(WL). In this prospective study, we compared the effects of WL from lifestyle intervention (LI) and bariatric surgery (BS) on WL-associated bone loss. We hypothesize that the higher WL from bariatric surgery will result in a greater decline in bone mineral density (BMD) and bone quality. ***Methods*** Twenty-nine obese subjects (BMI > 30 kg/m^2; weight: 107±19.3 kg) were included in the study; 13 participated in a LI study of WL (supervised diet+exercise) and 16 underwent BS. Assessments were done at 10% WL and at 6 months. Areal BMD and body composition were evaluated by DXA; bone micro-architecture and bone strength by microfinite element analysis-derived parameters as failure load (f.load) and stiffness at the distal radius and distal tibia were evaluated by high resolution peripheral quantitative computed tomography. Serum bone turnover markers, adipokines and cytokines were measured by Elisa. ***Results*** Participants in the LI arm were significantly older (71.3±4 vs 48.2±10 y.o., p < 0.001) and lighter (93.4 ± 8 vs. 118.5±18 kg, P=0.001) compared to the BS arm. Analysis adjusted for baseline age and weight showed no significant differences in areal BMD at all sites, volumetric BMD and bone microarchitectural features of the radius and tibia, except for higher cortical porosity (Ct.Po) at the tibia in the LI arm compared to the BS arm (3.0±0.3 vs 1.7±0.3%, p=0.04, respectively). The average WL at 6 months were -11.87±4.7 vs.-15.96±5.1%, p=0.07, for LI and BS, respectively. At 10%WL, the LI arm had a reduction in trabecular volumetric BMD (tb.vBMD) at the radius (-2.2±1.2 vs. 3.1±4.8% P=0.05) and tibia (-2.2±1.4 vs. 2.2±3.9 % P=0.02, respectively) compared to BS arm which had increases in this parameter. There was also a trend for reduced radius trabecular number and thickness in the LI arm at 10% WL. Meanwhile, there was a trend for reduction in total hip BMD, f.load and stiffness at the radius in the BS arm only. At 6 months, tb.vBMD at the radius was reduced in LI (-2.7±0.9%) relative to the increase in BS group (5.7±2.0%), p=0.008. There was a reduction in F.load (-5.3±2.4 vs 0.6±1.2%, p=0.09) and stiffness (-6.1±2.7 vs. 0.8±1.4%, p=0.08) of borderline significance at the tibia in the BS compared to no change in LI arm. BS arm showed a greater increase in serum C- telopeptide (28.1±48 vs. 81.3±30%, P=<0.05), an index of bone resorption, and in adiponectin (-0.7±8 vs.36.2±22.1%, P=0.01) compared to LI at 6 months. There were no significant differences in changes in lean and fat mass at 6 months in both arms. ***Conclusion:*** Although WL from LI resulted in reduced radial tb.vBMD, BS was associated with a greater increase in bone resorption and a trend for reduction in bone strength at the weight-bearing tibia at 6 months compared to LI. Results from this pilot project need confirmation in a larger study with longer duration of follow-up.

Neuroendocrinology and Pituitary

HYPOTHALAMIC-PITUITARY DEVELOPMENT AND FUNCTION

Functional MRI Study: Weight Loss Induced Changes in Taste Receipt-Induced Activation in the Striatum and Hypothalamus

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SAT-LB59

Background: Reward behaviors including those related to eating are influenced by output from the ventral striatum (VS), dorsal striatal [caudate(Cau) and putamen(Put)] and hypothalamus (HTH). We hypothesized that weight loss would induce modifications in activation in these regions of interest (ROI) during a consummatory reward task. **Methods**: We recruited metabolic abnormal obese (MAO) from the VA St.Louis Health Care System and Washington University in St.Louis (WUSTL). MAO was screened for by fasting insulin and plasma glucose, 2 hour 75 gram OGTT, and hemoglobin A1c. MAO was defined as prediabetes by ADA criteria and/ or elevated HOMA-IR. Functional magnetic resonance imaging (fMRI) scanning sessions were completed at the WUSTL Center for Clinical Imaging Research. A rapid event-related design was used to randomly deliver taste of chocolate milk (choc) or tasteless water (wat). Each taste receipt was proceeded by a cue of corresponding image of chocolate milk or a glass of water. A total of 5 runs, each with 24 trials were completed. Imaging analyses included preprocessing with fMRIprep including censoring excessive motion ≥ 0.5mm. Single subject GLM analyses were completed in AFNI. ROIs were designated bilaterally (lt and rt) except for HTH. A canonical HRF was applied to the food cue event and the AFNI tent function over 9 TRs was applied to the taste receipt event. To evaluate for an effect of weight loss (WL) on food cue and taste receipt-induced activation, repeated measures ANOVA for each region was completed with condition (choc or wat) as a covariate. Also in the model for taste receipt, repetition time (TR) was included as a covariate. Results reported as F(sign.). **Results**: Ten participants achieved at least 7% WL, (range 7-15%), 44±8 years, BMI 38±4kg/m2, f/m 4/6, fasting pg 105±11, 2 hour OGTT pg 132 ±49 mg/dL, HOMA-IR 3.9±1.8. One participant fulfilled criteria for T2D. For taste receipt several significant effects were found for WL: Cau_lt WL 5.9(0.02) and WL*TR 4.9(0.03), Cau_rt WL 8.6(0.004) and WL*TR 8(0.005), Put_lt WL 8.5(0.004), HTH WL*condition 5.4(0.02) and a trend for WL 3.3(0.07). All other comparisons were non-significant including all in the VS and all for food cue. **Conclusions**: Moderate weight loss in MAO modified taste receipt-induced activation in the Cau, Put, and HTH but not in the VS.

