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Inflammatory biomarkers of cognitive dysfunction in pediatric obesity: associations between Executive Function, C-Reactive Protein, Interleukin 6, and Tumor Necrosis Factor alpha

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OBJECTIVES/GOALS: Executive function (EF) deficits lead to poorer adherence and weight loss in obesity treatment. Conversely, untreated obesity leads to both EF impairments and risk of chronic disease. EF deficits in children with obesity have begun to be associated with biomarkers of chronic disease risk such as glucose and cortisol. Elevated pro-inflammatory biomarkers, such as C-Reactive Protein (CRP), Interleukin 6 (IL-6), and Tumor Necrosis Factor a (TNFa), indicate risk for obesity-associated chronic disease and may represent another candidate biomarker of EF deficits in pediatric obesity. These inflammatory markers tend to be elevated in obesity but have yet to be examined in association with EF in pediatric obesity. This represents an opportunity to identify potential biomarkers of EF which may serve as novel treatment targets that could improve outcomes and chronic disease prevention. Thus, the present study aims to explore associations between EF and blood serum CRP, IL-6, and TNFa. METHODS/STUDY POPULATION: Treatment-seeking children aged 8-12 years with BMI>95th percentile were recruited from a pediatric weight management clinic and attended baseline assessments for a family-based behavioral intervention program for pediatric obesity. Demographics and medical history were assessed via parent questionnaire. Height and weight were measured by research staff and converted to zBMI. Child performance-based EF was assessed via the NIH Toolbox Cognitive Battery iPad application. Blood draws, assays, and Dual-energy X-ray Absorptiometry (DXA; measuring adiposity) were conducted by trained research personnel. Pearson's correlations were conducted to explore associations between EF (NIH Toolbox Cognitive Battery, fully corrected T-scores) and CRP, IL-6, and TNFa. RESULTS/ANTICIPATED RESULTS: Children (n = 12) were primarily female (76.5%) and African American (64.7%). Correlation coefficients between inflammatory markers and EF were highly variable (r = −0.39 to 0.52). CRP showed small, negative associations with Cognitive Flexibility (r = −0.39) and Inhibitory Control (r = −0.34). IL-6 also demonstrated a small, negative association with Inhibitory Control (r = −0.37). TNFa was positively and moderately associated with working memory (r = 0.53). Remaining associations were weak (−0.3<r<0.3). DISCUSSION/SIGNIFICANCE OF IMPACT: Signals of higher inflammation, measured via CRP and IL-6, in association with EF deficits were identified in a small sample of children with obesity, as hypothesized. However, signals in the opposite direction were identified as well, measured via TNFa. CRP and IL-6 may represent candidate biomarkers of executive dysfunction in obesity that warrant further domain and biomarker-specific research, with potential long-term implications for improving pediatric obesity treatment.

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Influence of Vision and Proprioception on Motor Control in ASD

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OBJECTIVES/GOALS: Sensorimotor integration deficits are common in Autism Spectrum Disorders (ASD). There is evidence for both an over-reliance on visual and proprioceptive feedback during motor control in ASD, suggesting deficits in the ability to modulate sensory feedback processing in order to use the most reliable input. This study aims to test this hypothesis. METHODS/STUDY POPULATION: 40 persons with ASD (ages 10-33 yrs) and 25 age-, sex- and nonverbal IQ-matched controls completed precision gripping tasks under multiple proprioceptive and visual feedback conditions. Participants squeezed a force sensor with their index finger and thumb and tried to match their force output to a target force. Visual feedback of the target force (stationary bar) and their force output (bar that moved up/down with increased/decreased force) were displayed on a computer screen. Visual feedback was presented across low, medium, and high gain levels; the force bar moved a greater distance per change in force at higher gains. Proprioceptive feedback was manipulated using 80Hz tendon vibration at the wrist to create an illusion that the muscle is contracted. Force regularity (approximate entropy; ApEn) was examined. RESULTS/ANTICIPATED RESULTS: We have scored data from 18 participants with ASD and 13 control participants to date. Preliminary results from these participants indicate a Group x Tendon Vibration x Visual Gain interaction for ApEn (F = 1.559, p = 0.023). Individuals with ASD show slight increases in ApEn with 80Hz tendon vibration relative to no tendon vibration in all visual conditions. Controls showed increased ApEn during 80Hz compared to no tendon vibration at low visual gain but decreased ApEn with tendon vibration at high visual gain. These preliminary results indicate that controls shift to using a secondary source of sensory feedback (e.g., proprioception) when the primary source (e.g., vision) is degraded. However, persons with ASD do not reweight different sensory feedback processes as feedback inputs are degraded or magnified. DISCUSSION/SIGNIFICANCE OF IMPACT: Our preliminary results reveal that sensorimotor issues in ASD result from deficits in the reweighting of sensory feedback. Namely, persons with ASD fail to dynamically recalibrate feedback processes across visual and proprioceptive systems when feedback conditions change. Our results may aid treatment development for sensorimotor issues in ASD.

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Insulin Sensitizing Effects of Vitamin D Mediated through Reduced Adipose Tissue Inflammation and Fibrosis: Evidence from a Human Randomized Trial and Mice Studies

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OBJECTIVES/GOALS: Vitamin D [25(OH)D], known to have anti-inflammatory and anti-fibrotic effects in other tissues, may also impact adipose tissue. We designed parallel studies in humans and rodents to define the effects of vitamin D on adipose tissue inflammation and fibrosis, and on systemic insulin resistance. METHODS/STUDY POPULATION: We performed a randomized, double-blinded placebo-controlled trial to examine the effects of repleting vitamin D at to two levels (to >30 ng/ml and to > 50 ng/ml) in 25(OH)D-deficient (<20 ng/ml), insulin resistant, overweight-to-obese humans (n = 19). A comprehensive study of whole-body insulin action was undertaken with euglycemic stepped

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