

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

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The stress peptides corticotropin-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 immunofluorescence 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

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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