

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

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#### 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