on a 9-year-old girl with a 2.3 cm pituitary macroadenoma, whose ACTH and urinary 24-hour free cortisol were the highest recorded at our institution. Clinical Case: A 9-year-old pre-pubertal female presented with six months of frontal headaches, rapid weight gain, and hirsutism. Two months prior she developed fatigue and proximal muscle weakness and pain. On physical exam, she had plethoric round facies with acne and hirsutism, dorsal fat pad, central adiposity, and violet colored abdominal striae. Her pubertal development was tanner stage 3 for breast and 2 for pubic hair. BMI was 95th percentile and height was 40th percentile, previously 75th and 50th percentile respectively one year prior. 24 hour urinary free cortisol was 40,650 mcg/day [normal:100 mcg/day]. A 48 hour high dose dexamethasone suppression test was done as it is the most accurate in pediatric patients over 40 kg, morning cortisol was 100 mcg/dL [normal: 5-20 mcg/dL], ACTH 868 pg/ml [normal: 9-57 pg/ml], 24 Urinary Free Cortisol was 15,878 mcg/day [normal: 100 mcg/day]. A MRI Pituitary/Sella revealed a 2.3 cm pituitary macroadenoma superiorly displacing and flattening the optic chiasm, invading into the right cavernous sinus. She was referred to Neurosurgery, who did a partial transphenoidal resection, pathology consistent with ACTH producing tumor. Post-operatively she developed central diabetes insipidus and adrenal insufficiency for which she received desmopressin and oral hydrocortisone respectively. Her laboratory values eight months since surgery show normalization of ACTH and cortisol levels. The patient's general health has improved, headaches have resolved, strength has returned, and her hirsutism is reduced. Her BMI remains elevated at 88% but is declining and growth velocity is increasing back to her pre-disease level. Conclusion: Cushing Syndrome is exceedingly rare in pediatric aged patients and pituitary macroadenomas are atypical in this population.This is a unique case of an ACTH producing macroadenoma in a Pediatric patient, which has seldom been reported in the literature, and should be considered in patients with similar presenting symptoms.

Neuroendocrinology and Pituitary

ADVANCES IN NEUROENDOCRINOLOGY

Dissecting Type 2 CRH Receptor Signaling Characteristics in the Hypothalamic Cell Line MHYPOA-2/30

Viridiana Alcantara-Alonso, PhD[1], Patricia de Gortari, PhD[1], Robert Dallmann, PhD[2], Dimitris Grammatopoulos, PhD, FRCPath[3].

[1]National Institute of Psyquiatry, Mexico, Mexico City, Mexico, [2]Warwick Medical School, Coventry, United Kingdom, [3]Univ of Warwick Medical School, Coventry, United Kingdom.

SUN-267

The stress peptides coticotropin-releasing hormone (CRH) and urocortins (Ucns) exert anorectic effects acting mainly through the type 2 CRH receptor (CRH-R2) in the hypothalamus. Impairment of CRH-R2 signaling in chronically stressed rats has been linked with the development of hyperphagia (Alcantara-Alonso et al. *Neuropeptides*, 2017) however the exact mechanisms and molecular defects are unknown. In the present study we used the mHypoA-2/30, a hypothalamic immortalized cell line derived from adult mice (Belsham et al. *FASEB J*, 2009) to further explore the signaling molecules mediating the anorexigenic effect of the CRH-R2 cognate agonist urocortin 2 (Ucn2). Specifically, we investigated mRNA, protein expression and cellular localization of CRH-R2 in the mHypoA-2/30 neurons. Additionally, we examined the effects of Ucn2 on the phosphorylation of CREB and AMPK, as well as its transcriptional effects on genes of feeding-related peptides and molecules involved in modulation of circadian rhythms. Both CRH-R2 mRNA and protein expression were detected in mHypoA-2/30; indirect immunoflourescence experiments using a specific CRH-R2 antibody demonstrated widespread localization in the plasma membrane and cytoplasm. Moreover, the receptor sub-cellular localization was redistributed in response to activation by Ucn2 (100 nM), as the plasma membrane immunofluorescent signal was decreased after 4h of agonist treatment, suggesting CRH-R2 homologous internalization. We also observed a 50% increase in the phosphorylation of CREB associated with a concomitant decrease in AMPK phosphorylation after 30 min of Ucn2 treatment. Among the panel of hypothalamic genes analyzed, we identified after 24h of Ucn2 treatment increases in the gene expression of the anorexigenic peptides neurotensin and proopiomelanocortin. Interestingly, sustained CRH-R2 activation also led to an increase in the mRNA levels of Aryl Hydrocarbon Receptor Nuclear Translocator Like (ARNTL), a protein involved in the control of circadian rhythm. A luciferase reporter gene analysis of ARNTL showed that the mHypoA-2/30 cells also exhibit circadian patterns of expression and that the treatment with Ucn2 enhanced circadian amplitude of ARNTL reporter on these cells, which in turn may be involved in glucocorticoid release in circadian cycles and stimulating appetite during the activity phase of the animals. In conclusion, we found that the mHypoA-2/30 cell line expresses endogenous functional CRH-R2 that is linked to downstream regulation of anorexigenic gene expression. This cell line appears to be a useful *in vitro* tool to study hypothalamic CRH-R2 signaling machinery involved in central control of food intake and circadian cycles.

