MON-623

Introduction: Oral glucose tolerance test (OGTT) allows classification of subjects in 3 groups, depending on glycaemia 120 minutes after 75g glucose ingestion: normal (glycaemia < 1.4 g/L), glucose intolerant (1.4-2 g/L) and diabetic (>2g/L). Five insulin profiles following OGTT associated with different incidence rates of diabetes over 10 years of follow-up have also previously been described (Kraft J et al, *Laboratory Medicine,* 1975; Hayashi T et al, Diabetes Care.2013). Insulin measurement is very sensible to hemolysis and can advantageously be replaced by C-peptide determination. However, little is known about C-peptide reference values and response to OGTT.**Material and Methods:** 128 patients were included to evaluate glyceamia (COBASe801® ROCHE Diagnostics, France), insulin and C-peptide (LiaisonXL®, Diasorin, France) responses to OGTT.**Results:** According to Hayashi classification, 23 (18%) patients of the whole cohort harbored a physiological insulin response corresponding to profile I (peak of insulin during OGTT at 30 min and higher insulin level at 60 vs. 120 min). Others presented 5 pathological profiles: 14 (11%) patients were classified in profile II (peak of insulin at 30 min and lower or equal insulin level at 60 vs. 120 min), 56 (44%) in profile III (peak of insulin at 60 min), 26 (20%) in profile IV (peak of insulin at 120 min and lower insulin level at 30 vs. 60 min), and finally 9 (7%) in profile V (peak of insulin at 120 min and higher or equal insulin level at 30 vs. 60 min). Only 4 different mean C-peptide profiles emerged from the subgroups previously defined by insulin profile, mean C-peptide profile being substantially similar to mean insulin profile. The only major difference relied on a similar C-peptide profile corresponding to a growing curve from T0 to T120 in both patients with insulin profile IV and V. Mean and 95% confidence interval of C-peptide value at the different times of OGTT were also calculated in the subgroup of patients with both normal glycemic and insulin (pattern I) responses to propose reference values: respectively T0: 0.53 (0.26-0.77); T30: 2.2 (1.24-3.29); T60: 2.26 (1.36-3.68); T120: 1.88 (0.84-2.62) nmol/L. **Conclusion:** C-peptide response to OGTT profile seems to give globally the same information as insulin profile and should therefore also be predictive of the risk type 2 diabetes in case of hemolyzed samples. The slight differences observed between insulin and C-peptide profiles can be explained by their different metabolic pathways, insulin being quickly degraded in the liver and C-peptide undergoing a longer renal elimination. This work also allows us to propose for the first-time reference values for C-peptide at the different times of OGTT using Liaison XL®.

Pediatric Endocrinology

PEDIATRIC PUBERTY, TRANSGENDER HEALTH, AND GENERAL ENDOCRINE

Do Low Sex Hormone Binding Globulin Levels in Newborns Predict Weight Gain in Infancy and Early Childhood?

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SUN-077

Background: SHBG levels are low in obesity, and low SHBG levels are a biomarker for the development of T2DM and the metabolic syndrome. We sought to determine whether low SHBG in newborns will predict childhood obesity. **Methods:** We studied 94 healthy, singleton, full-term newborns, and measured their length, weight (BW), waist circumference, and skinfold thicknesses. We collected cord blood as well as day 2 venous blood samples for the measurement of SHBG and insulin (ALPCO, Salem NH). Maternal age, pre-pregnancy weight, pregnancy weight gain, and glucose screening test results were obtained from obstetrical records. Mothers with chronic diseases were excluded from the study. When babies were 2 years old, we administered a questionnaire to collect information about their eating, sleeping, screen viewing habits, and anthropometric measurements at ages 6, 12, and 24 months (n=47). Overweight was defined as a BMI SDS of ≥1 and <2.0, and obesity as ≥2 SDS. We used the Shapiro-Wilk test to determine if variables were normally distributed. Data were analyzed using the Mann Whitney U and Wilcoxon signed-rank tests, and by Pearson or Spearman correlation analyses. We report non-normally distributed variables as medians and interquartile ranges (IQR). Because of skewed distributions, log 10 transformed values for SHBG were used in the regression analyses. **Results:** SHBG levels on day 2 were significantly higher than in cord blood [22.0(28.7-16.9) vs. 19.0(24.6-14.5) nmol/L, p<0.001], whereas insulin levels were higher in cord blood than in day 2 samples [3.2(5.3-2.0) vs. 1.5(2.2-0.8) μIU/mL, p<0.001]. SHBG and insulin levels were similar in male (n=44) and female (n=50) babies at all time points. Babies with Ponderal index values in the highest quartile had lower day 2 SHBG [18.2(22.1-16.7) vs. 24.3(30.3-18.2) nmol/L, p=0.02] and higher cord blood insulin levels [5.0(7.4-2.6) vs. 2.9(4.8-1.5) μIU/mL, p=0.04] than the remainder of the cohort. At age 2 years, 32% (15/47) of babies were overweight or obese, 60% (28/47) were breastfeeding, 58% (27/47) were watching TV or iPads, and 55% (26/47) were eating sweet snacks. Toddlers watching TV or iPads (p=0.008), or eating sweet snacks (p=0.04) were heavier than their peers. Neither cord blood nor day 2 SHBG or insulin levels correlated significantly with any of the anthropometric measurements in the newborns. On the other hand, day 2 SHBG levels correlated positively with weight at 6 (r=0.311, p=0.04) and 24 months (r=0.353, p=0.02) of age. These associations remained significant after adjusting for gender, BW, gestational age, breastfeeding status and fruit juice intake at 6 months (R^2=0.28, p=0.048) and for gender, BW, gestational age, breastfeeding status, sweet snack intake and screen viewing habits at 24 months (R^2=0.33, p=0.046). **Conclusion:** Although the heaviest babies had lower SHBG levels at birth, low SHBG did not predict overweight at age 2 years.

