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Childhood obesity: A profile of measures of executive functions, emotional processing, and inflammation

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OBJECTIVES/SPECIFIC AIMS: Childhood obesity has become an issue of some concern worldwide. Some reviews and a recent study in adults have indicated that obesity-related inflammatory responses produce brain damage. However, studies exploring associations between inflammation and executive functions in children are overlooked. Therefore, the objective of this cross-sectional study is to determine whether difficulties in executive functions and emotional processing are associated with obesity and inflammation. METHODS/STUDY POPULATION: We have recruited 12 of a total of 60 children aged 6–8 years old. They have completed the NIH Toolbox Cognition Battery and the NEPSY II Affect Recognition tests. Samples of plasma and saliva were collected to quantify inflammatory biomarkers cytokines (IL-6 and TNF-α) assay by Luminex procedure. We performed descriptive analysis and Mann-Whitney *U* test to compare obese Versus nonobese groups. RESULTS/ANTICIPATED RESULTS: Obese children have lower scores in measures of affect recognition than healthy weight children. They also showed higher median scores in both salivary and plasma IL-6 and TNF-α. DISCUSSION/SIGNIFICANCE OF IMPACT: Although no statistical differences were found among groups in either measurement, these preliminary data based on the initial recruitment suggest that children with higher body mass index may have difficulties in emotional processing. More data will be available after completing recruitment to determine if the association between obesity and affect recognition is significant and if it is mediated by inflammation.

CLINICAL TRIAL

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Pharmacokinetic prediction of paclitaxel-induced peripheral neuropathy

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OBJECTIVES/SPECIFIC AIMS: Peripheral neuropathy is the dose limiting toxicity of paclitaxel treatment. Paclitaxel pharmacokinetics (PK), specifically the Cmax and amount of time the concentration remains above 0.05 μM (Tc > 0.05), have been associated with occurrence of severe, clinician-documented neuropathy. The objective of this study was to confirm that paclitaxel PK predicts progression of patient-reported neuropathy. METHODS/STUDY POPULATION: This observational trial enrolled breast cancer patients receiving weekly 1-hour paclitaxel infusions (80 mg/m^2 × 12 cycles) at the University of Michigan Comprehensive Cancer Center. Paclitaxel concentration was measured via LC/MS in plasma samples collected at the end of (Cmax) and 16–24 hours after (Tc > 0.05) first infusion. Patient-reported neuropathy was collected (EORTC CIPN20) at baseline and each cycle. The rate of neuropathy severity increase per treatment cycle is being modeled for each patient. Cmax and Tc > 0.05 values will be introduced into the model to confirm that PK independently contributes to neuropathy progression. RESULTS/ANTICIPATED RESULTS: PK and neuropathy data have been collected from 60 patients for ongoing analysis. Our initial model will characterize the expected severity of neuropathy after each cycle of paclitaxel treatment. The PK-neuropathy model will include either PK parameter to validate their contribution to the progression of neuropathy severity during treatment. We anticipate, based on our preliminary analysis of the first 16 patients, that both PK parameters will significantly contribute to the model but Tc > 0.05 will be more strongly associated with neuropathy progression. DISCUSSION/SIGNIFICANCE OF IMPACT: This project will generate a model that can be used to predict a patient's neuropathy severity throughout treatment using a single, conveniently collected and easily measured PK sample during their first cycle. The next steps of this project include identifying genetic and metabolomic biomarkers that predict which patients experienced more severe neuropathy than would be anticipated based on their paclitaxel PK, and a planned interventional trial of personalized paclitaxel dosing to enhance efficacy and/or prevent neuropathy.