Bone and Mineral Metabolism

OSTEOPOROSIS: DIAGNOSIS AND CLINICAL ASPECTS

Pelvic Bone Density Is Lower Than Bone Density of Hip and Femoral Neck in Postmenopausal Women

Mahshid Mohseni, MD[1], Roberto Civitelli, MD[2], Shannon Stum, RT[1], Bridgett Toennies, RT[1], Seth Eisen, MD[1].

[1]Washington University in St Louis, Saint Louis, MO, USA, [2]Washington Univ-St Louis, Saint Louis, MO, USA.

SUN-395

Pelvic Bone Density is Lower than Bone Density of Hip and Femoral Neck in Postmenopausal Women

Pelvic fractures represent 7% of all fragility fractures; they account for 5% of the cost of osteoporotic fracture care, and are commonly (> 50%) associated with loss of independence in the elderly. The incidence of pelvic fractures has increased significantly over the past 3 decades. However, little is known about the relationship between bone mineral

density (BMD) and pelvic fractures. We have conducted a pilot cross-sectional study to establish a method of measuring pelvic BMD and to correlate BMD of the pelvis with BMD at other skeletal sites. Postmenopausal women without a history of pelvis and hip fragility fractures were enrolled. Hip, spine, and pelvis DXA scans were obtained using a Hologic DXA machine. Pelvic BMD was calculated using Hologic Research Software from 3 areas of the pelvis (R1: public symphysis, R2: inferior pubic ramus, and R3: superior pubic ramus), corresponding to common fracture locations. Pelvis BMD was the average of the 3 pelvis sites. Pelvic BMD measurement precision error was calculated using the root mean square method (Recommended by International Society of Clinical Densitometry (ISCD)). Statistical analysis was used to compare BMD at different sites. Alpha error was set at 0.05. Of 73 postmenopausal women who were enrolled in the study (average age 64 years, average 15 years postmenopausal), 3% had chronic kidney disease, 7% had type 2 DM, 3% were on corticosteroids and none were smokers. BMD of femoral neck assessed on pelvic DXA was not significantly different from femoral neck BMD measured on standard DXA (P=0.09). To assess pelvis BMD measurement precision, 15 patients underwent 3 separate pelvic DXA images after repositioning. BMD precision error was 0.011g/cm^2 which is slightly lower than the precision total hip BMD at our center (0.007 g/cm^2). BMD of R1, R2, and R3 pelvic areas were measured as 0.44±0.15, 0.41± 0.15, and 0.62 ±0.19 g/cm^2, respectively. Notably, BMD of R3 was significantly higher than the other 2 areas (P<0.001, ANOVA). Average BMD (0.49±0.14 g/cm^2) of pelvis was significantly lower than BMD of femoral neck (0.72± 0.16 g/cm^2), total hip (0.86±17 g/cm^2) and spine (0.97± 19 g/cm^2)(P <0.001). Average BMD of pelvis was significantly lower in participants with osteopenia and osteoporosis of the hip and femoral neck compared to participants with normal BMD in those locations. In summary, we report a precise method of measuring BMD of commonly fractured areas of the pelvis. Pelvis BMD is lower than hip, femoral neck, and spine. Bone density of the pelvis correlates with hip and femoral neck bone density. The results of this pilot study can be used for future studies looking at pelvic low bone density in patients with pelvic fragility fractures which could help identify patients at risk for pelvic fragility fractures and change how osteoporosis is defined based on DXA images.

