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Candidate Genes and Quantitative Gastrointestinal Traits in Obesity Andres Acosta *Rochester Minnesota*, Michael Camilleri *Rochester MN*, Duane Burton *Rochester MN*, Jessica O'Neill *Rochester Minnesota*, Paula Carlson *Rochester MN*, Deborah Eckert *Rochester MN*, Mariza de Andrade *Rochester MN*, Adrian Vella *Rochester MN*

Background: Genetic predisposition contributes to obesity. In heterogeneous diseases, quantitative traits facilitate study of genetics in disease. We aimed to assess the association of candidate genes with gastrointestinal traits in obesity. **Methods:** In 274 overweight and obese participants, we studied on different days satiety, satiation, gastric volume, dual-phase gastric emptying; and gut hormones (ghrelin, CCK, GLP-1 and PYY). We prespecified genes to be examined with each quantitative trait based on their putative effects on receptor function, and previous epidemiological studies e.g. GWAS. Statistical analysis included association of summed allele risk score with BMI, univariate associations of variants of selected genes with quantitative GI traits (corrected for FDR) and multivariable linear regression using the principal components (PCA) adjusted by age, and gender. **Results:** The summed allele risk score was not associated with BMI. GNβ3 rs1129649 CCwas associated (p=0.009) with higher fasting plasma ghrelin, FTO rs9939609 AA (p=0.008) with accelerated GE of liquids, MC4R rs17782313 CC (p=0.01) with higher postprandial peak PYY, HTR2C rs518147 GG genotype (p=0.0007) with increased satiety, HTR2C rs1414334 CC genotype (p=0.01) with decreased satiety and UCP3 rs1626521 with satiety (p=0.005), and gastric volume and accommodation (p=0.005). On PCA (with FDR for number of genes tested), UCP3 rs2075577, UCP3 rs1626521, and HTR2C rs1414334contributed to 11.1% variance in satiation/satiety (p <0.0001); TCF7L2 rs7903146 contributed to 2.7% variance in gastric volume and accommodation (p=0.0167). **Conclusions:** Genetic variants may explain up to 11% of the variance in the gastrointestinal traits that are associated with obesity. Although, the variance attributable is limited, it is large compared to the variance attributable to genes based in epidemiological studies.

T-OR-2124-LB

Platelet mitochondrial function as a non-invasive marker for liver fat accumulation in health adults

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Background: Nonalcoholic fatty liver disease affects ~30% of population and is associated with obesity, insulin resistance, and metabolic syndrome. Means for detecting liver fat accumulation prior to disease development are needed. We tested the hypothesis that mitochondrial bioenergetic function in platelets could serve as a surrogate marker of hepatic fat content in healthy individuals. **Methods:** Participants were 21 healthy adults (60% female) aged 19-45 yrs (mean ± SD: 27 ± 7 yrs). Liver fat % was determined by quantitative MRI analysis using a modified 2-point Dixon sequence. Platelet mitochondrial oxygen consumption rate (OCR) was determined by an extracellular flux analyzer using a mitochondrial "stress test" with sequential addition of mitochondrial inhibitors. Measures included basal, ATP-linked, maximal and non-mitochondrial OCR as well as proton leak and reserve capacity (maximal – basal). **Results:** Average % liver fat was ~ -0.28 ± 0.20% (Range: -7.13-3.81%). Platelet basal, ATP-linked and non-mitochondrial OCR were significantly, inversely associated with % liver fat (r = -0.61, P = 0.003, r = -0.62, P = 0.003, and r = -0.50, P = 0.02, respectively). Proton leak was inversely associated with % liver fat (r = -0.40) at P = 0.07. % liver fat was not significantly associated with platelet reserve capacity or maximal OCR. Adjusting for age and sex did not change the results for any of the platelet OCR variables. **Conclusions:** Platelet mitochondrial function may have potential as a prognostic and diagnostic biomarker for liver fat accumulation.