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Fecal bile acids, fecal short-chain fatty acids and the intestinal microbiota in patients with irritable bowel syndrome (IBS) and control volunteers

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OBJECTIVES/SPECIFIC AIMS: Recent data suggest that fecal microbiota and intraluminal organic acids may play an important role in irritable bowel syndrome (IBS) pathogenesis through effects on intestinal secretion and motility. Understanding their contribution will be critical in developing diagnostic and treatment strategies. Objectives and goals of this study will be to: (1) compare fecal microbiota and fecal organic acids in IBS patients and controls and (2) investigate the association between colonic transit and fecal microbiota in IBS patients and controls. METHODS/STUDY POPULATION: We propose a prospective investigation of fecal organic acids, colonic transit and fecal microbiota in 36 IBS patients and 18 healthy controls. The target population will be adults ages 18–65 years meeting Rome IV criteria for IBS (both diarrhea predominant and constipation-predominant, IBS-D, and IBS-C) and asymptomatic controls. Exclusion criteria are: (a) history of microscopic colitis, inflammatory bowel disease, celiac disease, cancer, chronic infectious disease, immunodeficiency, uncontrolled thyroid disease, liver disease, or elevated AST/ALT > 2.0 x the upper limit of normal, (b) prior radiation therapy of the abdomen or abdominal surgeries with the exception of appendectomy or cholecystectomy > 6 months before study initiation, (c) ingestion of prescription, over the counter, or herbal medications affecting gastrointestinal transit or study interpretation within 6 months of study initiation for controls or within 2 days before study initiation for IBS patients, (d) pregnant females, (e) antibiotic usage within 3 months prior to study participation, (f) prebiotic or probiotic usage within the 2 weeks prior to study initiation, (g) tobacco users. Primary outcomes will be fecal bile acid excretion and profile, short-chain fatty acid (SCFA) excretion and profile, colonic transit, and fecal microbiota. Secondary outcomes will be stool characteristics based on responses to validated bowel diaries. Stool samples will be collected from participants during the last 2 days of a 4-day 100-g fat diet and split into 3 samples for fecal microbiota, SCFA, and bile acid analysis and frozen. Frozen aliquots will be shipped to the Metabolite Profiling Facility at Purdue University and the Mayo Clinic Department of Laboratory Medicine and Pathology for SCFA and bile acid measurements, respectively. Analysis of fecal microbiota will be performed in the research laboratory of Dr. David Nelson in collaboration with bioinformatics expertise affiliated with the Nelson lab. Colonic transit time will be measured with the previously validated method using radio-opaque markers. Generalized linear models will be used as the analysis framework for comparing study endpoints among groups. RESULTS/ANTICIPATED RESULTS: This study seeks to examine the innovative concept that specific microbial signatures are associated with increased fecal excretion of organic acids to provide unique insights on a potential mechanistic link between altered intraluminal organic acids and fecal microbiota. DISCUSSION/SIGNIFICANCE OF IMPACT: Results may lead to development of targets for novel therapies and diagnostic biomarkers for IBS, emphasizing the role of the fecal metabolome.

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Primary management of advanced-stage ovarian cancer: 1 year at a high-volume care center

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OBJECTIVES/SPECIFIC AIMS: To describe the use of primary debulking surgery and neoadjuvant chemotherapy in advanced-stage ovarian cancer patients treated at Memorial Sloan Kettering Cancer Center (MSKCC) over the period of 1 year. Specifically, identify a subset of patients that are medically eligible to be considered for surgery. Examine the ultimate treatment designation for those patients, assessing the application of the MSKCC resectability algorithm and its utility in guiding treatment choice. METHODS/STUDY POPULATION: Using the prospectively maintained Ovarian Cancer Database at MSKCC, we queried patients who presented for initial management of ovarian cancer from July 1, 2015 to June 30, 2016. All patients with stage IIIB-IV disease who received their primary treatment at MSKCC were included in our study. Patients needed to have pathology-confirmed ovarian cancer and all histological subtypes were included. Data were collected and analyzed in Excel. RESULTS/ANTICIPATED RESULTS: There were a total of 173 patients treated for stage IIIB-IVB ovarian cancer at MSKCC during the study period. Of those 98 patients received PDS, whereas 75 were directed to NACT, making MSKCC's overall NACT rate

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