Results: Kruskal-Wallis/Dunn test showed a significant difference in BMI between the urban group and the rural ones (KW: $X^2 = 11.987$, $p < 0.001$). Lower average light exposure between 7 am and 5 pm was significantly correlated with higher BMI (Spearman, $r = -0.296$, $p < 0.001$). Also, higher average light exposure at night (from 1 am to 6 am) was significantly correlated with higher BMI (Spearman, $r = 0.256$, $p = 0.002$). **Conclusions:** Our results support the hypothesis that low amplitudes of light exposure may be a risk factor contributing to the high prevalence of obesity worldwide. Studies have previously shown associations between BMI and social jetlag, suggesting the correlations found in our study may be related to higher levels of circadian misalignment, more often present where zeitgeber strength is lower, as in urban environments. Future research is needed to address causal relationships between light exposure and excessive body mass in humans. Provided light exposure is a risk factor for obesity, these results point to potential new targets for intervention and prevention strategies.

Adipose Tissue, Appetite, and Obesity

INTEGRATED PHYSIOLOGY OF OBESITY AND METABOLIC DISEASE

Baseline Metabolomic Profile as Potential Biomarker for Weight Change After Roux-en-Y Gastric Bypass Surgery

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Introduction: Weight loss surgery (WLS) has emerged as an effective treatment for severe obesity (BMI ≥ 40 kg/m2 in adults) and Type 2 diabetes (T2D). There is a wide spectrum of long-term response, both in weight change and resolution of T2D after WLS. Younger age at surgery, white race and the extent of weight loss prior to surgery are the known traits associated with favorable outcomes. The aim of this study was to investigate untargeted metabolite profile prior to surgery as a potential biomarker for long-term weight change response to WLS.

Methods: Latent class growth mixture modeling (LCGMM) was used to classify the longitudinal weight change trajectories in a cohort of individuals who underwent Roux-en-Y gastric bypass (RYGB). Untargeted metabolite profile was done on a 4-module Liquid Chromatography/ Mass Spectroscopy (LC-MS) platform on the pre-surgery fasting plasma samples from subjects with weight regain or sustained weight loss. Metabolite wide association studies followed by pathway analysis was undertaken using Mummichog and GSEA algorithms. Partial least-square discriminant analysis (PLS-DA), a supervised classification framework used for datasets with thousands of correlated variables and a small number of samples that performs variable selection and classification as a one-step procedure, was used to identify the informative features that defined the two groups.

Results: LCGMM identified 3-classes of weight change in a cohort of 1589 subjects who had undergone RYGB – a) typical trajectory with significant weight loss by 12 months with plateau at ~80% weight loss (n= 1357, 85.4%), b) sustained weight loss without plateau (SWL, n=116, 7.3%) c) weight regain (RGN, 116, 7.3%). Samples from 80 subjects each with RGN or SWL (age 42.5 ± 10 years, 55% F, Excess body weight 221 ± 40 lbs) were used for untargeted profiling of 37,570 metabolite features (564 known). After QC and adjusting for age, sex, race and fasting time, 1920 features (37 known) were associated with the weight category at nominal significance ($p < 0.05$). Amongst the known metabolites, the pathways represented in RGN were amino acid metabolism, branched chain and other essential amino acids that have been previously identified as markers of insulin resistance and T2D, while those with SWL were from sphingolipid metabolism. Dimethylguanidino valeric acid, a marker of liver fat and predictor of T2D was higher in individuals with SWL. Pathway analysis of the known and unknown metabolites together revealed pathways in urea cycle, pyrimidine, glutamate, essential amino acids, and butyrate metabolism. Features identified by PLS-DA overlapped with these pathways.

Conclusions: Untargeted baseline metabolites may serve as predictive biomarkers for weight change after RYGB. Future work will focus on developing a metabolite risk score and replication in other cohorts.

Adipose Tissue, Appetite, and Obesity

INTEGRATED PHYSIOLOGY OF OBESITY AND METABOLIC DISEASE

BIO89-100 Demonstrated Robust Reductions in Liver Fat and Liver Fat Volume (LFV) by MRI-PDFF, Favorable Tolerability and Potential for Weekly (QW) or Every 2 Weeks (Q2W) Dosing in a Phase 1b/2a Placebo-Controlled, Double-Blind, Multiple Ascending Dose Study in NASH

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Background: FGF21 is an endogenous hormone that regulates carbohydrate, lipid and energy metabolism. FGF21 analogs improve liver and metabolic abnormalities in non-alcoholic steatohepatitis (NASH). BIO89-100 is a long-acting glycoPEGylated FGF21, with promising tolerability and pharmacodynamic effects and potential for QW or Q2W dosing. **Methods:** This Phase 1b/2a trial enrolled 81 subjects with liver fat ≥10% by MRI-PDFF and either biopsy-confirmed NASH (BC-NASH) or phenotypic NASH (PNASH: central obesity with either type 2 diabetes mellitus or with evidence of liver injury by ALT or FibroScan