Group D, Controls (19 patients, 13 F and 6 M, mean±SEM age 40.26±2.87 ys, BMI 23.25±0.95 kg/m^2). The diagnosis of metabolic syndrome was made according to NCEP ATPIII criteria (2005 revision). GHD was diagnosed with dynamic test using Growth Hormone-Releasing Hormone (GHRH 50 μg i.v. + arginine 0,5 g/Kg), with a peak GH response between 9 and 16 μg/L when BMI was < 30 kg/m^2 or 4 and 9 μg/L when BMI was > 30 kg/m^2. Partial GHD was defined with dynamic test using GHRH, with a peak GH response < 9 μg/L when BMI was < 30 kg/m^2 or < 4 μg/L when BMI was > 30 kg/m^2.They were evaluated for: serum glucose and insulin, HOMA-index, QUICKI-index, Total/LDL/HDL cholesterol, triglycerides, IGF-1 and LCN2 (measured using ELISA kit DuoSet LCN2/NGAL, R&D systems).LCN2 plasmatic levels were significantly increased in METs, while no difference with control group was found in total and partial GHD. LCN2 levels were not influenced by BMI and HOMA-index. A significant positive correlation between LCN2 and HOMA-index was found in controls, while a trend-like, yet not significant, positive correlation was evidenced in partial GHD. No correlations between these parameters were identified in METs and GHD groups. Our data support the hypothesis that LCN2 plasmatic levels increase in metabolic syndrome. As previously shown (4), different inflammatory patterns characterize the two pathological conditions. However, the correlation between HOMA index and LCN2 suggest a possible modulatory action of LCN2 on insulin resistance in normal subjects and partial GHD ones.
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Diabetes Mellitus and Glucose Metabolism

IMPACTS OF METABOLISM ON CLINICAL CHALLENGES

Epinephrine Is Essential for Normal Renal Glucose Reabsorption via the Glucose Transporter GLUT2

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OR26-01

Humans and mice with Melanocortin 4 receptor (MC4R) deficiency remain protected from hyperglycemia despite chronic obesity and insulin resistance. We have observed that elevated glycosuria in MC4R deficient mice protects them from hyperglycemia. Moreover, our results indicate that circulating epinephrine may couple MC4R signaling with kidney glucose reabsorption. However, the direct role of epinephrine in regulating kidney glucose reabsorption remains unclear. We hypothesize that epinephrine is essential for maintaining glucose homeostasis via kidney glucose reabsorption. To test this hypothesis, we performed oral glucose tolerance tests (OGTTs) and intraperitoneal insulin tolerance tests (ITTs) in phenylethanolamine-N-methyltransferase (*Pnmt*) knockout (KO) mice that specifically lack epinephrine but have normal norepinephrine levels. *Pnmt* KO mice exhibited reduced insulin sensitivity compared to their Wild-Type (WT) littermates (Area under the curve for ITT: 9,700±256 vs. 8,482±417 mg/dL.min, p<0.05). Paradoxically, we observed improved rather than impaired glucose tolerance in *Pnmt* KO mice compared to their WT controls (Area under the curve for OGTT: 32,546±1,592 vs. 40,058±1,918 mg/dL.min, p<0.05). To ascertain if *Pnmt* KO mice, like MC4R deficient mice, show elevated glycosuria, we quantified their 24 urine glucose levels after oral glucose (250 mg) challenge. Indeed, *Pnmt* KO mice demonstrated elevated glycosuria compared to their WT littermates (Urine glucose: Baseline, 24.63±2.2 vs. 11.14±0.82 mg/dl; post glucose challenge: 67.83±5 vs. 16.09±1.13 mg/dl, p<0.001), again validating the phenotype similar to that of MC4R deficient mice. To determine the glucose transporters involved in mediating elevated glycosuria in the *Pnmt* KO mice, we measured the levels of different renal glucose transporters using western blot. We found that GLUT2 was decreased by ~26% in *Pnmt* KO mice compared to their WT littermates. Levels of other glucose transporters were not changed, indicating that suppression of renal GLUT2 mediates elevated glycosuria in the epinephrine deficient mice. We validated the direct effect of epinephrine on GLUT2 levels in vitro using mouse primary renal proximal tubule epithelial cells. Indeed, epinephrine selectively increased GLUT2, but did not affect other glucose transporters in the mouse kidney primary cells. Our findings establish the essential role of epinephrine in glucose reabsorption via the renal glucose transporter GLUT2. Therefore, modulating the renal adrenergic system, or, kidney-specific GLUT2 may afford alternative strategies to regulate glycosuria and ultimately mitigate diabetes.

Reproductive Endocrinology

CLINICAL STUDIES IN FEMALE REPRODUCTION I

AMH Is Higher Across the Menstrual Cycle in Early Post-Menarchal Girls Than in Ovulatory Women

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SAT-029

Ovaries of young girls contain healthy and degenerating follicles from the primordial to antral stage, suggesting coordination of growth and atresia. At age 6 yrs, antral follicle (AF) number and size increase; by late puberty, AF count is higher than at any other life stage. The discovery of AMH, a biomarker of AFs, has facilitated the study of the immature ovary. AMH, a granulosa cell product of preantral and small AFs, inhibits primordial follicle growth and AF selection. As a marker of AF count, AMH should be highest during puberty, yet cross-sectional studies suggest that AMH peaks in the mid-20's. In the current studies