status at 353 CpG sites. DNAm AA is the residual of DNA methylation age regressed on chronological age in a linear model. Spearman's correlations and linear regression examine the relationship between DNAm AA and depressive symptoms (Beck Depression Inventory) and cardiometabolic status. The potential association and impact of SES, trauma, substance use, and stress were also considered. RESULTS/ANTICIPATED RESULTS: Contrary to our hypothesis, DNAm AA did not associate with the severity of depressive symptoms. Correlation between DNAm AA and affective symptom subscore (BDI) approached significance ($p = 0.06$). We observed significant correlations between DNAm AA and specific depressive symptoms including participants' reported disappointment, disgust, or hatred toward themselves ($p < 0.05$), difficulty with making decisions ($p < 0.05$), and worry about their physical health ($p < 0.05$). DNAm AA was also significantly correlated with BMI ($p > 0.001$). Significant relationships were not evident in the subsequent regression analysis examining potential relationships between DNAm AA and depression. To our knowledge, this is the first study to examine associations between DNAm AA and depressive symptoms in AAW. DISCUSSION/SIGNIFICANCE OF FINDINGS: Depression limits life quality and quantity and is highly comorbid in CMCs. AAW have a high risk of comorbidity. This study deepens knowledge with respect to the associations between depression, CMCs, and aging with a clinically accessible marker in a population with disproportionate risk.

Mechanistic Basic to Clinical

66942

Metabolomic endotype of bioenergetic dysfunction predicts mortality in critically ill patients with acute respiratory failure

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ABSTRACT IMPACT: The pathophysiologic features of a metabolomic endotype that predicts patient outcomes due to sepsis have the potential to direct new therapies that target immune dysregulation and bioenergetic insufficiency. OBJECTIVES/GOALS: Acute respiratory failure (ARF) requiring mechanical ventilation is a frequent complication of sepsis and other disorders. It is associated with high morbidity and mortality. Despite its severity and prevalence, little is known about metabolic and bioenergetic changes that accompanying ARF. METHODS/STUDY POPULATION: In this study, semi-quantitative and quantitative ultrahigh performance liquid chromatography mass spectrometry (UHPLC MS) analysis was performed on patient serum collected from the Trial with Acute Respiratory failure patients: evaluation of Global Exercise Therapies (TARGET). Serum from survivors (n=15) and nonsurvivors (n=15) was collected at day 1 and day 3 after admission to the medical intensive care unit as well as at discharge in survivors. Pathway analysis of the biochemical changes was performed to determine whether the disruption in specific metabolic pathways can identify the bioenergetic and metabolomic profile of these patients. RESULTS/ANTICIPATED RESULTS: Significant metabolomic differences were related to biosynthetic intermediates of redox cofactors nicotinamide adenine dinucleotide (NAD) and NAD phosphate (NADP), increased acyl-carnitines, and decreased acyl-glycerophosphocholines in nonsurvivors compared to survivors. The metabolites associated with poor outcomes are substrates of enzymatic processes dependent on NAD(P), while the abundance of NAD cofactors rely on the bioavailability of dietary vitamins B1, B2 and B6. Changes in the efficiency of the nicotinamide-derived cofactors' biosynthetic pathways also associate with an alteration of the glutathione-dependent drug metabolism as characterized by the substantial differences observed in the acetaminophen metabolome. DISCUSSION/SIGNIFICANCE OF FINDINGS: This metabolomic endotype represents a previously unappreciated association between severity of outcomes and micronutrient deficiency, thus pointing to new pharmacologic targets and highlighting the need for nutritional remediation upon hospitalization to improve patient outcomes due to ARF.

Team Science

24234

Development of a computerized neurocognitive test of interhemispheric transfer for use in pediatric settings

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ABSTRACT IMPACT: As newborn screening is now available for X-linked adrenoleukodystrophy, there is a need to establish meaningful disease markers to detect the onset of the severe demyelinating cerebral form of this disease at the earliest possible stage, and to quantify early disease progression to evaluate the relative efficacy of therapies. OBJECTIVES/GOALS: Longitudinal testing of neurocognitive and motor function using smartphone and tablet-based applications holds promise for early detection and quantification of brain white matter changes in patients with adrenoleukodystrophy (ALD) and other rare demyelinating diseases, but this methodology requires validation in pediatric populations. METHODS/STUDY POPULATION: We developed an iPad application with a game-like interface to assess interhemispheric transfer across the corpus callosum, the brain structure where cerebral demyelinating disease typically begins in patients with ALD. Feasibility data from remote test administrations with healthy children were collected to analyze and speed and timing of finger tapping movements requiring bimanual coordination on a touchscreen. RESULTS/ANTICIPATED RESULTS: Among our pilot sample of healthy school-aged children, age-related improvements in finger tapping speed were observed in both single-hand and alternating-hand conditions. Results indicate that remote testing using iPad applications is a viable way to collect psychometric testing data rapidly in pediatric populations and is feasible during a pandemic. Next steps in this research project will be: (1) evaluating the stability of repeated test administrations (test-retest reliability), (2) assessing agreement between performance on our iPad application and validated measures of interhemispheric transfer and fine motor function, and (3) comparing performance of children with known corpus callosum white matter abnormality to performance of healthy children. DISCUSSION/SIGNIFICANCE OF FINDINGS: Brief neurocognitive tests that can be frequently administered may have the ability to capture subtle brain changes in developing children. Approaches enabling remote

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(virtual) testing will facilitate research during the covid-19 pandemic and are especially well-suited for data collection in rare disease populations.

