

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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### MON-593

**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<sup>2</sup>. 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<sup>2</sup>, 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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### SUN-561

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<sup>2</sup> 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

prevalence of FH in that small region in Brazil is related to inbreeding observed in the families investigated. In addition, a founder effect could also contribute to the elevated frequency of LDLR gene variants, mainly Asp224Asn. The data show the importance of molecular investigation on clinical conduct in FH Brazilian patients and their family members.

## Adipose Tissue, Appetite, and Obesity RARE CAUSES AND CONDITIONS OF OBESITY: PRADER WILLI SYNDROME, LIPODYSTROPHY

### *Comparative Comorbidity Burden Among Patients with Prader-Willi Syndrome: A Population-Level Cohort Study*

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#### SUN-595

Prader-Willi syndrome (PWS) is a rare, complex multi-system genetic disorder characterized by hyperphagia and abnormal food-related behaviors that contribute to severe morbidity and early mortality and to a significant burden on patients and caregivers. The hyperphagia seen in people with PWS can result in significant obesity. This study assessed rates of comorbidities associated with obesity, including type II diabetes (T2D), cardiovascular disease (CVD), and sleep apnea (SA) in a large US PWS vs. a non-PWS cohort.

**Methods:** T2D, CVD, and SA conditions for privately insured PWS and non-PWS patients aged <65 years were identified via ICD diagnosis codes in deidentified medical claims provided by IQVIA™ Health Plan Claims Data (1/2006 - 11/2018). Patients were grouped into age-bands of 0–2, 3–8, 9–17, 18–26, 27–34, 35–49, and 50–64 years. Patients were required to have ≥12 months of enrollment, and observations were segmented into 12-month patient years. Due to patient privacy, figures that represent fewer than 11 patients are not shared and are represented as a non-zero figure (NZF).

**Results:** 5,060 PWS and 31,093 non-PWS patient years representing 1,461 and 9,656 unique patients were eligible for analysis. T2D was detected in 8% of PWS patients age 9–17 (vs a NZF in non-PWS), 19% (vs 1%) in ages 18–26, and 27% in ages 27–34, 35–49, and 50–64 (vs 2, 5, and 13%, respectively). Comorbid CVD was detected in 25% of PWS patients age 0–2 (vs 1% in non-PWS), 11% (vs 1%) in ages 3–8, 15% (vs 1%) in ages 9–17, 29% (vs 4%) in ages 18–26, 44% (vs 11%) in ages 27–34, 60% (vs 27%) in ages 35–49, and 78% (vs 53%) in ages 50–64. Sleep apnea was detected in a NZF of non-PWS patients aged 0–2 and in all age groups 3–8, 9–17, and 18–26, compared to 37%, 22%, 17%, and 18% of PWS patients, respectively. Sleep apnea prevalence in PWS patients was 18% (vs 1% in non-PWS) in ages 27–34, 15% (vs 3%) in ages 35–49, and 16% (vs 4%) in ages 50–64.

The largest disparities between PWS and non-PWS T2D prevalence was observed in the 9–17 and 18–26 age groups. Manifestations of CVD in PWS patients ages 0–2 was characterized by high rates of congenital atrial septal and patient ductus arteriosus defects, and in adolescent and adult PWS patients featured markedly higher rates of hypertension and hyperlipidemia than non-PWS cohorts. The proportion of PWS patients with SA that also received continuous positive airway pressure or oxygen monitoring ranged from 38% to 71%.

**Conclusions:** Across all age groups, compared to non-PWS subjects, individuals with PWS experience markedly higher rates of CVD, T2D, and SA. The increased rate of CVD in the earliest age groups is consistent with previously observed increases in congenital heart defects with PWS. The frequency and early age of onset of hypertension, hyperlipidemia, T2D and SA emphasize the need for even more aggressive management of underlying drivers such as hyperphagia and the resulting obesity and metabolic dysfunction.

## Healthcare Delivery and Education

### EXPANDING CLINICAL CONSIDERATIONS FOR PATIENT TESTING AND CARE

#### *Gaps in Knowledge of Social Determinants of Health in an Endocrinology Fellowship*

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#### MON-127

**Background:** In June 2018, the Accreditation Council for Graduate Medical Education (ACGME) revised the common program requirements and identified a core requirement “to understand the social determinants of health (SDH) of the populations they serve and incorporate them in the design and implementation of the program curriculum, with the ultimate goal of addressing these needs and health disparities.” Trainees must “demonstrate an awareness of and responsiveness to the larger context and system of health care, including the SDH, as well as the ability to call effectively on other resources to provide optimal health care.” While Association of American Medical Colleges (AAMC) teaching hospitals comprise 5% of the total US hospitals, they provide 40% of charity care in the US. In this setting, trainees need to be aware of the challenges faced by the communities they serve. SDH are increasingly recognized for their importance in the care of patients with diabetes and explain the health disparities in diabetes that exist throughout the US. Endocrinology fellows and the faculty teaching them must therefore demonstrate knowledge of SDH and health disparities.

**Methods:** We investigated the knowledge gaps in SDH in an urban academic endocrinology fellowship. All fellows and faculty members completed a 10-question survey that assessed knowledge, confidence, and motivation to learn about SDH. Six fellows and 10 faculty members completed the survey.

**Results:** While 60% of faculty and 83% fellows reported having an understanding of SDH, no fellows or faculty could correctly identify all 6 SDH. When asked about their confidence level in identifying SDH, 20% of faculty had low