Diabetes Mellitus and Glucose Metabolism

CLINICAL AND TRANSLATIONAL STUDIES IN DIABETES

FDXR Regulates Iron Metabolism and Glucose Metabolism in Liver.

Ikki Sakuma, MD, PHD[1], Masataka Yokoyama, MD, PhD[2], Kazuyuki Yamagata, PhD[2], Naoko Hashimoto, MD, PhD[2], Akitoshi Nakayama, PhD[2], Gerald I. Shulman, MD, PhD[1], Tomoaki Tanaka, MD, PhD[2].

[1]Yale Univ Sch of Med, New Haven, CT, USA, [2]Chiba Univ Sch of Med, Chiba, Japan.

MON-635

Iron is an essential cofactor for many proteins that function in electron transport or oxygen transport as heme or iron-sulfur cluster. On the contrary, iron also has the potential to cause oxidative damage if not carefully regulated and when in labial iron excess. Clinical studies show that elevated serum ferritin levels are observed in most patients with type 2 diabetes and non-alcoholic fatty liver disease (NAFLD). In this context, p53 is shown to induces some mitochondrial iron regulatory genes. The role of crosstalk between p53 and iron metabolism has not been sufficiently examined in the pathogenesis of diabetes and NAFLD.

Here, we examined the role of ferredoxin reductase (FDXR), a key mitochondrial regulator for iron metabolism, as p53-inducible gene with focusing on the hepatocyte and liver. We confirmed that p53 induced FDXR expression in HepG2 cells and SKEHP1 cells. Biochemical analysis demonstrated that FDXR regulated ROS levels via iron metabolism. *In vivo* analysis, high-fat diet activated the p53-FDXR pathway in mice liver. We generated transgene expression in mice liver using adenovirus infection carrying shRNA or CRISPR Cas9 system. Treatment with the FDXR knockdown increased hepatic iron content and aggravated glucose intolerance. Besides, forkhead box protein O1 (FOXO1), a key transcriptional factor that induces phosphoenolpyruvate carboxylase and glucose-6-phosphatase increased ratio of nuclear localization, indicating hepatic gluconeogenesis activation. Consistently, biochemical analysis in HepG2 cells demonstrated that FDXR regulated insulin-dependent FOXO1 nuclear exclusion through oxidative stress.

In conclusion, p53-inducible FDXR regulates iron metabolism and oxidative stress. FDXR inhibits iron accumulation and oxidative stress in liver and links to suppression of hepatic gluconeogenesis via insulin-dependent FOXO1 nuclear exclusion. The results

of this study provide important new insights into relationship between iron metabolism and glucose metabolism as well as potentially identify novel therapeutic targets for the treatment of diabetes and NAFLD.

Pediatric Endocrinology

PEDIATRIC PUBERTY, TRANSGENDER HEALTH, AND GENERAL ENDOCRINE

Usefulness of a LHRH Test with Low Dose of Triptorelin Pamoate in the Diagnosis of Precocious Puberty in Girls

Juan Pablo Llano, MD[1], Mauricio Javier Llano, MD[2], Pineda Katherine, Msc[1], Teresa Ortiz Picon, MD[1], Gladys Laverde[3], Sonia Castro, MD[1].

[1]Laboratorio de Investigación Hormonal, Bogota, Colombia, [2]Centro Medico de los Andes, Bogota, Colombia, [3]Laboratory of Hormonal Investigation, Bogota, Colombia.

SUN-063

Objective: to determine diagnosis value of a new LHRH test for diagnosis or precocious puberty (PP) correlated with clinical and paraclinical pubertal changes. ***Methods***:79 girls under age 10 years old were referred to our laboratory with diagnosis of precocious puberty went thought a physical exam and bone age /pelvic US review to classify them clinically in probably PP or unlikely PP. A LHRH test was performed with measurement of at least 3 times including baseline measurement of gonadotrophins (LH / FSH) and