

microstructural changes in brainstem auditory pathway regions among children with SNHL. Longitudinal studies are warranted to assess the predictive value of DTI imaging for long-term outcomes and prognosticating intervention.

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A Preliminary Study on the Pharmacodynamics of Oral Cannabis Ingestion in Older Adults

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OBJECTIVES/GOALS: Our study explores the dose-related effects of THC on cardiovascular measures, self-reported effects, balance, and cognitive function among older adults. We also evaluate the acceptability and feasibility of study procedures, to inform future study designs employing this population. **METHODS/STUDY POPULATION:** Using a within-subject, double-blind, placebo-controlled design and standard behavioral pharmacology methods, reasonably healthy male and female adults aged 55-70 years undergo an eligibility screening, followed by a mock session and 3 experimental sessions (>7 days apart). During experimental sessions, participants are administered cannabis-infused brownies with varying THC doses. Prior to and at multiple intervals post-consumption, subjects complete assessments including self reports and observer ratings, psychomotor and cognitive performance measures, and vital signs. Follow-up interviews regarding the experience will be conducted one day after each session. **RESULTS/ANTICIPATED RESULTS:** We anticipate our results to mirror those of previously reported studies conducted in adults under 45 years old in that a dose-response relationship exists for subjective drug effects and vital signs with the caveat that this relationship may be exacerbated in our population. We additionally anticipate findings that indicate THC impairs balance and coordination, potentially increasing the risk of falls and accidents among this population, and cognitive function, affecting attention, memory, and executive functions. Feedback provided during the follow-up interviews will help refine procedures for future studies, ensuring that the methodology is acceptable and feasible for this population. **DISCUSSION/SIGNIFICANCE:** Prior work demonstrates the safety and efficacy of THC in conditions common among older adults, however, no conclusive data regarding tolerability and safety in this population exists. The presented work is vital groundwork for future research on THC as a potential therapeutic for older adults.

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Investigating the Impact of Inflammation on White Matter Tracts using Diffusion Tensor Imaging that may Contribute to Motivational Deficits and Negative Symptoms in Patients with Schizophrenia

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OBJECTIVES/GOALS: Previous research has linked inflammation to changes in brain reward circuitry and subsequent negative symptoms in patients with schizophrenia. This project aims to understand brain-immune interactions using diffusion tensor imaging (DTI) to investigate the impact of inflammatory markers on white matter (WM) tracts. **METHODS/STUDY POPULATION:** Patients with

schizophrenia, ages 18 to 45, were recruited at Grady Hospital in Atlanta, GA. All subjects were stable outpatients and underwent extensive medical screening to rule out medical causes of acute inflammation. DTI data was collected from 39 participants on a 3-Tesla Siemens scanner. Blood was collected between 9-11AM for later assay of serum inflammatory markers. Negative symptoms were assessed using the Brief Negative Symptom Scale (BNSS). A diffusion tensor imaging model will be fitted with the data to generate well-known diffusion tensor measures (fractional anisotropy and mean diffusivity). Linear regression will be used to analyze the relationship between DTI measures and inflammation (C-Reactive Protein, CRP), controlling for possible confounders. **RESULTS/ANTICIPATED RESULTS:** The hypothesis of this proposal is that decreased microstructural integrity in WM tracts between the nucleus accumbens (NAc) and insula will be associated with increased inflammation, which in turn are associated with increased negative symptoms. Negative symptoms include deficits in motivation/pleasure as well as diminished expressivity, and are strongly associated with poor functional outcomes. Based on previous data from this sample demonstrating relationships between CRP and negative symptoms as well as CRP and fMRI functional connectivity between the NAc and insula, we anticipate results that demonstrate similar relationships with WM microstructural integrity, such as functional anisotropy and mean diffusivity. **DISCUSSION/SIGNIFICANCE:** Given the lack of treatment options for negative symptoms, this research will provide key data to further our understanding of the potential role of inflammation on neural circuits that underlie these symptoms, including WM integrity. This research also has the potential to inform future anti-inflammatory therapies for patients with schizophrenia.

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Quantification of serum neurofilament light chain (NfL) in cubital tunnel

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OBJECTIVES/GOALS: The long-term goal of our lab is to develop clinical and intra-operative methods to aid in assessment of compressive and traumatic peripheral neuropathies. The overall objective of this project is to identify the potential of serum neurofilament light chain as a diagnostic biomarker for nerve injury. **METHODS/STUDY POPULATION:** The objective of this prospective study is to obtain data on serum NfL levels in patients with cubital tunnel syndrome and traumatic nerve injuries. Serum NfL from patients with cubital tunnel and traumatic nerve injuries will be compared to serum NfL of asymptomatic, sex and aged matched controls. Pre-operative and post-operative serum levels will be measured and compared to patient's pre-operative physical exam findings, motor and sensory function testing, electrodiagnostic studies, ultrasound, presence of intraneural vascularity, and post-operative patient reported outcome measures for cubital tunnel patients. For patients with traumatic nerve injury, acute phase and a subsequent serum NfL measurement will be used to assess temporal changes in NfL. **RESULTS/ANTICIPATED RESULTS:** The central hypothesis of this study is that symptomatic compression of the ulnar nerve or traumatic injury to the brachial plexus leading to axonotmesis will result in measurable increases in serum NfL proportional to the degree of nerve injury. This hypothesis has been formulated based on clinical experience and published studies demonstrating increased expression of serum NfL levels with axonal injury secondary to varying

forms of peripheral neuropathy. **DISCUSSION/SIGNIFICANCE:** The significance of this project is that characterization of the relationship of clinical symptoms, non-invasive imaging and expression of NfL will lead to better diagnostic and prognostic algorithms in the treatment of compressive and traumatic peripheral neuropathies.