Diabetes Mellitus and Glucose Metabolism

METABOLIC INTERACTIONS IN DIABETES

Role of HNF4a Isoforms in the Carbohydrate/Lipid Switch in the Liver and Responsiveness to AMPK

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SUN-LB119

Hepatocyte Nuclear Factor 4α (HNF4α), the master regulator of liver-specific gene expression, is regulated by two promoters (P1 and P2) which drive expression of two groups of HNF4α isoforms referred to here as HNF4α1 and HNF4α7. HNF4α is a known regulator of gluconeogenesis and is mutated in maturity onset diabetes of the young one (MODY1). Conventionally, it was thought that HNF4α1, but not HNF4α7, is expressed in the normal adult liver, with HNF4α1 downregulated and HNF4α7 upregulated in liver cancer. Now, we identify a previously undescribed role for HNF4α7 in the normal adult mouse liver - one involved in the diurnal variations of lipid and carbohydrate metabolism. More specifically, HNF4α1 appears to be a major driver of gluconeogenesis while HNF4α7 is a driver of ketogenesis: we hypothesize that alterations in the levels of the HNF4α isoforms during the day function as a **molecular switch** between the two. Moreover, our preliminary data show that HNF4α7 is required for increased levels of circulating **ketone bodies** in female mice, suggesting interactions with the estrogen pathway. AMP-Activated Protein Kinase (**AMPK**), an energy-sensing kinase that also plays a major role in carbohydrate and lipid metabolism, has been shown to phosphorylate HNF4α1 *in vitro*, but effects *in vivo* and on HNF4α7 are not known. In order to investigate the impact of AMPK on HNF4α isoforms, we employed HNF4α isoform-specific mice α7HMZ (express only HNF4α7) and α1HMZ mice (express only HNF4α1), as well as heterozygous mice which express both. Intraperitoneal injection of the mice with AMPK activator AICAR leads to a rapid decrease in glucose. Interestingly, half the α7HMZ males and all the females began seizing 30 min post injection, while very few α1HMZ males/females and none of the heterozygous mice seized. Moreover, there were differences in the survival of the different genotypes: a third of α1HMZ mice die within 24hrs, while two thirds of α7HMZ mice die within a week, with all heterozygous mice surviving. We suspect the seizures could be due to an electrolyte imbalance exacerbated by AICAR or extremely low glucose caused by AICAR. The α7HMZ females have significantly lower potassium levels compared to α1HMZ and wildtype mice. Additionally, AMPK is known to regulate Na+/glucose transporters, and HNF4α1 is expressed in the proximal tubules in the kidney (responsible for Na+ uptake). To elucidate the cause of the seizures, AICAR injections were repeated with α1HMZ males followed by a glucose or saline gavage. Interestingly, half of the glucose-gavaged mice died within 24hrs, while all of the saline-gavaged mice survived. Our work underscores the critical role that the HNF4α isoforms play in the metabolic switch, and suggests that the kidney as well as the liver could be involved.

Neuroendocrinology and Pituitary

CASE REPORTS IN SECRETORY PITUITARY PATHOLOGIES, THEIR TREATMENTS AND OUTCOMES

Fahr's Syndrome: A Rare Neurological Disorder Unmasked by a Psychiatric Illness

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SAT-LB50

Fahr's syndrome is a rare familial disorder characterized by abnormal accumulation of calcium deposits bilaterally at basal ganglia. It commonly affects middle-aged adults and presents with a range of neuropsychiatric symptoms. The exact prevalence of Fahr's syndrome is uncertain; however, intracranial calcifications suggestive of this disorder are detected incidentally in approximately 0.3 % to 1.2 % of CT imaging of the brain with a prevalence of 1/1,000,000. It may be idiopathic or secondary to numerous causes dominated by phosphorous and calcium disorders, with the most common etiology being hypoparathyroidism. We report the case of a 27 years old female patient with a medical history of insulin-dependent Diabetes Mellitus type 1, Bipolar disorder, Autoimmune Polyglandular Syndrome Type 1, Thalassemia major, Primary Hypoparathyroidism and Bronchial Asthma who was admitted to the hospital after presenting an episode of dizziness, slurred speech and involuntary movements associated to hypoglycemia. The patient had a medical history of recurrent episodes of conscious self-induced hypoglycemia with double doses of insulin therapy and noncompliance with home medications. Upon evaluation, patient presents aggressive and defiant behavior. Physical and neurological examination was difficult to assess since she refused to be examined. Laboratories were remarkable for serum calcium of 6.2mg/dl, albumin of 3.5g/dl, with corrected calcium levels of 6.5mg/dl, suggestive of severe hypercalcemia. Head CT scan showed bilateral subcortical, basal ganglia clouded, thalamic, and cerebellar calcifications with preserved gray and white matter differentiation. Treatment was tailored to symptoms control and correction of underlying abnormalities. These case present the most critical features of the diagnostic criteria of Fahr's syndrome. Pathologically, calcifications occur in the vascular walls and in the perivascular spaces of arterioles, capillaries, and veins. Clinical findings of Fahr's syndrome vary from neurological disorder to those mimicking Bipolar disorder. In this case, there were no neurological symptoms, and this patient only presented with psychiatric manifestations suggestive of bipolar disorder. For any psychiatric condition, it is essential to rule out organic brain disorders before labeling a patient, especially one who is young and has multiple endocrinopathies which could be associated with this rare condition.

Adrenal

ADRENAL - TUMORS

Repressive Epigenetic Programs Reinforce Steroidogenic Differentiation and Wnt/β-Catenin Signaling in Aggressive Adrenocortical Carcinoma

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