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A CTS Team Approach to Investigate Skeletal Muscle Diseases and Countermeasures in a Patient-Derived Bioengineered Muscle Platform

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OBJECTIVES/GOALS: Our team has developed a high-throughput 3D patient-derived muscle platform to study signaling pathways associated with skeletal muscle disease. This platform will be used to study pathologies of human muscle that arise from genetic mutations and processes of aging along with pharmacologic interventions to improve mass, function, and performance. **METHODS/STUDY POPULATION:** In the current study, 3D skeletal muscle is formed from young healthy male samples. Samples are treated with urocortin II (UCNII) or vehicle for ten days and evaluated for tissue performance. Functional assessments include real-time contraction magnitudes using digital image correlation (DIC) analysis of video collected during electrical pulse stimulation and end-point measures of initial and repeated tetanic force production. Functional measures provide indices of patient muscle synchronicity, strength, and endurance related to drug efficacy and toxicity which we will correlate to pro-growth protein signaling via Luminex. A subset of these samples will also be analyzed by histology and microscopy to assess muscle fiber density, type, and size, as well as myotube fusion index and sarcomere uniformity. **RESULTS/ANTICIPATED RESULTS:** We anticipate that healthy muscle treated with UCNII will have increased synchronicity and contraction magnitudes in DIC analysis throughout their seven-day electrical pulse stimulation protocol. We also expect to see sustained contraction magnitudes in DIC analysis at the end of electrical pulse stimulation indicating fatigue resistance in the drug treated group compared to no-drug control. Like our real-time DIC data, we anticipate increases to initial and sustained maximal force production in the drug treated group. We expect that drug treated muscle will present with an increased fiber density, fiber diameter, and fusion index with uniform sarcomeres. Finally, we expect heightened pro-growth signaling pathways in treated vs. controls. **DISCUSSION/SIGNIFICANCE:** The current study will serve as an initial investigation of the endogenous ligand UCNII for enhancing skeletal muscle mass and performance in human muscle laying the framework for future drug efficacy and toxicity studies. This platform will ultimately enhance the study of muscle diseases and translation of therapeutics to clinical settings.

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Improvement of health outcomes and quality of life of Hispanic older adults in Puerto Rico through participation in a Physical Activity (PA) Community-based Program

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OBJECTIVES/GOALS: The proposed study aims to improve physical and mental health outcomes among Hispanic older adults who live alone in a low-income San Juan, Puerto Rico community through weekly PA groups. Specific outcomes include measures of loneliness, social isolation, depression, physical mobility, metabolic indicators, and other health indicators. **METHODS/STUDY POPULATION:** Data will be collected at three time points: Pre

(Week 1), Mid (Week 6), and Post (Week 12) intervention. Currently, the community has 50 residents over 65 years old who live under the poverty index and receive multiple social benefits. Various tools will be implemented to measure loneliness (University of California Los Angeles – Loneliness Scale-10 items), social isolation (Lubben Social Network Scale-6 items), depression (Geriatric Depression Scale-10 items), physical mobility (Time Up and Go Test), metabolic health indicators (hemoglobin A1c and glucose) and other health indicators (i.e., blood pressure, cholesterol, as well as body mass index (BMI)). These measurements will determine if participation in PA groups is associated with improvement of the variables measured. **RESULTS/ANTICIPATED RESULTS:** It is expected that the baseline scores of older Hispanic adults in terms of loneliness, social isolation, depression, physical mobility, metabolic indicators (i.e., cholesterol level and hemoglobin A1c), and other health indicators (blood pressure or BP and BMI) will be lower compared to those after participation in the Physical Activity Program. More frequent participation will be associated with more significant improvement in measured variables. **DISCUSSION/SIGNIFICANCE:** Results from this study will determine the effectiveness of community-based PA interventions in addressing loneliness, social isolation, depression, physical mobility, and metabolic factors (hemoglobin A1c and glucose) in elderly minority Hispanic populations as a means of improving their health outcomes and quality of life.

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Radiographic Changes in the Auditory Pathway to Predict Outcomes of Children with Hearing Loss

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OBJECTIVES/GOALS: Early diagnosis of congenital sensorineural hearing loss (SNHL) is of paramount importance in preventing speech and language impairment. Diffusion tensor imaging (DTI) MRI can identify brain microstructural changes that may potentially contribute towards prognosticating rehabilitation. **METHODS/STUDY POPULATION:** We retrospectively reviewed pediatric patients with SNHL who obtained DTI MRI between 2011 and 2019, identifying 16 pediatric patients (age <18 years) with at least moderate asymmetric/bilateral SNHL, and gender-matched controls without neurological, developmental, or MRI-based brain macrostructural abnormalities. The following brainstem regions and tracts of the auditory pathway were assessed: superior olivary nucleus (SON), inferior colliculus (IC), ipsilateral tracts between the inferior colliculus and superior olivary nucleus (IC-SON). Diffusion values for bilateral regions and tracts were generated, then averaged to calculate a mean value for fractional anisotropy (FA) and mean diffusivity (MD) for each subject. **RESULTS/ANTICIPATED RESULTS:** Significant differences were identified in FA values of the SON between the SNHL cohort and controls (0.377 ± 0.056 vs 0.422 ± 0.052 ; $p=0.009$). No other FA or MD values were significantly different. In children ≤ 5 years, MD was significantly decreased in the SNHL cohort compared to controls in the IC (0.918 ± 0.051 vs 1.120 ± 0.142 ; $p<0.001$). In children >5 years, there were no significant differences in MD (1.124 ± 0.198 vs 0.997 ± 0.103 ; $p=0.119$). There were no significant differences in MD or FA in the white matter fibers of the IC-SON tract [applewebdata%3A//720AAf0C-C4CF-459C-A42A-6BAA56C4E4CA#_msocom_2]. **DISCUSSION/SIGNIFICANCE:** This is the first study to assess

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