CHRONIC DISEASE RISK AMONG ADULTS WITH CEREBRAL PALSY: THE ROLE OF PREMATURE SARCOPENIA, OBESITY, AND SEDENTARY BEHAVIOR

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Secondary health complications in Adults with CP

- Risk of overweight/obesity
- Decreased aerobic capacity
- Decreased strength
- Decreased levels of Physical Activity
  - Especially Health-Related PA

Like much of America...
Obesity Misclassification

- BMI does not discriminate adipose tissue and muscle, and lacks sensitivity to identify non-obese individuals with excess body fat.
  - Okorodudu et al. *Int J Obes.* 2010

  - ~30 million Americans, increased risk for MetS and early cardiovascular mortality
Intermuscular adipose tissue and Intramyocellular Lipid

- IMAT and IMCL also develop as a feature of certain disease processes (e.g. DMD, T2DM), spinal cord injury, sarcopenia, and obesity, as well as in conjunction with prolonged sedentary behavior *

Age as a covariate: When Muscle Turns to Fat…

25 Years Old

65 Years Old

Goodpaster et al, 2006
IMAT in CP?

Separation of AT from MRI of the midthigh of a prepubertal girl with QCP and D-F, a typically developing prepubertal girl. A and D contain subcutaneous, subfascial, and intermuscular AT; B and E contain only subfascial and intermuscular AT; and C and F contain only IMAT.
My Current Focus

Predictors, Confluence and Consequences of Frailty and Obesity in Adults with CP

1 K01 HD074706-01; Peterson (PI), National Institutes of Health... Pending...
Not so novel, novel concept

Physiological & Cognitive Frailty
- Diminished Aerobic Capacity
- Sarcopenia
- Weakness
- Functional Deficit
- Fatigability

Impaired Myogenesis
- Muscular Fibrosis
- Decreased Mitochondrial Density

Inflammation
- Ceramide Biosynthesis
- Incomplete beta-oxidation
- Dyslipidemia

Insulin Resistance
- Metabolic Inflexibility
- Hyperglycemia
- Impaired Insulin Signaling

Obesity
- Altered Nutrient Partitioning
- Cardiovascular disease and type 2 diabetes

Sedentary Behavior
- Cardiovascular disease and type 2 diabetes

High Fat Diet
- Cardiovascular disease and type 2 diabetes

Cerebral Palsy
- Chronic Neural Inflammation
- Exaggerated Sedentary Behavior
- Abnormal Musculoskeletal Development
- Muscle Spasticity

Oxidative Stress
- Muscle Pathology and Accelerated Functional Decline

Specific Aim 1: Exploratory

- Adults with and without CP will be matched and compared on measures of insulin sensitivity (FSIVGTT), and whole body and regional (IMAT) adipose tissue distribution (DXA and 3T MRI Dixon).
  - Also collected: Serum and tissue biomarkers of insulin signaling, ROS, inflammation, mitochondrial biogenesis, and glucose transport.

- Secondary Outcomes & Covariates:
  - Sedentary behavior assessment (accelerometry)
  - RMR and cardiovascular fitness (VO2)
  - Standard Anthropometry (e.g. BMI, WC, WHR).
Specific Aim 2

- Subjects with CP from aim 1 will be entered into an 8-week PA intervention to:

1. Assess the efficacy of multi-modality PA to elicit improvements in both health and function and
2. Determine the extent to which changes in adiposity are associated with improvements in insulin sensitivity
Specific Aim 3: Exploratory

- To examine within-subjects transcriptional and morphological differences in spastic versus non-spastic muscle from adults with hemiplegic CP and contrast with matched non-CP controls.

- **Markers**: proteins for insulin signaling, mitochondrial biogenesis, skeletal muscle and adipose macrophage phenotype (i.e. content and subtype), profibrotic markers
Of Particular Interest: Sedentary behavior... NIDRR FIR

- Time spent sitting correlates with an elevated risk of mortality for all causes and for cardiovascular disease
  - Dose-response relationship

- Sitting seems to have be associated with mortality independent of leisure time physical activity levels

- 56% of all deaths among overweight and obese, highly sedentary individuals are attributable to their SB.

- Never been considered a risk factor for cardiometabolic complications in CP. Can it be reduced?