Adrenal

ADRENAL - CORTISOL EXCESS AND DEFICIENCIES

Structural Instability as an Underlying Pathomechanism in Congenital Adrenal Hyperplasia

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MON-175

Congenital adrenal hyperplasia (CAH) is a group of autosomal recessive disorders affecting key enzymes of cortisol biosynthesis. In the majority of cases the underlying cause are detrimental mutations in the steroidogenic cytochrome P450 enzyme 21-hydroxylase (CYP21A2). Early diagnosis via newborn screening programs in most Western countries and lifelong oral cortisol replacement therapy enable survival, however quality of life often is reduced and co-morbidities are substantially increased. Treatment is a major challenge as disease control can only be achieved with supraphysiological glucocorticoid doses. In addition, the currently available drugs cannot ideally mimic the circadian rhythm and stress adaption of cortisol secretion. Currently, disease severity is classified by residual enzyme activity. The goal of our research is to better understand the specific biophysico-chemical pathomechanism of 21-hydroxylase deficiency in order to enable causative therapeutic approaches. To this end, we investigated the structural and stability properties of six clinically relevant mutant variants of CYP21A2 (V282G/L, P31L, D323G, R484Q/W). Difficulty in purification of these CYP21A2 variants and various biophysical studies suggest that the proteins were less stable than wild-type (WT). Structural and thermal stability assessment by circular dichroism (CD) spectroscopy of recombinant, purified CYP21A2 mutant variants revealed high α-helical content for the WT (65% α-helix) and the mutants at the position 282 (V282G: 60.6 %, V282L: 57.6%). Other mutations (P31L, D323G, R484Q/W) disrupt the α-helical organization of CYP21A2 in exchange for a slight increase in ß-sheet content but mainly for random coil. Temperature dependent CD spectroscopy showed that all mutant variants have reduced thermal stability (T_m: 41.3 - 45,6°C) compared to the WT (T_m: 47.1°C). Tryptophane fluorescence showed that mutant variants of the protein were more prone to local unfolding at the hydrophobic core compared to WT using urea as denaturant. Furthermore, in UV/Vis spectroscopy at 280 nm and 418 nm we could demonstrate that all mutant variants had a reduced heme incorporation (A_{418}/A_{280}: 0.20 - 0.63) compared to WT (A_{418}/A_{280}: 0.88). Our results show that correct structural folding and stability pose a major problem in specific mutations involved in CAH. Therefore we propose that structural protein instability, play a key role in the pathophysiology of CAH and thus might constitute a novel tailored therapeutic target for the treatment of affected patients.

Neuroendocrinology and Pituitary

ADVANCES IN NEUROENDOCRINOLOGY

Effects of Anti-Mullerian Hormone on the Expression of Gonadotropin Subunits in Pituitary Gonadotroph Cell Models

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SUN-250

Aim: We examined the effect of anti-Müllerian hormone (AMH) on the expression of gonadotropin subunits in pituitary gonadotrophs.**Methods:** The mouse pituitary gonadotroph cell line LβT2 was stimulated with AMH and the expression levels of gonadotropin subunits were determined by real-time PCR. We also examined the involvement of the Kiss-1 gene (encoding kisspeptin) and the kisspeptin receptor (Kiss-1R) in LβT2 cells. **Results:** A significant increase was observed in the expression level of the FSHβ subunit with AMH but not in the expression levels of gonadotropin α and LHβ subunits. A significant decrease was observed in the expression of Kiss-1 and Kiss-1R genes in LβT2 cells with AMH stimulation. Kiss-1 gene knockdown by siRNA did not alter the basal expression of gonadotropin subunits. When LβT2 cells overexpressing Kiss-1R were stimulated with kisspeptin, there was a significant increase in the gene expression levels of the gonadotropin subunits α, LHβ, and FSHβ. This inductive effect of kisspeptin was almost completely inhibited by AMH pretreatment. The GnRH-induced increase in gonadotropin subunit genes was unchanged in the presence of AMH. **Conclusions:** AMH can increase FSHβ subunit gene expression in pituitary gonadotroph cells. However, AMH decreases Kiss-1 and Kiss-1R gene expression within the gonadotrophs. Because AMH pretreatment abolishes kisspeptin-induced expression of gonadotropin subunit genes, AMH may control kisspeptin-regulated gonadotropin expression by inhibiting the expression and function of Kiss-1R within gonadotrophs.

Adipose Tissue, Appetite, and Obesity

NEURAL MECHANISMS OF OBESITY

Sex-Specific Modifications in MicroRNAs Contained in Exosomes of Astrocytes in Response to Palmitic Acid

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SAT-593

Communication between astrocytes and neurons is fundamental for correct functioning of the brain, in both physiological and pathophysiological situations. It is clear that astrocytes play an active role in metabolic control, but much is yet to be learned regarding how these glial cells and the neurons involved in energy intake/expenditure communicate to regulate energy homeostasis. We hypothesized that miRNAs contained in exosomes are an important means of cross-talk between these cells. Our objectives here were to determine whether the miRNA content of exosomes released by hypothalamic astrocytes changes in function of nutrient signals and if these signals are similar between males and females. To this end, primary hypothalamic astrocyte cultures were prepared from 2-day old male and female mice, using a standard protocol, and treated with