreactivity on Deiters' and pillar cells appears reduced in Vangl2 nulls compared to WT cochleae, suggesting that EPHRIN-A3 acts downstream of PCP signaling. DISCUSSION/SIGNIFICANCE: Results suggest that Eph/Ephrin signaling acts downstream of PCP signaling to mediate type II SGN guidance and EPHRIN-A3 switches its mode of activation. The clinical implications of these findings are that therapeutics targeting EPHRIN-A3 and/or VANGL2 in their given pathways could stimulate new OHC innervation following auditory damage.

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Brain Structural Alterations in Metabolically Healthy and Unhealthy Obesity: A Quantitative Comparison Using Coordinate-Based Meta-Analysis

Leen F. Abazid[1,2,3], Eithan Kotkowski[2,4], Crystal G. Franklin[2], Mary D. Woosley[2], Amy S. Garrett[2,4] and Peter T. Fox[2,3,4,5]
[1]University of Texas Health Science Center of San Antonio; [2]Research Imaging Institute; [3]Department of Radiology; [4]Department of Neurology and [5]Department of Psychiatry and Behavioral Sciences, The University of Texas Health Science Center in San Antonio at San Antonio, Texas, United States of America

OBJECTIVES/GOALS: The primary research goal was to identify brain alterations reliably associated with obesity using coordinate-based

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