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Digital Spatial Profiling of Allograft Loss in Kidney Biopsies with Chronic Allograft Dysfunction

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OBJECTIVES/GOALS: Assess molecular and cellular mechanisms of allograft loss in kidney biopsies using digital spatial profiling and clinical outcomes data. **METHODS/STUDY POPULATION:** Patients with chronic allograft dysfunction (CGD), enrolled in the Deterioration of Kidney Allograft Function (DeKAF) study, with or without eventual allograft loss, were included. CGD was defined as a >25% increase in creatinine over 3 months relative to a baseline. Kidney biopsy tissue was assessed by Nanostring GeoMX digital spatial profiling (DSP) after staining with anti-pan-cytokeratin, anti-CD45, anti-CD68, Syto-13, to identify specific cell populations, and Nanostring's Whole Transcriptome Atlas (WTA), to quantify the distribution of transcripts across the biopsy. Up to 14 regions of interest (ROIs) were selected, with or without glomerulus. CIBERSORT was used to perform cell deconvolution. Clinical and outcomes data were from the DeKAF study and United States Renal Data System. **RESULTS/ANTICIPATED RESULTS:** Macrophage (M1) cell population abundance was significantly different in ROIs with glomerulus between graft loss and no graft loss. Principle component analysis of differentially expressed genes resulted in transcriptomes in ROIs that cluster together by clinical outcome of graft loss or no graft loss. There were 203 DEGs in ROIs with glomerulus that were different by graft loss or no graft loss. By pathway analysis, these 203 DEGs were enriched in the T-cell activation, integrin signaling and inflammation pathways. **DISCUSSION/SIGNIFICANCE:** DSP of kidney allograft biopsies allows for the identification and quantification of specific cell types, such as macrophages and molecular transcripts as potential drug targets. This data can be used to understand mechanisms of kidney allograft loss and may lead to improved immune suppression in kidney transplant recipients.

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From discovery to the clinical laboratory: a methodological appraisal of untargeted metabolomics platforms to characterize inborn errors of metabolism.

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OBJECTIVES/GOALS: Untargeted metabolomics platforms are powerful biomarker discovery tools. However, the absence of uniform study design, data analysis, and reporting standards limits

translation of this research into the clinical lab. The goal was to critically appraise existing untargeted metabolomics platforms that analyzed inborn errors of metabolism. **METHODS/STUDY POPULATION:** A search strategy was conducted in MEDLINE via PubMed from January 16, 2013, to January 16, 2023. The search strategy was limited to primary literature articles written in English that evaluated human subjects with inborn errors of metabolism (IEMs). Articles that performed targeted metabolomic analysis or analyzed non-human samples were excluded. Information on patient cohorts analyzed, sample types, and method design were extracted using a template. Categorical data are summarized as frequencies and percentages. **RESULTS/ANTICIPATED RESULTS:** A total of 96 distinct IEMs were evaluated by the different untargeted metabolomics methods included in this review. However, most IEMs (55/96, 57%) were evaluated by a single platform, in a single study, with a limited cohort size. Only one study validated their results using a separate, validation cohort. There was considerable diversity in the separation techniques and mass spectrometry instrumentation used by the studies to create their untargeted metabolomics methods. Slightly over half (59%) of the studies identified at least some of the metabolites detected in their samples with the highest level of confidence. Importantly, most of the included studies reported adherence to quality metrics, including use of quality control material (65%) and internal standards in their analysis (61%). **DISCUSSION/SIGNIFICANCE:** Future studies analyzing IEM patient samples with untargeted metabolomics platforms should progress beyond single-subject studies and evaluate the reproducibility of the research using a prospective, or validation cohort as well as confirm metabolite annotations with reference metabolites standards to generate clinically useful data.

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Examining the clinical utility of dance to support social connection - Explorations at the level of the brain, heart, and body

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OBJECTIVES/GOALS: Social isolation/loneliness is a public health crisis and one that is unlikely to be solved through pharmacology. Nonpharmacological approaches, such as dance, are needed. The objective of this study is to investigate the physiological correlates of dance-induced improvements in social connection. **METHODS/STUDY POPULATION:** Participants were randomly assigned to participate for 4 weeks (2 times per week, 90-minute sessions) in either 1) improvisational dance training (experimental group; n=7); or a 2) dance movie watching experience (control group; n=7). Before and after the intervention, using mobile brain-body imaging techniques, participants and their instructor had their brain (via electroencephalography) and body physiology (via photoplethysmography) recorded during a series of verbal and nonverbal interactive experiences. Participants were also video recorded via 4 surrounding cameras for later motion capture analysis. Neuropsychological assessments were also conducted before and after the intervention. **RESULTS/ANTICIPATED RESULTS:** We found that dance significantly increased social skills including empathy, interpersonal skills, emotional regulation, mindfulness, and attention. Additionally, we found that dance significantly increased interbrain synchrony during nonverbal experiences including theta (4-8 Hz), beta (12-35 Hz), and gamma