Rebound Hyperphagia

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Gut-derived hormones have been successfully developed as the therapeutic targets to combat the increasing prevalence of diabetes and obesity. G protein-coupled receptors (GPCRs) in the gastrointestinal (GI) tract are involved in maintaining glucose and energy homeostasis by regulating the release of gut hormones in response to luminal dietary nutrients as well as microbial metabolites. We identified that an orphan GPCR, Gpr17, was expressed in the intestinal epithelium and found that loss of intestinal Gpr17 expression increased gut incretin hormone secretion from enteroendocrine cells (EECs). However, it is unknown how Gpr17 ablation in the intestinal epithelium affects feeding behavior and satiety regulation. To address this question, we used genetic knockout approach to generate intestinal Gpr17-deficient mice and analyzed their feeding behavior. Here we show that intestinal Gpr17-deficient mice had similar growth curve, body composition, and *ad libitum* food intake compared with littermate controls. Interestingly, intestinal Gpr17-deficient mice responded to fasting-refeeding challenge with reduced fasting locomotor activity and less food intake after refeeding, suggesting increased satiety during the phase of rebound hyperphagia. Moreover, we performed fasting-refeeding challenge with Gpr17-deficient mice fed on high-fat diet (HFD), and our meal pattern analysis revealed that these mice had reduced meal duration of the first meal after refeeding. In conclusion, our genetic knockout studies in rodents showed that ablating intestinal Gpr17 increased satiety during rebound hyperphagia in the fasting-refeeding experimental paradigm. Intestinal Gpr17 could be developed as a therapeutic target to treat obesity by improving energy balance through gut hormone secretion and meal pattern control.

Adipose Tissue, Appetite, and Obesity

NOVEL MECHANISMS CONTROLLING ADIPOSE TISSUE PHYSIOLOGY AND ENERGY BALANCE

Obesity and Covid-19: A Major Mortality Risk in Patients Hospitalized With Covid-19

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The coronavirus disease 2019 COVID-19 pandemic is a major public health crisis. Obesity has emerged as a significant comorbidity for COVID-19 severity. To study the association of both pandemics, we conducted an observational, retrospective cohort study involving 521 patients admitted with Covid-19 to an inner city, community hospital in Brooklyn, NY in the period March 20 to May 2, 2020. Of the cohort, 57.6% was men, mean age was 61.6±17.2 years, and mean BMI was 29.0 ± 8.2 kg /m2. 11% had BMI > 40 kg/m^2. 53.9% was Hispanic, 33.3% was African American, 7.1% was White, with a predominance of type 2 diabetes (99%). Diabetes, hypertension, coronary artery disease and chronic kidney disease were found in 45%, 41.5%, 15%, and 20.1% cases, respectively. Mean HbA1c was 5.8%± 1.1 in patients with no history of diabetes, 3% presented with diabetic ketoacidosis, mortality rate was 30.6%. Non-survivors were significantly older (median age 68 vs 56, $p < 0.03$) and had higher rate of microvascular and macrovascular diseases. In patients with diabetes, mortality rate was 40.1%. HbA1c was similar between survivors and non-survivors. Older age and hyperglycemia on admission were the risk factors for mortality. Only 30% of the cohort had normal weight (BMI<25), 30% was overweight and 40% was obese. In univariate analysis, the characteristics at admission significantly associated with mortality were age, BMI, hyperglycemia, diabetes and DKA in patients with or without diabetes. In age- and sex-adjusted multivariable analysis only BMI 30–39 kg/m^2 (OR = 1.63; 95% CI, 1.10, 2.43; p = 0.015), BMI >40 kg/m^2 (OR = 2.05; 95% CI, 1.22, 3.44; p = 0.007) and DKA (OR = 1.77; 95% CI, 1.18, 2.64; p = 0.005) remained positively associated with higher mortality. In summary, BMI, and DKA but not diabetes, were positively and independently associated with mortality in patients hospitalized with Covid-19. **Reference:** (1) Popkin et al., Obesity Reviews 2020 August;21(11):e13128. (2) Cariou et al., Diabetologia 2020 May;63(8): 1500–1515.

Adipose Tissue, Appetite, and Obesity

NOVEL MECHANISMS CONTROLLING ADIPOSE TISSUE PHYSIOLOGY AND ENERGY BALANCE

Pancreatic Ductal Adenocarcinoma Highly Expresses Activin A: Implications in Adipose Tissue and Cancer Cachexia

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Background: Pancreatic ductal adenocarcinoma (PDAC) is currently the third leading cause of cancer death in the United States and is projected to become the second leading cause by the year 2030. Prognosis for patients with metastatic disease remains dismal. Cancer cachexia is seen in over 85% of PDAC patients who often have the most severe degrees of cachexia and experience adipose tissue loss prior to skeletal muscle loss early in the disease process. Several factors have been proposed to induce cachectic symptoms in human patients, including inhibin subunit βA, or activin A. **Hypothesis:** While muscle wasting has been the most frequently studied mechanism in cachexia research, changes in adipose tissue are increasingly understood as important