Translational Science, Policy, & Health Outcomes Science

11979

Using whole-exome and mtDNA sequencing to develop a testing algorithm for diagnosis of mitochondrial disease in Puerto Ricans

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ABSTRACT IMPACT: Alterations in mitochondrial metabolism affect any tissue, especially those with the highest demand for energy. As the symptoms and clinical manifestations are heterogenous, disease diagnosis is challenging. The implementation of genetic-first approach in the diagnosis of mitochondrial diseases will expedite confirmation, treatment, management, and counseling of affected Puerto Rican individuals. OBJECTIVES/GOALS: Mitochondrial diseases are rare, and diagnosis is complex due to the heterogeneity of clinical manifestations. We aim to develop and implement a testing algorithm using a genetics-first approach, facilitating the identification of variants that contribute to mitochondrial disease's etiology and influence onset and progression in Puerto Ricans. METHODS/STUDY POPULATION: This is a cross-sectional study for characterizing clinical laboratory results from profiles used to evaluate metabolic diseases in individuals with suspected mitochondrial disorders from 2018 to 2021. A subset of 25 individuals from biochemical profile will be recruited to analyze their medical and family history, metabolic biomarkers in blood and urine, hearing test, imaging and chromosomal microarray. The implementation of a genetic testing algorithm using whole exome and mitochondrial DNA sequencing will be performed in a subset of 11 randomized individuals. Descriptive analysis will be reported, including a catalog of all variants. Multivariate analysis will be performed to estimate the statistical association between variants and phenotypes reported and adjusting for potential confounders. RESULTS/ANTICIPATED RESULTS: The biochemical profile of pediatric Puerto Rican individuals suspected of having mitochondrial diseases will be altered and can be used to differentiate among other metabolic causes. We expect to find altered levels of lactate, pyruvate and carnitines in serum, as well as altered organic acids in urine. The implementation of a testing algorithm using both, mitochondrial DNA and whole exome sequencing as first approach will be enabling the identification of disease-causing variants, thus enhancing and confirming the diagnosis of mitochondrial disease in Puerto Ricans. We will be able to identify rare/novel variants specific to our Hispanic population, for both nuclear and mitochondrial DNA. DISCUSSION/SIGNIFICANCE OF FINDINGS: This study will help to characterize the metabolic profile of pediatric Puerto Ricans. No previous study has been reported that describes testing algorithms for genetic diagnosis of mitochondrial disease in our population. Variants found will contribute to a deep understanding of the genetic contribution to phenotypes and disease susceptibility.

92811

Implementation of the Fitness, Lifestyle, and Optimal Wellness (FLOW) Program and Its Associated Health Outcomes

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ABSTRACT IMPACT: Through its interdisciplinary, tailored approach, the FLOW program could change the way that we approach promoting healthy lifestyle changes in the primary care field. OBJECTIVES/GOALS: The goal of this project is to assess patient outcomes associated with the implementation of the Fitness, Lifestyle, and Optimal Wellness (FLOW) Program. The ultimate aim of this program is two-fold: increasing patient-reported wellness and improving objective health measurements. METHODS/STUDY POPULATION: The FLOW program consists of a multidisciplinary team of sports medicine physicians, nutritionists, fitness trainers, and clinical psychologists. Patients who choose to participate in the program undergo a comprehensive physician-guided assessment, including lifestyle and metabolic evaluation, biomarker profile, and body composition analysis. Based on the patient's goals and results of evaluation, he/she is then connected with other members of the FLOW team to develop a comprehensive plan and offer resources for potential improvements in physical activity, nutrition, and/or behavior. The patient will undergo follow-up assessments and questionnaires at three and six months to track their objective measurements and reported progress. RESULTS/ANTICIPATED RESULTS: The anticipated results of the FLOW program are an overall improvement in patient health and wellbeing. More specifically, we anticipate seeing increased levels of exercise from initial reported levels, as well as better nutrition habits. We expect to see improvements in follow-up body composition assessments, with gains in fat-free mass and decreased body fat, in addition to patient-reported improvements in behavioral health as measured by PHQ-9, GAD-2, and the Perceived Stress Scale. We will also assess reported sleep health with the hopes to see improvement in follow-up assessments. DISCUSSION/SIGNIFICANCE OF FINDINGS: The FLOW program is designed to address health inequities that disproportionately affect the Deep South. Through this program, we propose a new role of the primary care team in promoting healthy lifestyle habits and disease prevention through exercise, nutrition, and behavioral health services.
Regulatory Science

Regulatory Science

Clinical Trial

95347

Examining the Impact of the BPCA: Promoting Pediatric Inclusion in Clinical Trials and Pediatric-Specific Drug Information

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ABSTRACT IMPACT: It provides insight in the relationship between pediatrics and clinical research and how pediatric

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