differences between sexes likely contribute to whole pituitary transcriptome changes we observed, however, to what extent remains to be studied. Together our study indicates that miRNAs play a substantial role in regulation of pituitary postnatal development but that differences in cellular composition may contribute more robustly to sex-biased gene expression.

Adipose Tissue, Appetite, and Obesity
OBESITY TREATMENT: GUT HORMONES, DRUG THERAPY, BARIATRIC SURGERY AND DIET

Single-Dose Effects of Anti-Obesity Drugs on Human Basal Metabolic Rate

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Design and rationale: Obesity results from energy intake exceeding energy expenditure (EE) over a prolonged period. Many anti-obesity drugs are designed to decrease energy intake. However, their potential impact on EE is not well documented. We designed a placebo-controlled, double-blind, randomized cross-over study to determine the acute effects of several FDA-approved anti-obesity drugs on basal metabolic rate (BMR) under well-controlled conditions.

Protocol and inclusion criteria: This ongoing study is limited to healthy males of all ethnicities aged 18–35 years with a BMI of 18.5 to 25.0 kg/m^2. Following an overnight stay in the Metabolic Clinical Research Unit, fasting subjects were measured from 8:00am to 12:00pm in a whole-room indirect calorimeter, which was maintained at a thermoneutral temperature (26.7±0.9°C) to prevent non-shivering thermogenesis. The six treatments include placebo, caffeine as the positive control (300 mg), phentermine (37.5 mg), topiramate (200 mg), Qsymia (phentermine 15 mg / topiramate 92 mg), and naltrexone (100 mg), with a 1-week outpatient washout period after each treatment. Drug-naïve subjects received a single dose of each drug to minimize potential metabolic adaptations that may occur with weight-loss or chronic use. The prespecified primary outcome was a ≥5% increase in BMR vs. placebo for each drug. This difference can be detected for 16 subjects with 0.83 power at α=0.05 allowing for ≤25% dropout. Secondary outcomes include respiratory quotient (RQ), heart rate (HR), mean arterial pressure (MAP), and self-reported hunger.

Preliminary data: To date, 7 subjects were recruited and 6 have completed the study (26.1±4.3 years, BMI 23.1±1.4 kg/m^2, body fat percentage 18.4±4.1%). Interim analysis using paired t-tests shows, compared to placebo, caffeine trended towards increasing EE (1.17±0.07 vs. 1.27±0.12 kcal/min; p=0.07) and increased MAP by 5.5±4.2% (88±2 vs. 93±4; p<0.05), but did not change heart rate (59±10 vs. 61±13 bpm). Naltrexone increased EE by 5.9±4.3% (p<0.05). No treatments altered resting RQ compared to placebo (0.83±0.05). Phentermine increased resting HR, both alone (15.7±7.9%, p<0.01) and in Qsymia (9.2±3.6%, p<0.05), compared to placebo. Of the five drug-treatments, only Qsymia reduced self-reported hunger scores compared to placebo.

Summary and future directions: Anti-obesity drugs may increase energy expenditure by upregulating sympathetic nervous system activity. Combined with appetite suppression, the impact on energy balance can lead to weight loss. We aim to complete our study to determine whether these drugs can acutely increase EE with minimal cardiovascular side-effects and compare our findings with long-term interventions.

Cardiovascular Endocrinology
PATHOPHYSIOLOGY OF CARDIOMETABOLIC DISEASE

Genetic Variants Related to Familial Hypercholesterolemia in Clusters from Minas Gerais - a Southeast State of Brazil

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Familial Hypercholesterolemia (FH) is an autosomal dominant genetic disease, characterized by high levels of the cholesterol fraction present in low density lipoprotein (LDLc). FH is associated to early atherosclerotic coronary disease, which can result in acute myocardial infarction and angina pectoris. Clinical diagnosis of FH in adults is based on elevated LDLc levels ≥ 4,9 mmol/L and total cholesterol (TC) ≥ 7,5 mmol/L; in untreated children and adolescents LDLc ≥ 4,0 mmol/L and TC ≥ 6,7 mmol/L, associated or not with physical signs (xanthomas, corneal arch). In Brazil, it is estimated that there are from 402,000 to 607,000 cases of FH. This study aimed to evaluate the genetic variants related to FH in a small region from Minas Gerais, a southeast state in Brazil. Fifteen index cases (IC) were selected in two cities (Bom Despacho and Moema), that comprise 1.416 km^2 in that region. Family members (n=69) were also selected, when possible, for genetic analysis, which was carried out by the NGS (Next Generation Sequencing) method, using Illumina® technology. Six different genetic variants were identified: 1) Pathogenic variants in LDLR gene - Asp224Asn in 74 individuals (10 IC); Cys34Arg in 1 individual (1 IC); Asp601His in 2 individuals (1 IC); and Ser854Gly in 2 individuals (1 IC); 2) Variant of uncertain significance (VUS) in APOB gene - Met499Val in 1 individual (1 IC); and 3) VUS in PCSK9 gene - Arg237TRP in 4 individuals (1 IC). All variants were identified in heterozygosis. The data suggest that the high