impact of self-reported stress on CGM data streams after excluding stress events associated with missing CGM data, nocturnal events (from 12 MN to 6 AM, too few events) and events for which subjects did not provide duration of stress. Thus, we analyzed 19.5 ± 7 events per patient from 6AM to 12MN. From 6 AM to 12 MN, the episodes lasted 179 ± 255 minutes with 83 % episodes being mild/moderate and 17% moderate/severe. Number of CGM readings during daytime stress episodes were 717± 1120 compared to 8768 ±1238 during non-stress periods. Impact of stress from 6 AM to 12 MN (Mid-Night) on CGM glucose was analyzed using matched paired t test. Mean glucose (160.6±41.9 vs 148.3± 28.6) and SD (53.2 ±17.7 vs 56.1±14.6) did not show a difference; however % of time spent below 70 mg/dl was less (4 ± 5) in patients during stressful periods compared to times without stress (6.3± 5.5, P value 0.02).

Conclusions: To our knowledge, this is the first study attempting to analyze the impact of self-reported stress using daily stress diaries on CGM data streams in T1D patients on SAP. The study revealed significant challenges experienced by patients in reporting adequate data. Self-reported stress was not associated with hyperglycemia. However, days of self-reported stress and periods during patients reported stress were characterized by less hypoglycemia on CGM data streams.

Pediatric Endocrinology

ADVANCES IN PEDIATRIC OBESITY AND CANCER

Novel Variants in Protein Kinase a Signaling-Related Genes Identified in Obese Children with and Without NAFLD

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Context: Nonalcoholic fatty liver disease (NAFLD) is estimated to affect nearly 10% of Americans age 2-19 and about 38% of those affected are obese. NAFLD is characterized by triglyceride accumulation in hepatocytes and can progress to nonalcoholic steatohepatitis, end stage liver disease and hepatocellular carcinoma. The underlying causes of NAFLD in youth are unclear although obesity, insulin resistance, type 2 diabetes mellitus and metabolic syndrome are risk factors. Genome-wide association studies and candidate gene studies have found several single nucleotide polymorphisms that affect susceptibility to and progression of NAFLD, but clinical translation for some of these genetics is lacking.

Study design: Because mouse models of dysregulated PKA signaling demonstrate the centrality of this pathway in hepatic lipid metabolism and glucose homeostasis, we hypothesized that defects in hepatic PKA signaling genes could affect susceptibility to or severity of NAFLD in children. We asked whether identified variants might be associated with differences in clinical markers in a cohort of obese pediatric patients (non-NAFLD, n=295; NAFLD, n=165) followed at Yale Medical School, where clinical data and genomic DNA were collected. Exon sequencing of 54 PKA-related candidate genes included those coding for PKA subunits, PDEs and other proteins integral to the hepatic PKA system. Variants were ranked by allele frequency and potential pathogenicity. Ongoing analyses aim to identify associations between single variants and potential additive effects with clinical parameters (anthropometric, liver function, glucose metabolism, plasma lipids).

Results: Gene variants were identified in ABCA1, ADCY4, ADCY5, AKAP7, CREB3L1, CREB3L4, CREM, CYP27A1, DHCR7, ERN1, GYS2, IL6, IL10RB, MC2R, PDE1B, PDE2A, PDE3B, PDE4A, PDE7B, PDE10A, PDE11A, PPARGC1B, PRKAR2A, and PRKAR1B. Reported variants met criteria of high to moderate impact based on 9 in silico analyses will help determine whether any of these variants may play a functional role in NAFLD.

Endnotes

1 Schwimmer JB, Deutsch R, Kahan T, Lavine JE, Stanley C, Behling C. Pediatrics. 2006;118(4):1388.
2 Vespasiani-Gentilucci U, Gallo P, Dell’Unto C et al. World J Gastroenterol. 2018;24(43):4835-4845.

Cardiovascular Endocrinology

HYPERTRIGLYCERIDEMIA; INFLAMMATION AND MUSCLE METABOLISM IN OBESITY AND WEIGHT LOSS II

18-Day Lifestyle Program Improves Metabolic Equivalent Measures, BMI, and Exercise Capacity Among Overweight and Obese Adults

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Introduction Various kinds of diets, workout programs, exist to lower one’s Body Mass Index (BMI), increase strength, and endurance. Metabolic Equivalent Measures (METS) is often used to measure exercise intensity1. A simple 18-day lifestyle program may be effective in raising METS, lowering BMI, and building endurance among overweight and obese adults. Methods Participants took part in an 18-day residential lifestyle program that encouraged daily outdoor exercise. Those with a BMI greater than 24.9kg/m2 were selected for this study. BMI, METS, and miles walked per day were measured at baseline and 14 days into the program. METS was measured using the Bruce Protocol while participants reported miles walked per
Reproductive Endocrinology

**FEMALE REPRODUCTION: BASIC MECHANISMS**

**Fertility Rates in Rats Characterized by Increased Hypothalamic CRH Secretion**

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**MON-018**

Certain strains of rats are characterized by hyperactive Hypothalamic-Pituitary-Adrenal axis responses to stress, increased hypothalamic Corticotropin-Releasing Hormone (CRH) production and decreased fertility rates. Activation of the HPA-axis and CRH secretion has been associated with suppression of the Hypothalamic-Pituitary-Ovarian axis primarily as a result of glucocorticoids. Here we examined the hypothesis that Fischer rats have decreased fertility rates because of hypothalamic CRH hypersecretion. Antalarmin, a CRH receptor type 1 antagonist, is known to suppress adrenocorticotropic hormone secretion and other CRH receptor type 1-mediated responses. Adult female Fischer rats were injected with antalarmin or placebo, twice a day, for 16 days. Mating was evidenced by the presence of spermatozoa in the vaginal smear performed every morning. After 16 days, 20% of rats (20%) treated with placebo became pregnant and 55% rats treated with antalarmin became pregnant. We have previously reported that administration of antalarmin after the first day of pregnancy does not affect blastocyst implantation in Fischer rats. Our data suggest that antalarmin improves fertility rates in Fischer rats by antagonizing the direct antireproductive role of hypothalamic CRH.

**Reproductive Endocrinology**

**MALE REPRODUCTIVE HEALTH - FROM HORMONES TO GAMETES**

**Follistatin-Like 3 (FSTL3) and Early Postnatal Testicular Development**

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**SAT-032**

Activin, a TGFβ family ligand, induces Sertoli cell (SC) proliferation during the early postnatal stage in mice. Overexpression of activin, however, leads to the disruption of spermatogenesis. FSTL3, a glycoprotein inhibitor of activin, is highly expressed in the testis and its expression is induced by activin creating an inhibitory feedback loop. FSTL3 deletion in mice is therefore expected to produce a mouse model of increased activin action. Contrary to overexpression of activin, however, as we have shown before, global deletion of FSTL3 in mice results in increased numbers of SC and increased sperm production in older males. Stereological analyses show that although the overall number of SC increases with age in both genotypes during pre-pubertal stages, increase in SC numbers is significantly higher in FSTL3 KO males. Here we show our transcriptomic analyses of WT and FSTL3 KO mice at 3d and 8wk. mRNA sequencing data showed that more than 1000 genes are differentially regulated between WT and FSTL3 KO at 3d. There is a much lower number of genes differentially expressed at 8wk. Among several canonical pathways that are altered at 3d in FSTL3 KO mice compared to WT we investigated the “Sertoli-to-Sertoli cell Communication” pathway. We found increased expression of junction proteins, including those that are involved in the blood testis barrier (BTB) as well as earlier establishment of BTB. Without the BTB, preleptotene spermatocytes cannot progress through the spermatogenic programme. Importantly, we found accelerated SYCP3 organisation, indicative of early entry into meiosis, concomitant with early establishment of BTB. To directly address whether FSTL3 deletion can induce SC proliferation we knocked down FSTL3 expression in the TM4 SC line. We found increased PCNA expression with FSTL3 siRNA compared to control siRNA transfection demonstrating FSTL3 impairment does induce SC proliferation. We are currently investigating the mechanisms for early establishment of BTB in FSTL3 KO testis and additional canonical pathways. The results of the study presented suggests that loss of FSTL3 promotes SC proliferation which likely allows establishment of SC-SC interactions including BTB formation earlier than in WT. Given that the difference in size between WT and FSTL3 KO testis persists at older ages, it is possible that the timing of increase in SC number and establishment of BTB has a sustained effect on testicular function later in life.